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Editorial

Research on Health Benefits of Coconut

Mohsin Masud Jan

Editor

Coconuts are rich in fibre and highly nutritious and improved heart health, weight loss and digestion. Yet its high in calories and saturated fats. Overall unsweetened Coconuts meat makes a great addition to balance diet. Coconuts milk contains unique proteins that may provide health benefits. Coconuts may kill and fight against viruses and bacteria. Much of its fat in Coconuts is in the form of medium – chain triglyceride.
Nutritional facts of one cup (80 gm) contains;

calories 283 gm, protein 3gm, carbohydrates 10gm, fat 27gm, sugar 5gm, fibre 7gm and vitamin C 11%, folate 10%, iron 22%, manganese 110%, potassium 18%, copper 32%, magnesium 22%, selenium 21%.

Its water contains lots of nutrients. In addition to being naturally sweet and hydrating, coconut water is loaded with several important nutrients, including minerals that many people don't get enough of. Coconut water contains 94 per cent water and very little fat. Studies show that coconut water contains antioxidants that help modify free radicals in body, which can help speed up recovery process after stress or injury. Moreover, coconut water is also effective at replenishing fluids and electrolytes after exercise. Comparable to other sports beverages which are high in sugar and caffeine, this is definitely a better choice.

It helps in lowering blood sugar. Research has shown that coconut water can lower blood sugar levels and improve other health markers in animals with diabetes. In a study from 2015, rats with diabetes that were treated with coconut water maintained better blood sugar levels than the control group. The same study also found that the rats given coconut water had lower levels of haemoglobin A1c, indicating better long-term blood sugar control.

However, another added blood sugar benefit of coconut water is that it's a good source of magnesium, which may increase insulin sensitivity and decrease blood sugar levels in people with type 2 diabetes and prediabetes.

With all this in mind, it's important to note that coconut water contains carbs (which are broken down into sugars in the body), so if you are living with diabetes or prediabetes, talk to your doctor or a dietitian before adding it to your diet.

It helps with digestion and gut health. Constipation is the result of a diet low on fibre. 61 per cent of coconut is all fibre, which is why your gut health and bowel movement stays in check. Coconuts are high in fibre, which helps bulk up your stool and supports bowel regularity, keeping your digestive system healthy. Since these fruits are likewise high in fat, they can help your body absorb fat-soluble nutrients, including vitamins A, D, E, and K.

Coconuts may improve immunity. Manganese and antioxidants in coconut may help boost your immune system and reduce inflammation. This fruit's MCTs may also have antiviral, antifungal, and tumour-suppressing properties

Further, it may reduce your risk of Alzheimer's. According to a study published in the journal 'Nutrient', Medium Chain Triglycerides (MCTs) are exclusively found in coconut and have ketogenic properties that might help in preventing Alzheimer's as well as other cognitive disorders. Basically, coconut fats have therapeutic properties that keep mental health in check.

Also it can improve your oral health. Coconut meat contains large amounts of medium chain fatty acids (MCFAs), a type of saturated fat that is much easier for the human body to digest than animal fats. These fats, also called medium chain triglycerides (MCTs), have been demonstrated to boost the endurance of trained athletes. The MCFAs found in coconut meat also contain antimicrobial properties. These can be useful in preventing infections related to root canals and other teeth issues. Although eating coconut meat is not a substitute for proper dental hygiene, it can help kill some of the unwanted bacteria found in your mouth and protect your gums and teeth from infection or cavities.

It also improves skin health. To keep your skin healthy and young, you need not look further than coconut oil. It contains antioxidants that slow down the aging process and protects your skin from harmful radiation from the sun. All you need to do is to apply a few drops of coconut oil on your skin. Use it before showering, so that it will be easier for the oil to be absorbed through your skin once your pores have opened up.

Original Article

Electromagnetic Radiation from Cell Phones: A Contributing Factor to Male Infertility

Sarwat Jabeen[1], Aisha Abdul Haq[1], Soofia Nigar[1], Sadia Iqbal[1], Surriyya Sarwat[2] and Sahar Mubeen[1]

ABSTRACT

Objective: To observe changes in thickness of germinal epithelium in seminiferous tubules of testis of Albino rats exposed to electromagnetic radiations emitted by cell phones.

Study Design: Experimental comparative study.

Place and Duration of Study: This study was conducted at the Department of Anatomy, Dow International Medical College Ojha campus of Dow University of Health Sciences from 1st February 2011 to 31st October 2011.

Materials and Methods: Male Albino rats (n=70) were taken from animal house of Dow University of Health Sciences. Rats were divided into Control Group A (n=35) and Exposed Group B (n=35). Exposed group was exposed to electromagnetic radiation from cell phones (3 hours/day) and subdivided into 5 groups according to the time of exposure. Exposed rats were sacrificed along with their control sub-groups. Germinal epithelium in seminiferous tubules was observed for thickness in both groups using a micrometer.

Results: The mean ±SD values of thickness of germinal epithelium of seminiferous tubules of control and respective exposed subgroup were compared, a significant decrease in the thickness of germinal epithelium of seminiferous tubules of exposed subgroup was observed with (P Value 0.000) C.I of 95%. Intragroup comparison of exposed groups between B1 and B2 showed a significant decrease in thickness of germinal epithelium (P-value 0.02) at C.I of 95%.

Conclusion: Electromagnetic radiation from cell phones has adverse effects on the germinal epithelium of seminiferous tubules of Albino rats. Exposed groups showed marked decrease in the thickness of germinal epithelium when compared with their controls.

Key Words: Cell phones exposure, electromagnetic radiation, germinal epithelium, cell phone, Infertility, seminiferous tubules.

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INTRODUCTION

At present cell phones are vital for our daily lives, these are used throughout the world and their use is also increasing gradually[(1)]. In 1987, the Global Mobile Communications System (GSM) was developed. The system is used by most European and Asian countries, including Pakistan. In GSM, the frequencies transmitted from mobile phones to mobile phone antennas range from 870 to 915 MHz, while the frequencies transmitted from antennas to cell phones range from 935 to 960 MHz.[(2)].

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Cell phones emit EMR (Electromagnetic radiation) which have adverse effects on body[(3)]. EMR is a self-propagating wave which has two components, an electric and a magnetic field which oscillate in phase perpendicular to each other and to the direction of energy propagation[(4).] James Clerk Maxwell, first described EMR, which was confirmed by Heinrich Hertz. Electromagnetic spectrum waves ranging from very long radio waves to very short gamma rays [(5).]

Literatures prove that radiofrequency electromagnetic waves from cell phones have several hazardous effects on human and animal system by penetration or absorption the human body [(6)]. Studies show that EMR produces changes in the brain electroencephalographic activity causing sleep disturbances, lack of concentration, headache, fatigue, decreased melatonin production[(7)]. A possible link between cell phone use and infertility has been established by studies[(8).] It is observed that most men carry their cell phones in pocket of their trouser while using wireless devices like blue tooth to communicate, which leads to the exposure of testes to a very high power mobile phone radiation as compared to be in "standby mode"[(9)]. In contrast few

studies reported no such adverse effects of EMR from cell phone in the animal experiments. Till now no clinical study was identified to assess the harmful effects of EMF on reproductive system in humans. However some studies suggested a negative impact of cell phone use on spermatogenesis[10].

Concern over the effects of EMR on male fertility has been growing, no conclusive data are available yet. Several data suggested that fertility is going to decline markedly as a result of excessive use of modern technologies like cell phones. There is lack of data available to find correlation between infertility and radiation effects of mobile phones on germinal cells of seminiferous tubules.

We exposed albino rats to radiation from cell phones, for variable time periods to observe the microscopic changes in thickness of germinal epithelium in relation to the duration of exposure. The findings of our study will certainly add new aspects in the field of reproductive science.

Our study was primarily aimed to explore the effect of EMW emitted from cell phones on thickness of germinal epithelium of seminiferous tubules. This could be then correlated with the possibility of infertility with the excessive use of cell phones that might cause destruction of spermatogenic cell series secondarily.

MATERIALS AND METHODS

An Experimental comparative study was done from 1st February 2011 to 31st October 2011at the Animal house and Dow Diagnostic Research and Reference laboratory of Dow University of Health Sciences.

Male albino rats (n=70) were divided into Control group A (n=35) and Exposed group B (n=35). Each group was further sub-divided into five groups of 7 rats each (A1, A2, A3, A4 and A5 and B1, B2, B3, B4 and B5, respectively). Subdivision of exposed group was according to the duration of exposure to EMR.

Adult male albino rats (n=70) of 90 – 120 days were included in the study. Exclusion criteria comprised of **f**emale rats, animals with age >120 days, weight > 250 gms, animals on experimental drugs.

Exposed group B, was subjected to EMR, emitted from conventional GSM cell phone which is a commonly used cell communication system all over the world [11]. The frequency used ranged from 1835 to 1850 MHZ. The rats were exposed to EMR 3 hours daily for 15 weeks. 8 phone sets were used in active silent mode in each cage. A small metal cage with a wooden bottom was used for our study. The rats were then exposed with EMR for a period of 3 hours. [12]. Animals of exposed subgroup B1, B2, B3, B4 and B5 were exposed to EMR from cell phones for a period of 30, 50, 70, 90 and 110 days, respectively. Rats were then sacrificed after giving anesthesia, testes were removed after giving vertical abdominal incision, washed and fixed in 10% formalin.

Testes from each animal was examined histological changes. Testes were kept in 10% formalin and Bouin's fluid respectively for 24 - 48 hours, dehydrated in ascending grades of alcohol from 70% to100%, further cleared in xylene and embedded in paraffin, then blocks were prepared for sectioning. Hematoxylin and Eosin method was used to stain 4 µm thick sections.

To calculate the thickness of germinal epithelium, roughly circular or oval seminiferous tubules were selected, and calculated using the ocular micrometer scale under 10x objective and 8x lens. Ten sections were selected for observation from each animal. Five fields were examined in each section.

Statistical Analysis: Statistical analysis was performed by SPSS version 16. Two sample independent t –test was applied to compare mean differences in the thickness of germinal epithelium amongst the exposed subgroups (B) and respective control subgroup (A). One Way Analysis Of Variance was applied to find significance differences in the thickness of germinal epithelium among exposed subgroups (B1-B5). Statistically significant p value of ≤ 0.05 is taken as significant with 95% confidence interval.

RESULTS

Microscopic study of control group (Group A) showed normal architecture of seminiferous tubules with interstitial tissue, containing leydig cells (Fig: 1). Seminiferous tubules consist of germinal epithelium which comprises of 2 types of cells i.e. spermatogenic cells and sertoli cells surrounded by basal membrane. Sertoli cells are distinguished from spermatogenic cells due to the presence of large, oval and vesicular nucleus. All lineage of spermatogenic cells are visible.

In exposed group (group B), irregularities were observed in the germinal epithelium and basal membrane of the seminiferous tubule, together with vacuolization between germinal epithelial cells, undulations in the basal membranes of numerous seminiferous tubules, non-matured germinal epithelial cells in the lumen and vacuolar degeneration were also observed (Fig:3).

The mean ±SD values of thickness of germinal epithelium of seminiferous tubules in control subgroups A1, A2, A3, A4 and A5 were 93.57±2.93, 92.85±4.29, 93.71±6.94,92.71±5.87 and 89.71±2.36µm respectively.

Mean ±SD values of the thickness of germinal epithelium of seminiferous tubules in exposed subgroups B1, B2, B3, B4 and B5 were 43.17±17.09, 27.16±11.18, 19.91±0.97, 15.93±2.20 and 9.23±0.57µm respectively.

The mean±SD values of thickness of germinal epithelium of seminiferous tubules of control and exposed subgroup was compared, significant change was observed. Reduction in the thickness of germinal epithelium of exposed subgroup was observed with (P Value 0.000) at C.I of 95%. (Table I and Fig: 2)

Statistically insignificant decrease in thickness of germinal epithelium of seminiferous tubules was seen .while comparing, B2 and B3, (P-value 0.58), B3 and B4 (P-value 0.92), B4 and B5 (P-value 0.65) at C.I of 95%. Subgroups B1 and B2 (P-value 0.02) at C.I of 95% showed a substantial decrease in the mean thickness of germinal epithelium of seminiferous tubules.

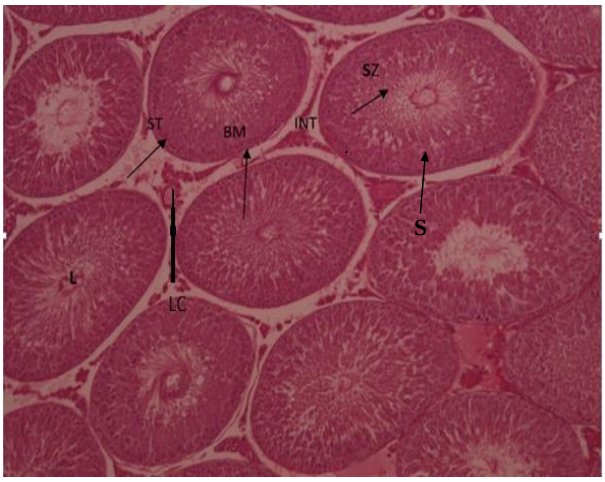

Figure No.1: H & E stained, 4µm thick section from control group(A), shows compact arrangement of seminiferous tubules (ST) with intact basement membrane (BM), interstitial space (INT), Leydig cell (LC), St (Sertoli cell), lumen (L) of tubule containing spermatozoa (SZ) X 100.

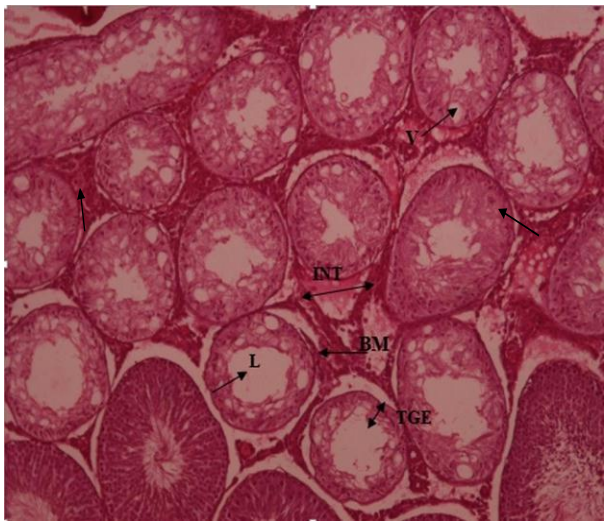

Figure No. 2: H & E stained, 5 µm thick section of testis from group B5, shows distorted seminiferous tubules with vacuoles (V), reduction in diameter of the tubule, distorted basement membrane (BM), reduced thickness of germinal epithelium (TGE) reduction in sertoli cells (St) and widening of interstitial spaces (INT). Leydig cells (LC) can be seen. X100.

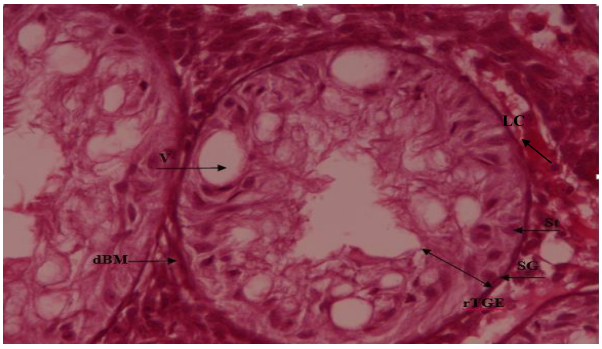

Figure No.3: H & E. stained, 5 µm thick section of testis from group B3, shows thickened, distorted basement membrane (dBM), sertoli cells (St), spermatogonia (SG), reduced thickness of germinal epithelium (rTGE), leydig cells (LC), vacuole (V). X1000 (oil immersion).

Table No.1: Comparison of Mean thickness of germinal epithelium (µm) among control (A) and exposed Subgroups (B)

Animal Subgroups (n=7)	Control Group A (n=35) A1-A5	Exposed Group B (n=35) B1-B5	P-value
30 Days	93.57±2.93	43.17±17.09	0.000***
50 Days	92.85±4.29	27.16±11.18	0.000***
70 Days	93.71±6.94	19.91±0.97	0.000***
90 Days	92.71±5.87	15.93±2.20	0.000***
110 Days	89.71±2.36	9.23±0.57	0.000***
Mean ± SD	92.51±4.74	23.08±14.66	0.000***

DISCUSSION

Currently, the development of cell phones and wireless technology have attained a crucial role in growing technology leading to increased usage and exposing more people are to EMF which could eventually contribute to serious public health problem[13]. Some studies have shown that EMFs cause hostile effects on the morphology and physiology of human and animal tissues**.** Cell phone exposure has an impact on male infertility[14], causing a fall in sperm count, affecting sperm motility, viability and morphology. Many studies identified these findings as a result of oxidative stress[15].

The findings of the present study suggest that a significant decrease in the thickness of germinal epithelium of seminiferous tubules when exposed to cell phones radiation for 2 hour daily for 4 months. This may be due to vulnerability of germinal epithelium to electromagnetic radiation or apoptosis resulting from heat or stress induced by radiation [15]. Study by Bin-Meferij et al. identified the same result, that apoptosis of cells which usually effect spermatogonia may leads to decrease in height of germinal epithelium. This ultimately results in impairment of whole cycle. [16].

Numerous data on animals and humans study showed harmful effects of EMR exposure on histology of testes and affecting male fertility [17], while others contradict

them. The study by Rajaei et al. also ruled out that exposure to EMF for long period might result in reduction in the height of epithelial cell [18]. This is consistent with our finding of decrease in height of spermatogenic cell series in exposed group.

In contrary to our study, that established decrease in the thickness of germinal epithelium in response to EMR, Trosic identified that irradiation of male rats for an hour per day with 915 MHz RF field for 2 weeks produces no changes in function or histological structure of testes. We can conclude that short-term intermittent RF radiation exposure does not represent a significant risk factor for rat reproductive function. However, long-term exposure, should be ruled out for adverse effects [19]. The study by Ozguner found out mean height of germinal epithelium were considerably decreased in EMF group (P<.0.05), expose to radiation by RF generator, frequency ranging between 869-894MHZ.[20]. This is in agreement with our study that too proved a reduction in thickness of germinal epithelium in exposed rats.

It has been suggested that long-term exposure to an EMF could affect the proliferation and differentiation of spermatogonia. In a study by Lee Set al. the number of spermatogonia was reduced, with concomitant increase in exposure to radiation. Histologically, EMF exposed groups showed vacuoles in basal membrane of seminiferous tubules, edema in the intertubular space. Seminiferous tubule diameters and germinal epithelium thickness were reduced and higher apoptotic index was observed [21]. These finding are similar to our study where reduced thickness of germinal epithelium is supposed to be due to apoptosis in the germinal epithelium [13]. This study validated our finding where decrease in thickness of spermatogenic cell series was observed with increase in duration of EMW exposure.

Study by oh JJ et al. support our study, the rats were divided into 4 groups on the basis of length of exposure and distance. Bottom of cage is provided with EMF device. After exposure of 28 days animals were sacrificed. Histological findings showed atrophy of seminiferous tubule, arrest of spermatogenesis, hyperplasia of Leydig cell, edema of interstitium and increase thickness of the basal lamina [22]. These findings are consistent with our result that showed a significant reduction in the height of germinal epithelium on exposure to 110 days as compare to expose for a shorter duration.

In a recent study by Okechuku, histological changes in the testes of rats receiving radiation from cell phones for 6 hours a day for a month include reduction in number of sperms, degeneration of Leydig cell, spermatogenic arrest and tubular necrosis. These findings are consistent with our study.[23].

CONCLUSION

EMR from cell phones has adverse effects on the germinal epithelium of seminiferous tubules of Albino rats. Exposed groups showed marked decrease in the thickness of germinal epithelium when compared with their controls. This eventually may be associated with infertility.

Author's Contribution:

Concept & Design of Study:	Sarwat Jabeen
Drafting:	Sahar Mubeen
Data Analysis:	Sadia Iqbal, Aisha Abdul Haq
Revisiting Critically:	Surriyya Sarwat
Final Approval of version:	Soofia Nigar

Conflict of Interest: The study has no conflict of interest to declare by any author.

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Original Article

Efficacy of Evening Primrose Oil in Treatment of Atopic Dermatitis

Jamshida Iqbal Khattak[1], Shahzad Rashid Awan[2], Saddiq Ullah[3], Naseem Ullah[4], Shah zeb[5] and Mohammad Sohail[1]

ABSTRACT

Objective: To find out efficacy of evening primrose oil in treatment of atopic dermatitis.
Study Design: Randomized controlled clinical trial
Place and Duration of Study: This study was conducted at the department of dermatology Mian Rashid Hussain Memorial Hospital Pabbi, Nowshera and Alkhidmat hospital Peshawar for duration of six months from November 2020 to April 2021.
Materials and Methods: Totally, 300 patients were included in the study. Each primrose oil and control group comprise of 150 patients. All the information was recorded at the baseline and each following visit for five months.
Results: All mean values in the evening primrose oil group have gradually and continuously decreased on their 5 successive monthly evaluations in comparison to the baseline values. Intensity and itchiness ratings also declined significantly. In contrast, the average results in the control group have been delayed, less pronounced and uneven. Overall, at the completion of the 5th month, improvement was observed in 147 (98 %) in EPO and 40 (60 %) in control group patients. At any stage of evaluation in either group no major adverse effects were recorded.
Conclusion: Our study concludes that evening primrose oil is effective and safe for the management of atopic dermatitis.
Key Words: Evening primrose oil, Atopic dermatitis, Linoleic acid

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INTRODUCTION

Atopic dermatitis (AD) is inflammatory, recurring chronic skin condition. In this problem trans-epidermal water loss increases along with erythema, skin dryness and itching [1, 2]. AD is heterogeneous and characterized by complex immunologic aberrant responses, which include degradation of epidermal barrier, hereditary factors, and climatic influences. According to several studies, AD may be linked to irregular metabolism of fatty acid, particularly inappropriate gamma-linolenic acid (GLA) synthesis [3-5].

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The functional impairment of delta-6 desaturase has been suggested as a risk factor for AD in certain AD patient groups [6, 7]. The diagnosis is confirmed primarily on physical examination, and the Hanifin and Rajka criteria are the most frequently employed criteria[8]. This illness often starts in childhood, affects both males and females, and has been gradually increasing in frequency over the last several years[9]. It is critical for these individuals to avoid documented precipitating or exacerbating variables such as extreme temperatures, frequent washing and scrubbing of the skin, stress and anxiety, contact irritants, and aeroallergens. Apart from this, an elimination diet trial, skin hydration with a bathing accompanied by emollients application, needful use of antihistaminics and antibiotics, topically use of glucocorticoids, and tacrolimus constitute the first line of treatment for AD. In severe instances, second-line therapies may include phototherapy, photo-chemotherapy. The natural source of linoleic acid (LA) and gamma linolenic acid (GLA) is considered as evening primrose oil (EPO). As blood concentrations of GLA and DGLA rise, the intake of GLA found in EPO is thought to induce an anti-inflammatory response [9]. Many investigations have also indicated that evening primrose oil has a detrimental impact in AD [10], although other investigations have revealed conflicting results[11]. Evening primrose (Oenothera biennis), a small herb with beautiful yellow blooms flowering in the

evening and belonging to the rosebay willow herb family, is one of the adjuvant therapeutic medicines for AD [12]. It is currently cultivated as a commercial crop, and the valuable oil is extracted from its small seeds. Although some research varied, numerous clinical trials have shown positive benefits of EPO in atopic dermatitis. According to the literature no research has been done on the in Pakistan on the effectiveness of evening primrose oil in the treatment of atopic dermatitis. Therefore we conducted this research to determine the effectiveness of EPO in the treatment of atopic dermatitis in the Pakistani population.

MATERIALS AND METHODS

This research study was randomized controlled clinical trial conducted at the department of dermatology Mian Rashid Hussain Memorial Hospital Pabbi, Nowshera and alkhidmat hospital Peshawar Khyber Pakhtunkhwa Pakistan. The duration of was this research work was six months from November 2020 to April 2021. The inclusion criteria for our research work was all the patients of both the gender diagnosed with atopic dermatitis based on criteria of Hanifin and Rajka [13] having ≤ 10 EASI [14] score while exclusion criteria were patients having other skin issues along with atopic dermatitis, finding of infection, patients with systematic disease and un-controlled chronic problems. Those with another skin condition in combination to AD, an infection finding, a systemic disorder or an untreated chronic illness were eliminated. Pregnant women, lactating women, epileptic patients, peptic ulcer history, phenothiazines intake, in the previous month UVB phototherapy or photo-chemotherapy, and patients taking systemic steroid or other immunosuppressive medications in the last three months were also excluded. Institutional Review Board approved our study. Consent form was signed from all the participants in written form. Totally, 300 patients were included in the study. They were categorized into two groups. 150 patients were included in evening primrose oil group while 150 patients were enrolled in control group. The patients in the evening primrose oil group were treated with topical steroid and emollient in addition to evening primrose oil while patients in control group were treated with only steroid and emollient. Each patient received treatment for a total of 5 months. A baseline assessment of the illness was made and documented in a pre-designed Performa on the initial appointment, in addition to collecting a thorough history, systemic assessment and general assessment. The disease extent, severity, itching and dryness were all definitely documented according to previous study [15]. Each following visit included a clinical assessment of the change in disease state in comparison to the baseline. We considered a marked improvement if the overall score reached 25% of the baseline. It was considered moderate improvement if the overall score was more than 25% but less than 50% of the baseline. Mild improvement was defined as a score more than 50% but less than 75% of baseline. In the instance of marginal improvement, the score was more than 75% but less than 99 percent of the baseline. It was termed static if the score stayed the same. Deterioration was defined as a score higher than the baseline value. No improvement was assigned to the last three kinds of changes (marginal improvement, stasis, and deterioration). Patients were monitored for any adverse effects at each appointment, and if any were observed, they were documented. Data from all the patients of both groups were entered and analyzed using SPSS version 23. Unpaired t test was used to test the significance of the data. P value of <0.05 was measured as significant.

RESULTS

In this study female patients were dominant in both the group. There were 90 (60%) female and 60 (40%) male in evening primrose oil group while there were 86 (57.33%) female and 64 (42.67%) male in control group. (Figure 1) According to the age wise distribution, number of patients in evening primrose oil group of ≤10 years were 66 (44%), 11-20 were 42 (28%) 21-30 20(13.33%) were, 31-40 20(13.33%) and ≥41 were 2(1.33%) while in control group they were 55 (36.67%), 40 (26.67%), 28 (18.67%), 23 (15.33%) and 4 (2.67%) respectively. (Figure 2) According to the status of baseline disease, in evening primrose oil group, the number of patients in moderate, mild and severe atopic dermatitis were 18 (12%), 114 (76%) and 18 (12%) while in control group they were 20 (13.33%), 120 (80%) and 10 (6.67%) respectively. (Figure 3) In the evening primrose oil group, 93 (62%) were with family history of atopy while in control group 87 (58%) were with family history of atopy. (Figure 4) All average values in the evening primrose oil group have gradually and continuously decreased on their 5 successive monthly evaluations in comparison to the baseline values. Substantial decrease in intensity and itching occurs at the completion of the first month. Subsequently, the decrease in average scores of each clinical parameter and the overall score assumed level of significance statistically. Intensity and itchiness ratings also declined significantly. In contrast, the average results in the control group have been delayed, less pronounced and uneven. (Table 1) Improved intensity of all measures except control was also transitory since it did not continue until the completion of the testing period. Table 2 summarizes the AD outcomes in the two patient groups based on a decrease in the disease's overall score. Overall, at the completion of the 5th month, improvement was observed in 147 (98 %) in EPO and 40 (60 %) in control group patients. Treatment outcomes of both the groups were significantly different ($P < 0.00001$, t test).At any stage of evaluation in either group no major adverse effects were recorded.

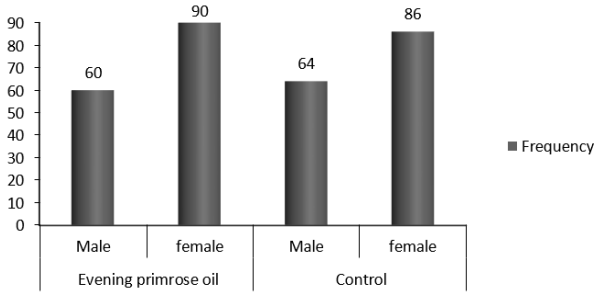

Figure No.1: Distribution of patients based on gender

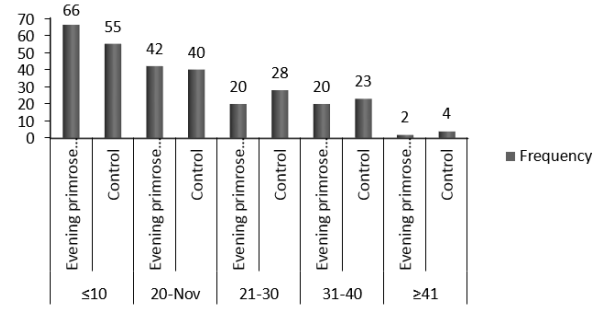

Figure No.2: Distribution of patients based on different age groups

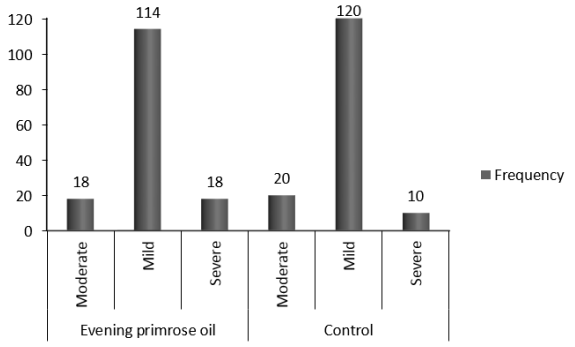

Figure No.3: Distribution of patients based on baseline disease status

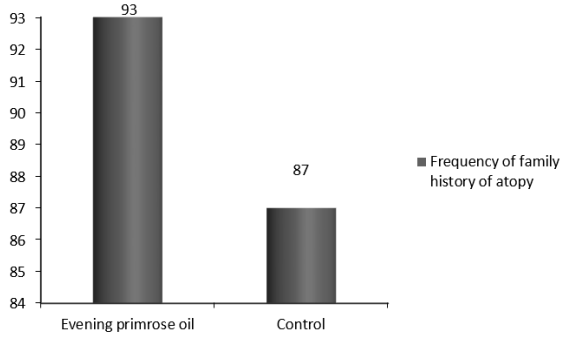

Figure No.4: Distribution of patients based on family history of atopy

Table No.1: Score of the cases during follow up study in both the group

Time (Month)	Group	Extent	Intensity	Itching	Dryness	Total score	P value
Baseline	Evening primrose oil	1.88±0.4	2.08±0.54	1.72±0.42	1.16±0.3	6.84±1.66	0.001
	Control	1.80±0.5	1.44±0.51	1.72±0.42	1.52±0.5	5.48±1.93	
1st month	Evening primrose oil	1.64±0.3	1.56±0.32	1.08±0.4	1.16±0.2	5.44±1.22	0.001
	Control	1.80±0.6	1.40±0.55	1.52±0.2	1.36±0.4	6.08±1.75	
2nd month	Evening primrose oil	1.40±0.5	1.04±0.4	0.96±0.2	0.84±0.3	4.24±1.4	0.03
	Control	1.52±0.2	1.24±0.22	1.40±0.3	1.24±0.2	5.4±0.92	
3rd month	Evening primrose oil	1.0±0.31	0.88±0.34	0.52±0.4	0.84±0.3	3.24±1.35	0.001
	Control	1.48±0.4	1.28±0.42	1.44±0.5	1.16±0.5	5.36±1.82	
4th month	Evening primrose oil	0.84±0.7	0.84±0.22	0.44±0.2	0.52±0.3	2.64±1.42	0.002
	Control	1.48±0.4	1.16±0.66	1.56±0.2	1.08±0.6	5.28±1.86	
5th month	Evening primrose oil	0.64±0.3	0.68±0.49	0.28±0.4	0.48±0.4	2.08±1.59	0.001
	Control	1.72±0.5	1.72±0.32	1.56±0.2	1.12±0.7	6.12±1.72	

Table 2: Outcomes of both the treatment group during follow up

Parameter		Group	1st month	2nd month	3rd month	4th month	5th month
Improved	Marked	EPO	0	0	18 (12%)	54 (36%)	54 (36%)
		Control	0	0	0	15 (10%)	0
	Moderate	EPO	0	45 (30%)	90 (60%)	90 (60%)	84 (56%)
		Control	0	18 (12%)	27 (18%)	15 (10%)	15 (10%)
	Mild	EPO	42 (28%)	90 (60%)	60 (40%)	30 (20%)	9 (6%)
		Control	27 (18%)	42 (28%)	39 (26%)	45 (30%)	45 (30%)
	Marginal	EPO	45 (30%)	27 (18%)	12(8%)	21(16%)	15 (10%)
		Control	29(19.33%)	45 (30%)	21(16%)	21(16%)	39 (26%)
Not improved	Static	EPO	60 (40%)	15 (10%)	0	0	0
		Control	69 (46)	18 (12%)	42 (28%)	39 (26%)	21 (14%)
	Deterioration	EPO	0	0	0	0	0
		Control	27 (18%)	42 (28%)	21(16%)	21(16%)	48(32%)

DISCUSSION

Evening promise, herb of the Onagraceae family, is named because of its blooming during night time. The promise of evening seed oil includes a great quantity of LA and GLA. After being brought to Europe in the 17th century, Evening promise was utilized as a popular folk remedy [15]. GLA has been extracted for the first time from seeds of the evening promise [10, 16]. In the present study the effectiveness of evening primrose oil in treatment of atopic dermatitis was determined. In the current research, we observed that evening primrose oil is both beneficial and safe in the treatment of atopic dermatitis. Therapy with EPO resulted in improvement in overall disease severity beginning as early as the end of the first month of treatment, with 98 percent of patients showing improvement by the end of the 5th month of treatment. There were no side effects associated with the medication. Numerous well organized research investigations conducted in the western countries showed a comparable positive impact of EPO on atopic dermatitis in the pediatric age range [6, 17, 18]. In addition, some improvement in the extent, intensity, itching, and dryness of the symptoms were seen in our patients who received a placebo. These findings, on the other hand, were uneven, non-uniform and non-progressive in nature. The beneficial impact of topical emollient, inherent placebo response and natural fluctuations in the course of AD are all possible explanations for the inconsistent improvement seen in some control-treated individuals. Unfortunately, no researches have been able to show that evening primrose oil has a substantial impact on the therapy of atopic dermatitis. Another earlier research of 102 patients at the Leicester Royal Infirmary in the United Kingdom showed that essential fatty acid supplementation had no impact on atopic dermatitis. Dietary supplementation did not avoid the manifestation of AD in babies with a high family risk, but it did seem to reduce the severity of AD in these children later in life [19, 20]. Numerous covariates, including as racial characteristics, concurrent corticosteroid usage, and other factors that are currently being revealed by new research may explain for previously reported uneven patient response to EPO [10]. Recent studies have revealed new complexity in metabolism of fatty acid and immunologic response in atopic dermatitis that go beyond what has been previously described, and they may soon assist identify subgroups of non-responders and those who may consistently benefit. There are few studies on the effectiveness of EPO in Pakistani individuals with atopic dermatitis. Atopic dermatitis is known to be influenced by genetic and environmental factors. Since our randomized placebo-controlled research found EPO to be helpful in the treatment of atopic dermatitis, we may logically expect comparable studies in Pakistan to have positive findings.

CONCLUSION

Our study concludes that evening primrose oil is effective and safe for the management of atopic dermatitis. Better improvement in management of atopic dermatitis was observed in our study. For better understanding of the effectiveness of evening primrose oil in management of atopic dermatitis further studies having large sample size and follow up for long period of time is recommended.

Author's Contribution:

Concept & Design of Study:	Jamshida Iqbal Khattak
Drafting:	Shahzad Rashid Awan, Saddiq Ullah
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Revisiting Critically:	Jamshida Iqbal Khattak, Shahzad Rashid Awan
Final Approval of version:	Jamshida Iqbal Khattak

Conflict of Interest: The study has no conflict of interest to declare by any author.

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Original Article

Evaluation of Mean Vertical Distance Between Mesial Incisal Edge of Maxillary Central Incisors and Incisive Papilla in Various Arch Forms of Patients

Syeda Sameen Zehra Rizvi[1], Aamir Rafique[2], Muhammad Uzair Riaz[3], Naila Zakria[4] and Aeman Choudhary[5]

ABSTRACT

Objective: To evaluate the mean vertical distance between the mesial incisal edge of maxillary central incisor and incisive papilla in various arch forms.

Study Design: Descriptive/ Cross sectional study

Place and Duration of Study: This study was conducted at the Department of Prosthodontics, de' Montmorency-College of Dentistry/Punjab Dental Hospital, Lahore for 6 months from February 2018 to August 2018.

Materials and Methods: The study consisted of 100 patients attending the Prosthetic outdoor department of Punjab Dental Hospital, Lahore meeting the inclusion criteria. The vertical distance between mesial incisal edges of central incisors and the center of the incisive papilla was evaluated using vernier caliper, after mounting the casts on surveyor. Center of the incisive papilla was transferred on the labial surface of central incisor with the help of carbon marker. Arch forms were assessed by using Diagnostic Orthoform Template as recommended by 3M Unitek. Data was analyzed on SPSS version 21.0. Chi-square test was applied for statistical significance.

Results: The vertical distance between mesial incisal edge of maxillary central incisors and incisive papilla ranged from 6.89 mm to 7.03 mm with the mean vertical distance of 7.00±0.026 mm. The mean papillo incisal distance(PID) was 6.99±0.027 mm in ovoid, 6.98±0.020 mm in square and7.01±0.018 mm in taper arch form.

Conclusion: The results can be used by the dentist and laboratory technician as a foundation for construction of maxillary occlusal rims that are used for the establishing the occlusal plane in different arch forms, in conjunction with the support of other anatomical landmarks.

Key Words: Vertical distance, incisive papilla, incisal edge, central incisors, arch forms

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INTRODUCTION

Restoration of esthetics is an important aspect in the treatment plan of edentulous patients[1]. The goals of prosthetics rehabilitation are to restore phonetics, aesthetics and dentofacial harmony.

Display of anterior teeth with the lips in repose or in functional position determine the outcome of any prosthesis in anterior esthetic region[2]. According to Frush and Fisher, placement of anterior teeth near to their natural position almost always provide the best aesthetic outcome[3]. So, when artificial teeth are placed correctly speech, esthetics and normal functions will be automatically restored[1].

For tooth positioning, neutral zone theory for setting anterior teeth seems to be logical, but sometimes the desired esthetic outcome may be compromised[4]. So, pre-extraction records may aid in determining the correct positioning of artificial teeth[1]. When these records are also not available anatomical landmarks are used to achieve correct placement of anterior teeth.[5] The incisive papilla is a firm, immovable and reliable milestone in the arrangement of artificial teeth. It acts as a guide to determine midline[3], labiolingual[6] as well as incisocervical arrangement of maxillary central incisors.[3]

The association, in vertical dimension, between incisive papilla and incisal margins of the central incisors in maxilla in various arch forms would serve as a benchmark for inciso-cervical placement of anterior teeth in denture base according to the individual requirement of the edentulous patients. So, the goal of this study is to evaluate vertical distance between maxillary central incisor and incisive papilla in

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different arch forms. This helps in determining the correct incisal display of maxillary central incisors in both removable as well as in fixed prosthesis.

MATERIALS AND METHODS

The study was carried out in the Department of Prosthodontics of de' Montmorency College of Dentistry, Lahore for duration of six months from February 2018 to August 2018 after approval from CPSP with reference no CPSP/REU/DSG 2015-077-1553. The study consisted of 100 patients attending OPD of Prosthodontic department. Non probability consecutive sampling technique was used to include the patients in study. Subjects included in the study were patients of both genders with age ranging from 20 to 40 years. Patients with aligned full complement of natural permanent teeth up to maxillary 1st molar, class I maxillomandibular relationship and well traceable incisive papilla were involved in the study. Patients with missing, supraerupted or carious central incisors and 1st molars in maxillary arch, midline diastema, attrition/wear of central incisors, gingival hyperplasia or periodontally compromised teeth, history of maxillofacial trauma, orthodontic treatment or restorative treatment of maxillary central incisors were excluded.

After taking consent, patient's demographic information like age and gender was obtained. History was taken, followed by the clinical examination of the patient. Maxillary impressions of the selected subjects were made with irreversible hydrocolloid (Tropicalgin by Zhermack Spa) following the directions given by the manufacturing company for mixing of material. Alginate was hand mixed using rubber bowl and loaded on to stainless steel perforated tray. The tray was then introduced into patient's oral cavity and the material was allowed to set intraorally for three minutes to ensure complete and final setting before removal. The impression was then removed, washed with water and disinfected with suitable disinfectant before pouring casts. Cast was then poured with type 4 dental stone and base was formed using base formers. The casts were homogenized by generating a horizontal base that was parallel to the occlusal plane. Retrieved casts were divided into square, ovoid and taper arch form by using Diagnostic Orthoform Template as advocated by 3M Unitek. Casts were secured on cast holder of the surveyor and tripoding was done. Reference points used were mesiolabial incisal edge of maxillary central incisor anteriorly and mesio-buccal cusp tips of maxillary right and left first molar posteriorly. The center of incisive papilla was marked and transferred to the labial side if maxillary right central incisor with the aid of carbon marker. The line drawn in this region is refer to as "IP line". Measurements were made from IP line to mesial incisal edge of central incisor with the help of Vernier Caliper with precision of 0.01mm. This recorded measurement is the mean vertical distance between incisive papilla and maxillary central incisor. All the procedure was done by the researcher itself. All this information was recorded in a pre-designed proforma.

Data was entered into SPSS version 21.0 used for analysis. Mean and standard deviation were evaluated for quantitative variables like age and mean vertical distance. Frequency and percentage were calculated for qualitative variables like gender and arch forms prevalence in sample. Chi Square was applied and p-value ≤ 0.05 was considered significant.

RESULTS

A total number of 100 patients of both genders including 53 males and 47 females i.e. 53% and 47% males and females respectively meeting the inclusion criteria were included in the study. Frequency and percentage of gender distribution and arch forms of patients in study is shown in table 1 and table 2 respectively.

Table No.1: Frequency and Percentage of Gender of Patients

	Frequency	Percentage
Male	53	53%
Female	47	47%
Total	100	100%

Table No.2: Frequency and Percentage of Arch Forms

Arch Forms	Frequency	Percentage
Ovoid	49	49%
Tapering	37	37%
Square	14	14%
Total	100	100%

Table 3 mentions the mean age of patient. The mean and standard deviation of age is 29.77±6.19. Minimum age was 20 years and maximum age was 40 years.

Table No.3 - Mean and Standard Deviation of Age of Patients

Age (years)	N	100
	Mean	29.77
	SD	6.197
	Minimum	20
	Maximum	40

Table No.4: Mean and Standard Deviation of Vertical Distance (Analysis of Gender and Vertical Distance)

	N (No. of Patients)	Mean of Vertical Distance	Standard Deviation of Vertical Distance	p-value
Male	53	6.96	0.045	0.00
Female	47	6.99	0.023	
Total	100	6.97	0.039	

Table 4 shows mean and standard deviation of vertical distance in males and females. Mean vertical distance for males is 7.00 ±0.024mm and for females mean and standard deviation is 6.99±0.025 mm.

Table 5 illustrates the mean and standard deviation of vertical distance in different arch forms with significant p-value.

Table No.5: Mean and Standard Deviation of Vertical Distance in Different Arch Forms

Arch forms	Genders		Mean	Standard deviation	
	Males (n %)	Females (n %)			
Ovoid	26 (49%)	23 (48.9%)	6.99	0.027	P-value 0.00
Tapering	21 (39.6%)	16 (34.0%)	7.01	0.018	
Square	6 (11.3%)	8 (17.0%)	6.98	0.020	

DISCUSSION

Restoration of natural appearance of edentulous patients that need rehabilitation with complete dentures either removable or implant supported, especially in upper arch, is an essential part of treatment. Although prosthesis cannot exactly replace the natural dentition, however if some measurable parameters are used in correct manner for the prosthesis fabrication, the resulting prosthesis will not only be functionally secured but also biologically and aesthetically workable[7].

Arrangement of artificial teeth close to their natural position can be guided to a certain extent by available pre-extraction records such as pre-extraction radiographs, anthropometric records, casts, and photographs. Various other guidelines such as phonetics, upper lip, lower lip and smile line are used to establish the maxillary incisal edge position[8]. Most commonly used parameter is phonetics, where "S," "Z," and "C", "F" and "V" sounds were proposed by Payne and Pound and Robinson for position of incisal edges of upper teeth. Sharry, Heartwell, Ellinger, et al. and Landa proposed that the occlusal plane of maxillary occlusal rims should extend approximately 1-2 mm below the upper lip in resting position and then phonetics should be used to adjust this vertical position.[9]

Although, above mentioned guidelines had been utilized for anterior teeth setting but they vary greatly depending on anatomy of individual. In the present study, vertical position of maxillary central incisal edge was determined from incisive papilla. The incisive papilla is an important landmark[10] and a useful guide for positioning of the anterior teeth as referred by Harper RN, Martone AL and Hickey J, et al[11,12,13]. They studied pre- extraction casts as well as post resorption models over a period of seven years. As a result, they concluded a stable incisive papilla, thereby forming a reliable basis for replacing the maxillary central incisors in correct horizontal and vertical position.[14] The anterior part of the incisive papilla is usually destroyed and scarred during extraction of maxillary anterior teeth. Another reason is the bone resorption that takes place following the loss of teeth making the anterior part of papilla less reliable guideline. On the contrary, the center and posterior part of the papilla is more likely to remain constant[1]. For this reason, center portion of papilla is used as reference point in this study.

Guldag et al in his study on Turkish population found the mean vertical distance between maxillary central incisors and incisive papilla to be 6.70±0.81 mm The range of vertical distance was 5.51 mm to 8.89 mm[15]. Chalsuthipan and Boonsiri evaluated the vertical distance between maxillary central incisors, canines and the incisive papilla in Thai population. They found that vertical distance between posterior part of the incisive papilla to incisal edge of the maxillary central incisors was ranging from 6.94 to 7.23 mm. The mean vertical distance in their study was 7.08 mm[16]. The mean value variation between Chalsuthipan and Boonsiri and present study is 0.08 mm. The reason behind this difference is maybe the differences in reference points on the incisive papilla because the most posterior border of the incisive papilla was used by authors, but in the present study, we used the center portion as a reference.

In literature, several methods have been proposed to define the arch forms by using the partitioning around medoids clustering and silhouette method[17]. Some authors prefer to classify dental arches into ovoid, tapering and squarish, this classification of arch forms was used in the present study by using Diagnostic Orthoform Template as advocated by 3M Unitek. The majority of the subjects had an ovoid arch form 49% where as 37% had tapering and 14% had squarish arch.[2] A study by Mersel et al on Israeli patients investigated vertical distance in different arch forms. The vertical distance range from 5-14 mm in ovoid arch form, 6-11 mm in square arch form and 6-10 mm in tapered arch form.[18] The result of present study gave the vertical distance of 6.99±0.027 mm in ovoid, 7.01±0.018 mm in tapering and 6.98±0.020 mm in square suggesting the positive correlation of vertical distance between the two landmarks with the p-value of 0.00. A direct comparison of the two studies between the results cannot be made because of the difference in reference points i.e. Mersel took posterior border while present study used mid part of incisive papilla.

Further, a long term prospective study with larger sample size and their variation with age, race, dental and skeletal morphology is required to authenticate IP line as a landmark for arrangement of maxillary anterior teeth.

CONCLUSION

The suggested mean vertical distance between central incisor and incisive papilla for placing prosthetic central incisors is 7.00 mm. There is a higher presentation of ovoid arch forms. Arch form parameter being statistically significant according to gender can also be considered. The statistical information obtained from the study can be an exemplary point to start fabrication of occlusion rims and vertical placement of central incisor in different arch forms.

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Conflict of Interest: The study has no conflict of interest to declare by any author.

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Original Article

Frequency of Malaria Among Pregnant Women

Malaria Among Pregnant Women

Muhammad Abas Khan

ABSTRACT

Objective: To find out frequency of malaria among pregnant women who presented to a tertiary care hospital in Peshawar.

Study Design: descriptive study

Place and Duration of Study: This study was conducted at the Department of Medicine, Lady Reading Hospital, Peshawar, from December 2020 to May 2021.

Materials and Methods: Data collection was done by non-probability consecutive sampling technique. Patients who were pregnant and above 15 years of age were involved in the study. Frequency of malaria was established. Data was evaluated using SPSS version 23.

Results: Among 140 pregnant women patients, 30(21.4%) patients were diagnosed having malaria. The mean age was 30 ±11.62 years. malaria was found in 30 (21.4%) patients with pregnancy. In the positive blood samples, 24(80%) were infected with plasmodium falcipram and 14(10%) were infected with P.malairia,7(5%) with p.vivax and 7(5%) with P. falciparum. Women with age group of 20-30 years were found more prone to the plasmodium infection. In maximum patients, plasmodium density 1 was noted.

Conclusion: increased frequency of malaria in patients having pregnancy was noted

Key Words: Malaria, Pregnant Women, Parasitemia

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INTRODUCTION

Malaria is a chief public health challenge.228 million cases of malaria happened globally and 405,000 deaths occurred in 2018. Maximum cases of malaria (93%) and deaths (94%) happened in the World Health Organization Africa Area, with Plasmodium falciparum which accounted for 99.7% of the cases [1]. Women having pregnancy are at high malaria risk[2,3]. In sub Saharan Africa 11 million out of 38 million (29%) pregnant women had been exposed to malaria in 2018 [1]. Though frequently asymptomatic, P. falciparum infection during pregnancy is related with harsh pregnancy consequences e.g. low birth weight, stillbirth, pre-term delivery, anemia in mother and abortion[4–6]. Frequency of malaria in women having pregnancy heightens in the 2nd trimester. Malaria in pregnant women is valuable indicator for surveillance of malaria at level of community [7,8] with commonest risk factors of young age and a prim gravida [2,9,10].

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In Pakistan 3.5 million established malaria cases are stated every year. As stated by world health organization in 2018[11], Pakistan is amongst the 6 World health organization Eastern Mediterranean countries having around 100 percent of the population at risk. Plasmodium vivax parasite is commonly found in Pakistan but P. falciparum is increasing from 35 to 40 percent[12]. Nearly 300 to 500 million people are effected from malaria and 2 to 3 million peoples dies every year[13]. Fifty million women having pregnancy are infected with malaria called (PAM) pregnancy-associated malaria globally and 2,500-10,000 maternal deaths occur each year [14-15].

5 diverse human malaria species are found E.g P. vivax, P. falciparum, P. malariae, P. ovale and P. knowlesi. In 2016 216 million malaria cases and deaths of 445,000 cases happened globally[16]. Malaria is transmitted over 91 countries and 80 percent of cases occurred in countries from sub-Saharan African region [16,17]. Every year 25 million women who were pregnant in sub-Saharan Africa are at P. falciparum risk. 2 institution-based studies conducted amongst women with pregnancy in Nigeria displayed malaria frequency as 41.6%[19] and 7.7% [19]. Additional study in Eastern Sudan disclosed 13.7% of women with pregnancy had P. falciparum[20]. Studies in Burkina Faso [21], and Malawi[22] displayed the frequency to be 18.1%, and 19% separately. One community-based study done in Ethiopia disclosed the frequency of malaria amongst women with pregnancy to be amid 2.83 and 16.3% [23–25]. Malaria in pregnant women is risk to fetus and mother[26]. Malaria leads to anemia in mother, premature delivery, spontaneous abortion, low birth weight and

fetal death[27,28]. Anemia related to malaria effects 10,000 maternal deaths every year in Africa[29]. Risk factors for malaria include age[19,31] educational status[22,31] gravidity, gestational age[32], parity[22,33] and Insecticide Treated Net usage[25]. In spite of higher risk malaria there is partial proof around malaria load amongst women with pregnancy. Hence, a requirement was sensed to find the frequency of malaria in women having pregnancy in our local situation. Objective of this study was to find the frequency of malaria in women having pregnancy who presented with fever in tertiary care hospital. This study will generate local data and generate attentiveness in physicians, and epidemiologists concerning frequency of malaria in women having pregnancy**.**

MATERIALS AND METHODS

This descriptive study was conducted at the Medicine department, Lady Reading Hospital Peshawar from December 2020 to May 2021. Data collection was done by non-probability consecutive sampling technique. patients who were pregnant of any duration presenting with history of fever and age above 15 years of age were included in the study. Patients having no pregnancy and having fever due to other etiology were excluded. Patients who were previously diagnosed as malaria based on medical records were taken as chronic malaria and were excluded from study. Sample size was 140 patients and was calculated on the basis of 10% frequency of malaria in women having pregnancy with 95% confidence level and 5% absolute precision[34]. clinical malaria was operationally defined as having malaria parasite in blood and a temperature in axilla of ≥ 37.5 °C or a having fever within the previous 48 hours, while asymptomatic malaria was defined as any level of parasite in the blood without fever. Patients having fever with headache or loss of consciousness with malaria parasite positive were diagnosed as cerebral malaria. Ethical Approval was taken from institutional ethical committee and the research was conducted on the principle of Helsinki declaration. Informed written consent was taken from each patient or their attendants after the aim of our study was explained and making them assure of confidentiality. All patients having malaria were confirmed with thick and thin smears and rapid antigen detection. Patients admission was done in medical unit of Lady Reading Hospital, Peshawar through outpatient and emergency department.

Malaria blood slides were prepared in Unit of parasitology in lrh Peshawar. Briefly, 2 µL and 6 µL of blood was utilized to make thin smears and thick smears, respectively. Thin smears fixation was done on absolute methanol, allowing it to air dry and both thin and thick smears staining was carried out with 10% Giemsa stain in phosphate buffered water (pH 7.2) for ten minutes. Thick film examination was done utilizing a Microscope with × 10 eyepiece and ×100 oil immersion objective to find the existence, type and stage of parasite. Thin smears were utilized to confirm type and count of parasites. Parasite density (parasites per µL of blood) calculation was done utilizing WBC (white blood cell) or RBC (red blood cell) count of participants determined on an automated hematological analyzer. An examination of minimum of 100 fields were done before a slide was marked to be negative. History and physical examination was carried out and thermometer was used to measure the fever. Neurologic system was examined in detail to assess the level of consciousness in cases of cerebral malaria. Also abdominal ultrasound was performed to look for hepatosplenomegaly. All other relevant investigations (blood sugar level, serum creatinine, complete blood count and erythrocyte sedimentation rate). Moreover, categorization was done as plasmodium falciparam, plasmodium vivax, plasmodium ovale and plasmodium malaria. Analysis of data was done utilizing SPSS version 23. Percentages and frequencies were used for categorical or qualitative variables like frequency of malaria, gender etc. calculation of SD and mean was done for numerical or quantitative variables malaria duration and age. Chi square test application was done for comparison of malaria frequency in both genders. P value <0.05 was considered significant.

RESULTS

In 140 patients having prenancy, 30(21.4%) patients were diagnosed as having malaria. The patients age ranged between 15 to 60 years (mean 30 ±11.62 years) with most patients between 20-50 years (mean 66.18 ±11.91 years). Patients who had malaria parasite were in the age group of 20-30 years followed by 30-40 years and then 40-50 years (detail in Table 1). Patients were from different districts of Khyber Pakhtunkhwa with inclusion of (FATA) federally Administered Tribal Areas. Majority of the patients were belonging to District Peshawar 58 (41.43%) persuaded by Charsadda 33(23.57%), Nowshera 14(10%) Swabi 15(10.71%), Mardan 20(14.29%) and other districts 15(10.71%).

Table No.1: Age wise distribution of malaria in pregnant women

Maternal age	Malaria in pregnant women		
	Yes	no	
<20	5(16.67%)	10(9.09%)	15(10.7%)
20 to30	12(40%)	44(40%)	56(40%)
30 to 40	10(33.33%)	39(35.45%)	49(35%)
40 to 50	3(10%)	15(13.63%)	18(12.8%)
50 to 60	0(0%)	2(1.81%)	2(1.42%)
Total	30 (21.4%)	110 (78.6%)	140(100%)

In total of 140 patients having pregnancy, malaria was noted in 30 (21.4%) cases. In these patients plasmodium falcipram was found in 24(80%) of cases.

Plasmodium malaria in 14(10%). Plasmodium ovale 7(5%) and plasmodium vivax in 7(5%). Table no 2.

Table No.2: Types of malarial parasites isolated

Malaria parasite type	Total
Plasmodium Falcipram	24(80%)
Plasmodium malaria	14(10%)
Plasmodium ovale	7(5%)
Plasmodium vivax	7(5%)

Overall frequency of malaria parasite in the blood was 21.4%. The frequency of malarial parasite in the blood was high in women aged < 25 years that is 101(72%) patients in comparison to those ≥ 25 years 39(28%), (table 3) and also higher in prim gravidae 95(68%) in comparison to patients who were multigravida 45(32%) (table 4). Plasmodium falciparum was found in highest number.

Table No.3: Frequency of malarial parasite according to age of patients

Age of patient	Number of patient with malarial parisite
<25	101(72%)
>25	39(28%)
Total	140(100%)

Table No.4: Frequency of patients having malarial parasite according to parity of patients

parity	Number of patients with malarial parasites
Primary gravida	95(68%)
multigravida	45(32%)
total	140(100%)

Number of plasmodium parasite per field under microscope called as plasmodium density. The extreme Plasmodium vivax density was recorded 3 in 5 patients, whereas the lowest Plasmodium vivax density was 2 in 7 patients. The Plasmodium vivax density 1 was recorded in 3 patients. Similarly, 5 patients have lowest of 02 Plasmodium falciparum density, while 10 patients have extreme 02 Plasmodium falciparum densities (Table 5).

Table No.5: Plasmodium density in pregnant women

number	P.vivax density	number	P.falciparm density
3	1	10	2
7	3	5	2
5	3		

DISCUSSION

in our study the frequency of malaria was 21.4% which is similar to study completed by khan F et al in 250 pregnant women where result was 22.8%.[33].the minor variance is because of comparatively larger sample size in khan F et al study.in khan F et al study Amongst the positive, 52 (20.80%) samples of blood were P. vivax and 5 (2.00%) samples of blood were P. falciparum. it is in different to our study in which plasmodium falciparum was noted in high frequency 80% followed by plasmodium malaria 10%, in maqsood A et al study Plasmodium Vivax found in frequency of 55.8%, P. Falciparum for 41.9%, and P. Ovale 2.3% of infections.in another study done by doso et al in 1655 pregnant women over all frequency of malarial parasite was 20.4% which is similar to our study results.in this study frequency was maximum (33.2%) in primi and secondi gravidae having age < 25 years and lowermost (14.1%) in multi gravidae having age greater than 25 years. This is again similar to our study.[34] In Gontie et al study the frequency of malaria was noted as 10.2% which is lesser than our study because a whole of 498 patients having pregnancy were involved in study. Two studies done in Nigeria disclosed the frequencies to be 58% because malaria is endemic in Nigeria[35]. In omer SA et al in which a whole of 836 women with pregnancy were observed where 219 (26.2%) were infested with Plasmodium falciparum. According to it persons having age between 21-30 years were mostly vulnerable to plasmodium and is in similarity with the present study.[36] In Adefioye OA et al study who carried out examination of 250 blood samples, amongst these 180 (72%) were having Plasmodium falciparum. individuals having age 36-39 years were having high frequency 15 (88.2%), while those having age (>40) years were having lesser susceptibility to the malaria parasite i-e 2 (40.00%)[37].

CONCLUSION

So it is decided that the malaria is very grave and lethal in women having pregnancy as in majority of cases it leads to abortion. In addition to this the study helps us for the enhancement of control of malaria and other deliberate plan amongst the pregnant women who are pregnant in Khyber pukhtoonkhwa.

Recommendations: Patients having pregnancy presenting with fever need to be evaluated for the presence of malaria. Suitable preventive and therapeutic measures are needed in patients with pregnancy presenting with fever to reduce related morbidity and mortality duty to malaria.

Author's Contribution:

Concept & Design of Study:	Muhammad Abas Khan
Drafting:	Muhammad Abas Khan
Data Analysis:	Muhammad Abas Khan
Revisiting Critically:	Muhammad Abas Khan
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Conflict of Interest: The study has no conflict of interest to declare by any author.

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Original Article

Surgically Induced Astigmatism

Evaluation of Surgically Induced Astigmatism (SIA) at 10'O Clock Limbal Incision 2.8mm After Phacoemulsification

Attaullah Shah Bukhari[1], Shahid Jamal Siddiqui[1], Suhail Ahmed Shah[2], Sarmad Jamal Siddiqui[3], Imran Ali Pirzado[4] and Arif Rabbani[5]

ABSTRACT

Objective: To evaluate surgically induced astigmatism (SIA) at 10'o clock Limbal incision 2.8mm after phacoemulsification procedure.

Study Design: Experimental study

Place and Duration of Study: This study was conducted at the Khairpur Medical College Teaching Hospital from the duration of July 2018 to December 2018.

Materials and Methods: 100 patients who had astigmatism of less than 1.5D were selected on the basis of convenience sampling technique, and were divided into groups based on eye involvement, with one group having 50 patients in which the incisions site was Superotemporal, and the other 50 had incision site at Superonasal. The incision was given at 10'o clock 2.8mm with the wound being close with corneal hydration without using sutures. Pre and post-operative K1 and K2 measurements were recorded Data was analyzed using SPSS, with the paired t-test being applied to determine the statistical significance which was kept at ≤0.05.

Results: In a study of 100 people, 64 were male and 36 were female with the mean age of male patients being 52.31 and female being 54.35. No significant difference was observed in the pre and post-operative K1 and K2 value in Superotemporal incision (K1:0.986, K2:0.384). Similarly, no significant difference was seen in the pre and post-operative K1 and K2 value in Superonasal incision (K1:0.352, K2:512).

Conclusion: Limbal Incision can be used after phacoemulsification surgery as it doesn't enhance SIA post-operatively.

Key Words: Evaluate Surgically Induced Astigmatism (SIA), Limbal Incision, Phacoemulsification

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INTRODUCTION

Cataract surgery and refractive surgical procedures are very common in the population, with the amount of procedures basking in several millions worldwide[1].

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A study carried out in Denmark alone showed the wide amount of cataract procedures of approximately being 46,000 each year[2]. Cataract surgery has undergone various modernization and advancement in the field ever since its inception. It has finally reached new heights through the development of phacoemulsification cataract surgery[3]. Pakistan a third world country faces cataract the same way as other middle and low-income countries do, accounting for 47.8% blindness worldwide and being the leading cause of blindness in Pakistan[4-5]. Phacoemulsification and extra-capsular cataract extraction (ECCE) are the most common surgical modalities available to the surgeons for removing cataracts[6]. Phacoemulsification is a procedure that is much more demanded by the patients, and patients have high expectations regarding its outcomes. However, Phacoemulsification is widely associated with many post-operative complications[7-10]. One of the many complications seen with Phacoemulsification is surgically induced astigmatism (SIA). SIA is a very important factor in determining the desired refractive outcome[11]. SIA can be modulated by more than one method during cataract surgery. To

achieve the best surgical results, it is vital to rapidly restore visual acuity by reducing SIA and correcting any residual astigmatism[12]. Various types of small-incision cataract wounds, such as sclera, posterior Limbal tunnel, and clear corneal have been created surgically at various locations including Superotemporal, Temporal, Superior, and Superonasal. Studies have been carried out on these to determine how these aforementioned incisions have resulted in SIA[13]. Furthermore, the size of incision has also been studied and assessed if incision size has any effect on the amount of SIA created[14]. In Pakistan, studies have also been done on Phacoemulsification and SIA but the amount of studies is very minimum[15]. Considering the amount of cataract surgeries that take place in the country, a study was conducted to evaluate SIA at 10' o clock Limbal Incision 2.8mm after Phacoe-mulsification.

MATERIALS AND METHODS

This study was done at Khairpur Medical College Teaching Hospital from the duration of July 2018 to December 2018. This experimental study included 100 patients on the basis of convenient sampling. The patients with the keratometric astigmatism of 1.5D or less, had no history of ocular trauma, surgery or other underlying diseases that could alter the corneal refractive power were included in this study. The patients were divided into two groups on the basis of eye involvement and site of incision. 50 were involved in Superotemporal and 50 were involved in Superonasal incisional site. After taking an ethical approval from the concerned authority, the study was conducted and written and informed consent from each patient was acquired before they can be included in the study. The same surgeon performed the procedure on each patient, and K readings were recorded pre and post operatively included K1 and K2 readings. The procedure was performed by giving topical anesthesia drop (Alcane). Incision was given at ten o'clock by 2.8 keratom in right eye supra temporal and in left eye supra nasal cataract was removed by phaco procedure, and flodable Intra ocular lens was implanted. Wound was closed by corneal hydration without suture. The data was recorded and enter on data sheet. The data was analyzed through SPSS version 21, and compare the mean of k readings the paired *t* test was applied and level of significance was kept at $P \leq 0.05$.

RESULTS

- The Mean age of the patients on the basis of gender were present in figure 1.1
- The Demographic data was presented in figure 1.2
- The Mean pre and post-operative K reading of both supra temporal and Supra nasal including K1 and K2 readings were shown in figure 1.3
- The level of significance on comparison of Mean values of in both groups was shown in Table-1.

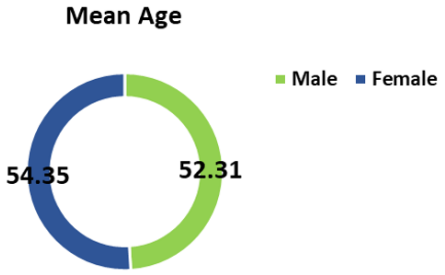

Figure No.1.1: Mean age of the patients on the basis of gender

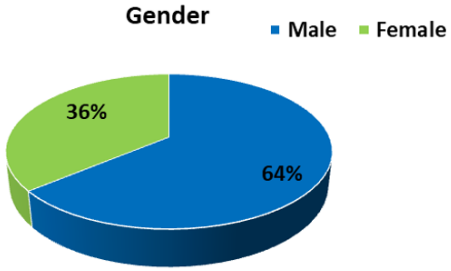

Figure No. 1.2 shows the Percentage of gender based

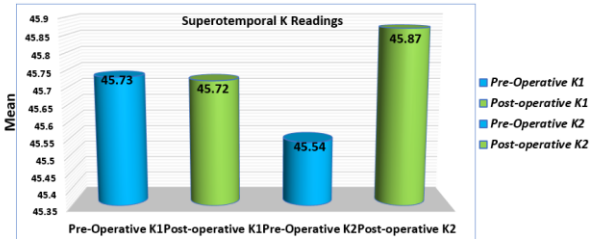

Figure: 1.3 shows the Mean Pre and Post-operative K1/K2 readings in Superotemporal incisional site

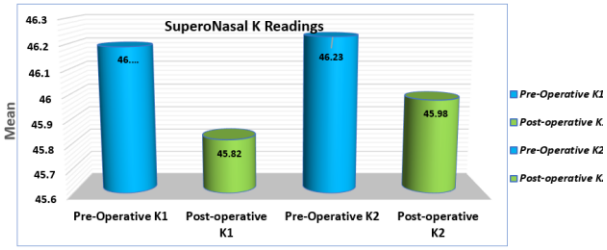

Figure: 1.4 shows the Mean Pre and Post-operative K1/K2 readings in Superonasal incisional site

Table No.1: Level of significance on comparison of Mean K reading among different incisional sites

Compare the Mean Superotemporal K Readings		
P value	Pre-Operative	Post-Operative
K1	0.986	
K2	0.384	
Compare the Mean Superonasal K Readings		
K1	0.352	
K2	0.512	

DISCUSSION

The aim of the study was to determine if Limbal incision performed at 10'o clock position will develop concerning levels of SIA, or will instead reduce astigmatism. Since cataract is a widely concerning issue in Pakistan, surgeons should be aware of what type of incision is best and has the lowest rate of developing surgically induced astigmatism. SIA depends mostly on site and size of the incision, as well as the presence of pre-operative astigmatism[16]. The prevalence of post-operative astigmatism is less in small sutureless incision as compared to large incisions of extracapsular lens extraction. Our study showed that when carrying out Limbal incision, there was no significant different in pre and post-operative astigmatism development. Therefore SIA didn't develop significantly to cause caution while carrying out Limbal incision either Superonasally or Superotemporally. Although there was no difference in pre and post-operative astigmatism, However many incisions have led to a reduction in post-operative astigmatism. Piao et al (2020) showed that clear corneal incision leads to a statistically significant reduction of astigmatism[17]. Warren et al (2011) compared both Limbal incision and clear corneal incision to assess SIA, in which he showed that 2.2mm square posterior Limbal incision induced significantly less SIA compared to same-sized clear corneal incision, furthermore which will improve refractive outcomes[18]. This result is in line with our study in which there was no increase in post-operative SIA. Nikose et al (2018) in his study compared SIA in temporal clear corneal incision and superior clear corneal approach and concluded that temporal clear corneal incision is evidently better concerning SIA[19]. Whereas another study showed that there was no significant difference in SIA between Superotemporal incisions and Superonasal incisions after clear corneal incision[11]. Our study compared pre and post-operative SIA in same groups, future studies can be done to compare SIA in Superotemporal and Superonasal Limbal incisions. Limbal Incision can be carried out in a similar manner to clear corneal incision, these both are strong incision methods that don't increase SIA and rather reduce it.

CONCLUSION

Limbal Incision at 10'o clock position doesn't enhance SIA after Phacoemulsification and therefore can be used in cataract procedures.

Author's Contribution:

Concept & Design of Study:	Attaullah Shah Bukhari
Drafting:	Shahid Jamal Siddiqui, Suhail Ahmed Shah, Sarmad Jamal Siddiqui
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Final Approval of version:	Sarmad Jamal Siddiqui

Conflict of Interest: The study has no conflict of interest to declare by any author.

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Original Article

Effectiveness of Levetiracetam as a First Line Anticonvulsant for Neonatal Seizures

Muhammad Hayat Khan, Syeda Shireen Gul, Qaiser Zaman, Nadeem Ahmad and Qurrat-ul-Ann

ABSTRACT

Objective: To determine the effectiveness of levetiracetam as a first line anticonvulsant in neonates presenting with seizures at a tertiary care hospital.

Study Design: Prospective study.

Place and Duration of Study: This study was conducted at the Department of Neonatology, Pakistan Institute of Medical Sciences (PIMS) Hospital, Islamabad from 23rd December, 2020 to 22nd June, 2021.

Materials and Methods: One hundred and thirty eight neonates having clinical seizures with and without having documented EEG abnormality were enrolled. Levetiracetam as 50 mg/kg loading dose (diluted in 20 ml normal saline) was administered intravenously in 20 minutes, followed by a maintenance dose of 20 mg/kg intravenously every 12 hours. An additional 20 mg/kg loading dose of levetiracetam was administrated in case of persistent seizures despite initial levetiracetam load. Response to the levetiracetam was considered as the cessation of seizures clinically within a time frame of 30 minutes.

Results: There were 79 (57.2%) males. Overall, mean age was 6.27±6.5 days. Mean birth weight was 2.33±0.64 kg. There were 80 (58.0%) neonates who belonged to urban areas of residence. There were 42 (30.4%) neonates who were born pre-term. Lower segment cesarean section was the commonest mode of delivery noted among 70 (50.7%) cases. Most frequent etiology of seizures was found to be sepsis 57 (41.3%) while hypoxic ischemic encephalopathy was reported in 49 (35.3%). Levetiracetam treatment was found to be successful in 122 (88.4%) neonates. No drug related serious adverse events were reported.

Conclusion: Levetiracetam was found to be highly effective as a first line anticonvulsant in neonates presenting with seizures. No drug related serious adverse events were observed.

Key Words: Levetiracetam, Anticonvulsant, Neonate, Seizures

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INTRODUCTION

Seizure in neonates is a common medical emergency. The incidence of seizures in estimated to be more in pre-term newborns (ranging between 0.6-5/1000 live-births).[1] Most commonly observed etiologies of neonatal seizures are hypoxic-ischemic encephalopathy, congenital malformations, infection, intracranial hemorrhage, thrombosis and inborn metabolic disorders.[2]

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Neonatal seizures are considered to be an important cause of neurological impairments, delay and it is associated with increased risk of neonatal mortality.[3]

Data from developed countries show that there are controversies regarding optimal management options for neonatal seizures.[4,5] In the past, phenobarbital followed by phynytoin or fosphenytoin have been the mainstay of treatment in neonatal seizures.[6]Currently FDA approved anti-epileptic options including phenobarbital and phenytoin exhibit efficacy in less than half of the neonates suffering with seizures while adverse events related with these drugs also common.[7,8] Levetiracetam has a unique mode of action where it binds to unique site. Levetiracetam has rapid absorption, renal excretion and has not been reported to modulate Na, K or Ca channels while no cardiotoxicity has been reported with its therapeutic dosages.[9]Due to these benefits, levetiracetam can be preferred over its contemporary drugs.[10]A study by Kreimer et al[11]reported seizures control in 47% patients using levetiracetam monotherapy.

While a study by Falsaperla et al[12] reported that levetiracetammono-therapy is effective in 100% patients for the treatment of seizures. While another study by Ragunathan and Chandrasekhar[13] reported seizures control in 64.7% patients presenting with seizures using levetiracetam monotherapy. The aim of the present study is to determine the effectiveness of levetiracetam as 1st line anticonvulsant in neonates presenting with seizure at a tertiary care hospital. The findings of this study were thought to help to determine the success rate of levetiracetam for seizures control in our local population.

MATERIALS AND METHODS

This prospective study was conducted at Department of Neonatology, Pakistan Institute of Medical Sciences (PIMS) Hospital Islamabad from23rd December, 2020 to 22ndJune, 2021, and comprised 138 neonates. Inclusion criteria was neonates having clinical seizures (focal/ generalized clonic/tonic, myoclonic, subtle) with and without having documented EEG abnormality. Neonates having prior treatment with antiepileptic drugs other than benzodiazepines, were excluded.

After inclusion of the neonates, levetiracetam as 50 mg/kg loading dose (diluted in 20 ml normal saline) was administered intravenously in 20 minutes, followed by a maintenance dose of 20 mg/kg intravenously every 12 hours. An additional 20 mg/kg loading dose of levetiracetam was administrated in case of persistent seizures despite initial levetiracetam load. Response to the levetiracetam was considered as the cessation of seizures clinically within a time frame of 30 minutes from the initiation of the intravenous drug therapy. If the seizures did not stop within 30 minutes after starting the infusion, additional 20 mg/kg loading dose of levetiracetam was administrated. Cessation of seizures as observed clinically within this additional time frame was also considered as the response to the drug. If the seizure episode did not cease within the total time frame of 60 minutes, it was considered as treatment failure. In failed cases, intravenous phenytoin (20 mg/kg diluted in 20 ml of normal saline) was administered. All the study relevant information was noted. The collected information was analyzed with SPSS version 26. P value ≤0.05 was considered as significant.

RESULTS

There were 79 (57.2%) male. Overall, mean age was 6.27±6.5 days (ranging between 1 to 28 days). Mean birth weight was 2.33±0.64 kg (ranging between 1kg to 3.5kg). There were 80 (58.0%) neonates who belonged to urban areas of residence. There were 42 (30.4%) neonates who were born pre-term. Lower segment cesarean section was the commonest mode of delivery noted among 70 (50.7%) cases. Most frequent etiology of seizures was found to be sepsis 57 (41.3%) while hypoxic ischemic encephalopathy was reported in 49 (35.3%) [Table 1].

Figure 1 showing effectiveness of levetiracetam in the neonatal seizures and it was noted that levetiracetam was successful in 122 (88.4%) neonates. No drug related serious adverse events were reported.

Table No.1: Demographic information of the neonates (n=138)

Variable	No.	%
Gender		
Male	79	57.2
Female	59	42.8
Age (days)		
≤7	108	78.3
>7	40	21.7
Birth weight (kg)		
<2.5	62	44.9
≥2.5	76	55.1
Area of residence		
Urban	80	58.0
Rural	58	42.0
Gestational maturity		
Term	96	69.6
Pre-term	42	30.4
Gravidity status		
Primigravida	53	38.4
Multigravida	85	61.6
Mode of delivery		
Normal vaginal delivery	68	49.3
Cesarean section	70	50.7
Gestational diabetes mellitus	6	4.3
Eclampsia	17	12.3
Birth asphyxia	53	38.4
Etiology of seizures		
Idiopathic	11	8.0
Hypoxic ischemic encephalopathy	49	35.3
Metabolic	15	10.9
Sepsis	57	41.3
Hemorrhage/thrombosis	3	2.2
Meconium aspiration syndrome	3	2.2

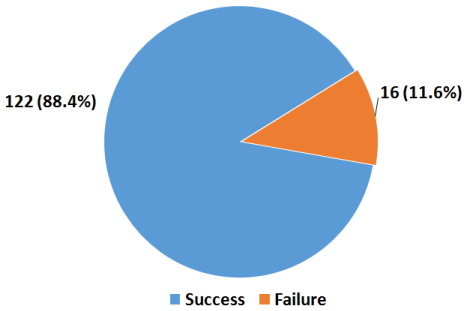

Figure No. 1: Effectiveness of levetiracetam in neonatal seizures

No significant association was found among study variables and treatment effectiveness (p>0.05) except mode of delivery as normal vaginal delivery where 75.0% neonates with failure of treatment had normal vaginal delivery in comparison to 45.9% who had successful outcomes (p=0.029) [Table 2].

Table No.2: Stratification of neonatal characteristics with respect to treatment effectiveness (n=138)

Characteristics of Neonates	Treatment effectiveness		P value
	Success (n=122)	Failure (n=16)	
Male gender	72 (59.0%)	7 (43.8%)	0.246
Age ≤7 days	98 (80.3%)	10 (62.5%)	0.104
Birth Weight <2.5 kg	57 (46.7%)	5 (31.2%)	0.242
Rural Area of Residence	53 (43.4%)	5 (31.2%)	0.353
Pre-Term	40 (32.8)	2 (12.5%)	0.097
Primigravida	50 (41.0%)	3 (18.8%)	0.086
Mode of delivery as normal vaginal delivery	56 (45.9%)	12 (75.0%)	0.029
Gestational diabetes mellitus	5 (4.1%)	1 (6.3%)	0.691
Eclampsia	16 (13.1%)	1 (6.3%)	0.432
Birth asphyxia	49 (40.2%)	4 (25.0%)	0.241
Etiology of seizures			
Idiopathic	11 (9.0%)	-	0.634
Hypoxic ischemic encephalopathy	47 (38.5%)	2 (12.5%)	
Metabolic	15 (12.3%)	-	
Sepsis	52 (42.6%)	5 (31.2%)	
Hemorrhage/Thrombosis	3 (2.5%)	-	
Meconium aspiration syndrome	3 (2.5%)	-	

DISCUSSION

Commonly adopted anticonvulsant options like phenytoin have a relatively low efficacy while adverse events related to phenytoin are also common.[14] Newer antiepileptic treatments are being proposed by the researchers but the data is only limited to case reports and case series.[15,16]Intravenous levetiracetam has become a common 2nd line anticonvulsant choice among pediatric population but evidence about its effectiveness is not abundant.Levetiracetam is a broad-spectrum anti-epileptic agent having approval of usage for seizure prophylaxis in both focal and generalized sizures.[9,10]Intravenous levetiracetam is widely available for those cases who cannot intake oral form.

In this study, we found that levetiracetam had successful treatment outcome in 88.4% neonates while 11.6% did not respond to levetiracetam treatment. These findings are very similar to a study conducted by Reiter et al[16] assessing IV levetiracetam in the management of acute seizures in children who showed that 89% of children remained seizure-free at 1 hour.A study done by Venkatesan et al[17], evaluating 127 neonates who developed seizures after being diagnosed with hypoxic ischemic encephalopathy, found that levetiracetam was effective as either initial or following phenobarbital in 84% neonates while phenobarbital as initial therapy was successful in 61% cases.Levetiracetam is easy to administer and can be given as a five minute infusion into a peripheral IV cannula without the increased risk of serious adverse events (including hypotension, cardiac arrhythmias, extravasation or death). Furthermore, levetiracetam is compatible with both dextrose and normal saline infusion and has limited drug interactions. A study done by McTague et al[18] from UK revealed that intravenous levetiracetam was effective in 81% children having repeated seizures and status epilepticus. Levetiracetam was also found to be safe in the same study.

Our study had some limitations as well. As this was a single center study with a relatively small sample size, the findings of this study cannot be generalized. As we did not have any comparator or control group in this study, further studies should be conducted having randomized controlled design to judge the efficacy of levetiracetam with other available anticonvulsants. We only evaluated immediate outcome of levetiracetam in the present study so studies aiming to evaluate long-term outcomes should also be conducted.

CONCLUSION

Levetiracetam was found to be highly effective as first line anticonvulsant in neonates presenting with seizures. No drug related serious adverse events were observed. Further research should be conducted having randomized controlled design to judge the efficacy of levetiracetam with other available anticonvulsants in the local population.

Author's Contribution:

Concept & Design of Study:	Muhammad Hayat Khan
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Revisiting Critically:	Muhammad Hayat Khan, Syeda Shireen Gul
Final Approval of version:	Muhammad Hayat Khan

Conflict of Interest: The study has no conflict of interest to declare by any author.

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Original Article

Clinical Spectrum, Nutritional Status and Outcome of Visceral Leishmaniasis in Children – Tertiary Care Hospital Experience

Syed Sajid Hussain Shah[1], Shahzad Najeeb[1], Farrukh Addil[2], Khyal Muhammad[2], Ejaz Hussain[1] and Fiaz Khan[3]

ABSTRACT

Objective: The objective of this study was to enlighten the clinical spectrum of Visceral Leishmaniasis (VL) in children presenting to tertiary care hospital along with nutritional status and outcome in hospital.

Study Design: Retrospective Study

Place and Duration of Study: This study was conducted at the Ayub Teaching Hospital, Abbottabad from January 2018 to December, 2019.

Materials and Methods: Patient diagnosed case with VL were and clinical features, nutritional status and outcome was documented on specific proforma. Clinical spectrum was taken as presenting features of patients with pallor, bruises, and edema. Patient's nutritional status was assessed by doing serum albumin and plotting weight for age on growth chart for sex. Outcome taken as discharge, expiry or transfer out. Data was analyzed by SPSS 20 and results taken significant with p value < 0.05.

Results: There were 36 patients, 25 (69.4%) male and 11 (30.6%) females. Patient's age ranged from 05 months to 6 years, mean age of 27.86 ± 20.49. Pallor was main presenting feature. Mean serum albumin of patients were 2.51 ± 0.44 and mean Hb was 6.79 ± 1.83. Out of 36 patients, 34 patients (94.4%) were having Hb less than 9 gm/dl. Majority of patients (66.7 %) were below 5th percentile for weight for age on growth chart. Most of underweight patients were female and there was significant relationship between gender and underweight (p value 0.041). There was one expiry and 35 (97.2%) patients improved and discharged from hospital.

Conclusion: Pallor and under nutrition are main presenting feature while females are more malnourished. Appropriate treatment leads to complete recovery.

Key Words: Clinical spectrum, nutritional status, outcome, visceral Leishmaniasis

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INTRODUCTION

Visceral Leishmaniasis (VL) has been enlisted as one the neglected parasitic infectious disease by World Health Organization (WHO).[1,2] Though Visceral leishmaniasis (VL) is endemic in many parts of world including Pakistan yet it can lead to severe manifestations and even death if not treated in time and with proper dose and duration. VL infections present as sub clinical in many cases.[3] VL is endemic in most of the countries of world as it is estimates that almost 100 countries are endemic.

New cases of VL are estimated to 0.7 to 1 million yearly.[4] As in few countries, VL is highly endemic, it affect the country economy badly as health system is under constant constrain due to high mortality and morbidity.[5] Sand fly is responsible for the transmission of VL as the parasite affects the macrophages and replicates in bone marrow, spleen and liver.[6] Though the majority of patients with VL present with fever, loss of appetite leading to weight loss especially in children and splenomegaly yet VL can also have atypical presentation as gastrointestinal symptoms including portal hypertension, pneumonia and even absence of splenomegaly.[7] The objective of this study was to enlighten the clinical spectrum of VL in children presenting to tertiary care hospital along with nutritional status and outcome in hospital.

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MATERIALS AND METHODS

This study was done in Paediatric B ward of Ayub Teaching Hospital, Abbottabad. This was retrospective study. Data had been retrieved form files of patients from January 2018 to December, 2019 who were admitted to Paediatric B ward with diagnosis of VL after approval from institutional review board. Recorded from data, the presenting features of patient including fever, edema, rashes (petechial/bruise), history of contact with Leishmaniasis patient, complete blood count findings, Leishmaniasis antibody or bone marrow for diagnosis, serum albumin and outcome from hospital in form of discharge, expiry or transfer out was documented on specific proforma. Patient age, sex, weight was recorded on proforma. Data was analyzed by SPSS and results taken significant with p value < 0.05. Clinical spectrum was taken as presenting features of patients with pallor, bruises, and edema. Patient's nutritional status was assessed by doing serum albumin and plotting weight for age on growth chart for sex. Patients with serum albumin less than 3.0 gm/dl were taken as less nourished and patients having less than 5th percentile on weight for age growth chart taken as malnourished. Patients with platelet count less than 20 k /cmm and bruises and petechial rash were given platelets transfusion. History of Leishmaniasis in family, neighborhood and village was also recorded along with pet dog at home.

RESULTS

In this there were total of 36 patients. Out of 36 patients, 25 (69.4%) were male and 11 (30.6%) were females. Age of patients ranged from 05 months to 6 years with mean age of 27.86 ± 20.49. Of total 36.1% patients were below one year, 25% patients were between one to two years and 38.9% patients were above 2 years. Weight of patients ranged from 3.80 to 14 kg with mean weight of 9.33 ± 2.42 kg. Patient acute state of nutritional was check by doing serum albumin. There were 35 (97.2%) patients with serum albumin less than 3.0 gm/dl. Mean serum albumin of patients were 2.51 ± 0.44. (Table 1). Hb ranged from 3.6 to 12.5 gm/dl with Hb of 6.79 ± 1.83. Out of 36 patients, 34 patients (94.4%) were having Hb less than 9 gm/dl. Majority of patients (66.7 %) were below 5th percentile for weight for age on growth chart. Leishmania antibody was done is 35 (97.2%) patient and it was positive. Only in on patient Leishmania antibody was not done as bone marrow was done in the patient for diagnosis. Overall bone marrow was done in 3 (8.3%) patients. There was history of Leishmaniasis in neighborhood in 5 (13.9%) patients. Family history of Leishmaniasis was present in 3 (8.3%) patients. Patients with Leishmaniasis were present in village and surrounding area in 16.7% cases. Dog as pet were kept at home in 30.6% patients with Leishmaniasis. Majority (94.4%) patient's presented with history of pallor and 30.6% patients presented with edema. At presentation 15.7% patients were having bruises on the body. At presentation 27.8% patients were having platelets less than 20K / cmm and needed platelet transfusion. Majority of underweight patients were female and there was significant relationship between gender and underweight with p value of 0.041. (Table 2). There was one expiry during hospital stay and 35 (97.2%) patients improved and discharged from hospital.

Table No.1: Age, Weight, Albumin, CBC

	Min.	Max.	Mean	Std. Deviation
Age (months)	5.0	72.0	27.861	20.4927
Weight (kg)	3.80	14.00	9.3278	2.42483
Albumin (gm/dl)	1.5	4.0	2.514	0.4441
ALT (IU/L)	10	64	33.39	12.311
TLC (thousand/ul)	1.60	13.10	4.8808	2.52112
Platelets (thousand/ul	1.6	169.0	60.625	45.8019
Hb (gm/dl)	3.6	12.5	6.789	1.8261

Table No.2: Gender versus percentile cross table

Gender		Percentile		Total
		Above 5th percentile	Below 5th percentile	
Sex	Male	11	14	25
	Female	1	10	11
Total		12	24	36

DISCUSSION

VL is a major public health problem leading to severe morbidity and mortality if untreated, mainly affecting children. It is caused by parasite which is intracellular obligate and transmitted by female sand fly. Literature has shown that even VL cases are resistant to pentavalent antimony compounds requiring amphotericin B and interferon gamma for treatment.[8] Incidence of Leishmaniasis has increased in last few decades due to multiple factors including human travelling, expansion of population and increase susceptibility to infections due to malnutrition and human immunodeficiency virus (HIV). It is evident in the literature that children presenting with pyrexia of unknown origin showed the VL in bone marrow of 13.3% patients.[9] This study was done to enlighten the clinical spectrum of VL in children presenting to tertiary care hospital along with nutritional status and outcome in hospital.

Presentation and clinical spectrum of VL ranges from self-healing skin ulcer to lethal systemic presentation. Clinical features include history of prolong fever, loss of appetite and weight loss, enlargement of liver and

spleen and complete blood count showing pancytopenia.[10] Adam GK et al[11] did their study in Eastern Sudan and investigated the mortality rate and incidence of VL. It was retrospective study and data was collected from ministry of health. The data was of 14 year from 2002 to 2015. This study included 51773 patients. In 2002 the fatality rate was 4.8% and it declined to 1.1% in 2014. Case fatality rate was more in patients who live in rural area. There was significant relationship between death and rural area residence with p value of 0.021. In our study almost all of the patients were from rural area. The mortality was 2.8% as only one patient died. But majority of patients were malnourished as 66.7 % were below 5th percentile for weight for age on growth chart. In one of study by Al-Warid HS et al[12] in Iraq objective was identification of VL association with age and sex. In their study males were at higher risk as compare to females and VL more in children less than 5 years of age. In our study apart from few patients, rests of the patients were less than five years of age and majority of them were males. It is comparable to the findings of Al-Warid et al study results. Ahuja A et al[13] in their research article highlighted the spectrum of VL including unusual presentation as patients presented with infectious etiology to malignancy. There were six patients and presentation was with or without fever as four patients had splenomegaly, one patient each with unilateral pleural effusion and renal failure. In our study none of the patient presented with unusual presentation.

Bezerra GSN et al[14] in their review article discussed about the diagnosis of VL by using urine sample. Due to non-specificity of clinical symptoms of VL, diagnostic test with high sensitivity and specificity are required. There is relationship between Leishmania DNA and renal impairment even the DNA is there in urine without renal involvement. In our study the main diagnostic test was by Leishmania antibody and only two patient's diagnosis was made on bone marrow aspirate. Al-Eryani A et al[15] did one study in Yemen about the patient description and characteristics of children presenting with VL. Most of children were having weight loss (93%), pallor (86%) and malaise (86%). In our study 66.7% children were underweight, 94.4% children at presentation were pale, 97.2% children were having serum albumin less than 3.0 gm/dl and 30.6% children had edema at presentation.

Skenderi E et al[16] presented one case report and diagnosis was VL as it one important cause of fever of unknown origin. In 20 months old child, presenting feature was with fever. In our study all patients were having history of fever. Goto Y et al[17] in their review article performed systematic review regarding anemia in patients with VL. They review estimated that prevalence of anemia was in more than 90% and degree of anemia was moderate to severe with mean Hb of 7.5 gm. In our study pallor was present in 86% patient while Hb less than 9gm was present in 94.4% patients. Cloots K et al[18] in their research article concluded that males are at risk for developing VL. The disease pathogenesis is related to biological sex related differences. In our study majority of patients were male (69.4%) while females were 30.6%. Kimutain R et[19] studied the efficacy of sodium Stibogluconate and Paromomycin in combination in Eastern Africa and found it to be safe except in older and HIV positive patients. In our study all patients were given sodium Stibogluconate and they responded well as 97.2% patients improved and discharged from hospital. Altaf C et al[20] did study in Muzaffarabad. In their study the median age of patients were 18 months where as in our study the median age was 24 months. In their study the mortality was 3.28% while in our study it was 3.8%. All of patients responded well to the antimony based drug as that of our study. There is predominantly helper T cell (Th) 2 response in VL and there are high levels of interleukin-10 (IL-10). Patients who are cured of VL, immune response is by Th1 predominantly and high level of interferon-gamma (IFN-γ). Post Kala-azar Dermal Leishmaniasis (PKDL) in the presentation in which the immune response characteristics are of Th2 and Th1, leading to dissociation between immune response in the skin and manifestation in form papulonodulare or macula. The interval between VL and PKDL is from 0 to 3 years in different regions of world.[21] In our study none of the patient had PKDL till completion of treatment but there should be study involving patients for development of PKDL.

There were limitations in this study. Due to retrospective study, follow up could not be done and complete recovery status could not be ascertained. Also improvement in malnourishment status could not be documented on follow up.

CONCLUSION

Pallor and under nutrition are main presenting feature of children presenting with VL. Females are more at risk for having underweight as compare to male children. Timely diagnosis and treatment leads to complete recovery.

Author's Contribution:

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Data Analysis:	Khyal Muhammad, Ejaz Hussain, Fiaz Khan
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Original Article

Short-Term Outcome of bilateral Internal Mammary Artery Harvesting

Muhammad Moeen, Shafqat Hussain, Iftikhar Paras, Muhammad Ali Khan and Muhammad Hamid Chaudhary

ABSTRACT

Objective: To describe our experience about the short-term outcome of bilateral internal mammary artery (BIMA) harvesting for coronary artery bypass grafting (CABG) at our tertiary care hospital.

Study Design: Prospective Cross-sectional study

Place and Duration of Study: This study was conducted at the Ch. Pervaiz Elahi Institute of Cardiology, Multan, Pakistan from January 2018 to December 2020.

Materials and Methods: A total of 42 patients of both genders undergoing BIMA harvesting for CABG were included. Among these cases, both left and right Internal mammary arteries were harvested by semi skeletonization technique. Demographic characteristics along with clinical features, comorbid conditions, underlying diseases and severity were recorded among all study cases. Short-term outcomes in terms of 3-months operative death, stroke, renal dysfunction or renal failure, need for re-operation, duration of ventilation, superficial and deep wound infection, and arrhythmias were noted for possible outcomes among all study cases.

Results: Among a total of 42 cases, mean age was noted to be 49.52+8.1 years while most the patients, 23 (54.8%) were between 40 to 60 years of age. There were 39 (92.9%) male patients while mean BMI was noted to be 25.1$\pm$3.6 kg/m^2. Hypertension was the most commonly found co-morbidity noted among 34 (81.0%) patients, dyslipidemia in 24 (57.1%) while diabetes mellitus was noted in 18 (42.9%). There were 31 (73.8%) patients who were found to have triple vessels disease. Mean number of anastomosis were recorded to be 3.62+0.85. Mean duration of ICU stay was recorded to be 6.14+1.78 days. Superficial wound infection was noted in 2 (4.8%) patients while pleural effusion was the commonest post-operative complications seen in 4 (9.5%) patients. No mortality was recorded.

Conclusion: The short-term outcome of bilateral internal mammary artery harvesting was found to be acceptable.

Key Words: Mammary Arteries, coronary artery bypass, dyslipidemia.

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INTRODUCTION

Coronary artery bypass grafting (CABG) is done commonly to treat coronary artery disease globally.[1] Since the introduction of saphenous vein graft (SVG) in 1967, lots of advancements have been made in the past few decades regarding conduit in the form of graft patency, decline in re-occlusion as increase in patient's survival.[2]

Literature establishes that due to better long-term patency and less chance of angina pectoris or subsequent cardiac events, arterial grafts are much better than SVGs.[3]

Researchers have found bilateral internal mammary arteries (BIMA) grafts to have advantages over single internal mammary artery (IMA) grafting as BIMA demonstrates better overall outcome and much longer cardiac events free survival.[4,5] Contrary to SVGs, IMA provides us options of utilizing it as a pedicle, a skeletonized or as a free graft.[2,6] There are advantages and disadvantages linked to various methods of harvesting but irrespective of these, BIMA grafting has been found to be superior in terms of long-term outcomes and survival rates in comparison to one IMA grafting.[4,5] A study done by Hemo E et al revealed that BIMA harvesting was associated with 10% risk of re-intervention at 10 year duration in comparison to 20% with those who had one IMA harvesting while the risk of re-intervention increased to 30% in those patients who had no IMA.[7]

Not many local studies have been published describing outcomes of BIMA harvesting in Pakistan so the current study was planned to describe our experience about the short-term outcome of BIMA harvesting for

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CABG at our tertiary care hospital. The findings of this study were thought to present safety and efficacy aspects of BIMA harvesting so that local cardiac surgeons are aware the potential risks and benefits related with this technique.

MATERIALS AND METHODS

This prospective cross-sectional study was carried out at Ch. Pervaiz Elahi Institute of Cardiology, Multan, Pakistan from January 2018 to December 2020. Approval from institutional ethical committee was acquired whereas written consent was sought from all study participants.

A total of 42 patients of both genders undergoing BIMA harvesting for CABG at Ch. Pervaiz Elahi Institute of Cardiology, Multan, Pakistan were included. Internal mammary arteries were harvested by semi skeletonization technique while one IMA was utilized to bypass left anterior descending artery whereas second IMA was use to bypass either right coronary artery or left circumflex artery as per surgeon's preference according to position of the targeted vessels. Thirty-nine procedure were done on pump while three cases were done off pump beating heart.

Demographic characteristics along with clinical features, comorbid conditions, underlying diseases and severity were recorded among all study cases. Short-term outcomes in terms of 3-month operative death, stroke, renal dysfunction or renal failure, need for re-operation, duration of ventilation, superficial and deep wound infection, and arrhythmias were noted for possible outcomes among all study cases.[8]

A special proforma was designed to record all study information. Data was analyzed using SPSS version 26.0. Gender, co-morbid conditions, types of vessel disease and post-operative complications like arrhythmias, pleural effusion, renal dysfunction and superficial would infection were represented as frequency and percentages. Age (years), BMI (kg/m^2), number of anastomosis, duration of intensive care unit (ICU) stay (days), duration of ventilator (hours) and duration of inotropic use (hours) were shown as mean and standard deviation.

RESULTS

Among a total of 42 cases, mean age was noted to be 49.52+8.1 years (ranging 30 to 75 years) while most the patients, 23 (54.8%) were between 40 to 60 years of age. There were 39 (92.9%) male patients while mean BMI was noted to be 25.1±3.6 kg/m^2. Hypertension was the most commonly found co-morbidity noted among 34 (81.0%) patients, dyslipidemia in 24 (57.1%) while diabetes mellitus was noted in 18 (42.9%). There were 31 (73.8%) patients who were found to have triple vessels disease. Table 1 is showing baseline characteristics of patients undergoing BIMA Harvesting in the present study.

Table No.1: Characteristics of Patients undergoing bilateral Internal Mammary Artery Harvesting (n=42)

Characteristics		Number (%)
Gender	Male	39 (92.9%)
	Female	3 (7.1%)
Age (years)	<40	10 (23.8%)
	40-60	23 (54.8%)
	>60	9 (21.4%)
BMI (kg/m^2)	<25	23 (54.8%)
	25-30	15 (35.7%)
	>30	4 (9.5%)
Diabetes Mellitus		18 (42.9%)
Hypertension		34 (81.0%)
History of Myocardial Infarction		18 (42.9%)
History of Smoking		20 (47.6%)
Dyslipidemia		24 (57.1%)
Chronic Kidney Disease		5 (11.9%)
Chronic Obstructive Pulmonary Disease / Asthma		4 (9.5%)
Calcified Aorta		2 (4.8%)
Ejection Fraction < 40%		4 (9.5%)
Types of Vessel Disease	Double	11 (26.2%)
	Triple	31 (73.8%)

Mean number of anastomosis were recorded to be 3.62+0.85. Mean duration of ICU stay was recorded to be 6.14+1.78 days. Superficial wound infection was noted in 2 (4.8%) patients while pleural effusion was the commonest post-operative complications seen in 4 (9.5%) patients. No mortality was recorded. Table 2 is showing short-term outcomes and complications among patients who underwent BIMA in the present study.

Table No.2: Short-Term Outcomes and Complications among Patients who underwent bilateral Internal Mammary Artery Harvesting

Short-Term Outcomes and Complications	Number (%) / Mean±SD
Duration of ICU Stay (days)	6.14±0.78
Duration of Ventilator Required (hours)	6.29±4.07
Duration of Inotropic Use (hours)	17.71±8.79
Frequency of Superficial Wound Infection	2 (4.8%)
Frequency of Arrhythmias	2 (4.8%)
Frequency of Pleural Effusion	4 (9.5%)
Frequency of Renal Dysfunction	1 (2.4%)

DISCUSSION

In the past, researchers have found BIMA harvesting to be associated with significantly better short-term as well as long-term outcomes in comparison to single IMA harvesting or venous grafts alone.[3-6] A study done by Lytle BW et al revealed 15% increase in terms of

20-years survival among cases undergoing BIMA harvesting.[9] When comparing to venous grafting, IMA grafting is also known to induce increased release of endothelial-derived relaxing factor (NO) at molecular level and as we know that NO is found to regulate blood-flow and it induces inhibition of platelet functioning and helps allowing lesser neutrophil adhesion to the endothelium coinciding with increased short-term as well long-term vessel patency.[10,11] Some cardio-thoracic surgeons are of the view that BIMA grafting should not be used in routine aiming coronary revascularization as it is complicated procedure requiring longer duration to perform needing optimum surgical skills while a compromise in the said features could contribute to in-hospital mortality and morbidity especially deep sternal wound infections.[12] Due to all these controversies, this study was carried out to present our local experience about BIMA harvesting and short-term outcomes related with it. We found BIMA harvesting to be a relatively safe and effective technique as no peri-operative or post-operative mortality was recorded in the present set of patients. Superficial wound infection was noted in 2 (4.8%) patients while pleural effusion was the commonest post-operative complications seen in 4 (9.5%) patients. A previous local study from Agha Khan University Hospital Karachi evaluating short-term efficacy and safety of BIMA grafting revealed it to be clinically good.[13]

Some researchers have advocated BIMA grafting to be done in relatively young patients who have greater life-expectancy.[14] Mean age in the present study was noted to be 49.52+8.1 years. Our findings are quite consistent with a study done in Bangladesh where mean age of the patients undergoing BIMA was recorded to be 48.73+8.42 years.[15] Local data also recorded mean age among patients undergoing BIMA to be 48+9.4 years[13] which is quite similar to the present findings. In the present study, 42.9% of the patients had diabetes mellitus wile researchers in the past have highlighted diabetes mellitus to be risk factor for post-surgery deep sternal wound infection.[16] We had aimed strict diabetes control among our diabetic patients and it was seen that no major post-operative complications were seen among diabetic patients in the present study.

Safety of IMA grafting have been evaluated on the basis of in-hospital deaths, arrhythmias, sternal infections of post-surgery myocardial infarctions in the literature.[13,17] We did not note any peri-operative or post-operative deaths in our patients while frequency of superficial wound infection and arrhythmias was noted to be in 4.8% each in the present study.

There were few limitations to this research. As this was a single center study from South Punjab, Pakistan, our findings cannot be generalized regarding short-term outcomes of BIMA grafting aiming coronary revascularization. There was no comparative group or any other contemporary techniques compared in the present study so further studies with better comparative designs are required to further establish the short-term outcomes related to BIMA in our local population. We only evaluated short-term outcomes in the present study so further studies evaluating long-term outcomes of BIMA grafting should be done to further enlighten us about different aspects of BIMA grafting.

CONCLUSION

The short-term outcome of bilateral internal mammary artery harvesting was found to be acceptable. Studies involving large sets of patients from multiple centers with long-term follow ups and outcomes should be done to further elaborate the safety and effectiveness of bilateral internal mammary artery harvesting.

Author's Contribution:

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Original Article

Preferences and Attitudes of Orthodontic Patients on Use of Social Media in Saudi Arabia

Rabia Bilal

ABSTRACT

Objective: The objective of the study was to find out how orthodontic patients use social media sites to share their treatment-related experiences and attitudes, whether orthodontic patients use the Internet and social media sites as a source for orthodontic information

Study Design: cross sectional study

Place and Duration of Study: This study was conducted at the E-Questionnaire was shared on various social media accounts and data was collected from January to March 2017.

Materials and Methods: The questionnaire included questions pertaining to socio-demographic characteristics, availability of social media accounts, whether the patients follow any oral health related accounts; and, whether their reliability on those accounts depends on the number of followers, the comments, before and after photos or the reliability of the account owner.

Results: 86.80% of males said that they have never shared their orthodontic experience online, 87.20% of females said that they rely on the information if the owner of the account was an orthodontist. A small percentage of patients (23.4%) said they rely on information available to them on social media. The reason of reliance was that the owner of that social media account is an orthodontist. Only 6% of the participants stated they followed the account because of the number of followers.

Conclusion: Twitter was the most used social networking site among orthodontic patients, followed by Instagram. The majority of patients had never shared their Orthodontic experience on social networking sites and most patients would like their healthcare providers to communicate with them, providing the information via videos.

Key Words: Social media, orthodontic treatment, twitter, Instagram, face book

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INTRODUCTION

Social Media sites have recently increased in popularity and it is changing the behavior of society in many different ways. Application of these sties allows new forms of interactions with others, and modify how people consume products and services. This phenomenon permits people to be connected with others all the time and anywhere. Also, it is often used to share thoughts, experiences, and opinions and seek support about patient's health issues. Although some health professionals remain resistant to new technologies, the reality is that more than 1 billion people have an account just on Facebook, which is the most used social media site worldwide; also, there are many other social media platforms, such as YouTube, Twitter and Instagram[1,2]. Twitter is an example of a new means for the public to communicate health concerns with each other and with their health care professionals[3]. Facebook and YouTube may be more efficient media outlets for oral health literacy promotion and education among adolescent school children when compared to twitter[4]. These sites have recently been used to evaluate the experiences of dental patients. Heaivilin and colleagues found that nearly 14% of Internet-based social media users sought advice on dental pain from the Twitter community, with 15% describing its impact on their daily lives[3]. With such a wide breadth of users and an information-rich database, could these sites provide the dental profession with insight into the problems and issues experienced by orthodontic patients?[5,6]

The increasing dependence of patients on social media websites as a source of health care information indicates a need for future studies to assess their impact on health care utilization and outcomes[7]. The aim of this study was whether orthodontic patients use the Internet and social media sites as a source of orthodontic information and, a tool to share their

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orthodontic experience. Also, to investigate the reasons to rely or not to rely on social media applications for the orthodontic information.

MATERIALS AND METHODS

This was a cross-sectional descriptive study. The study was approved by the ethical committee under the code EA/5990 /2017. Convenience sampling technique was used and e-questionnaire was filled by a total of 1880 individuals comprising of 25.2% males and 74.8% of females. The sample covered the whole Kingdom, as there was a good representation from all the regions of Kingdom. The questionnaire consisted of 8 items close ended instruments developed by the author of the study.

The following variables were included in the questionnaire:

Demographic data.

Social media account availability.

The use of social media to share experience related to orthodontic treatment.

Whether they follow any dental/orthodontic related social media accounts and if it is their first choice to gather orthodontic health information.

Preference of gathering dental health care information through social media sites or dentists themselves.

Whether they rely on social media dental health accounts and if depends on the number of followers, the comments, before and after photos or the reliability of the account owner.

The need of dental healthcare providers with patients through social media.

Sharing of information preference via texts, photos or videos.

The data were transferred to the computer for analysis using SPSS program for Windows (version 17). Descriptive statistics (percentage and frequency) of different variables of cancelled and missed appointments were assessed. Statistically significant difference was evaluated using the Chi-square at significance level set at $P < 0.05$.

RESULTS

The demographic data showed the most percentage of participants were between 18-23 years of age (52%) followed by 24-29 years (31%). This was followed by 30 years or above individuals (9.3%) and least number of participants was between 12-17 years of age (7.8%).

The demographic data for regional distribution amongst different regions across kingdom showed most number of participants were from central region (50.5%), followed by western province (28.7%), eastern province (12.9%), Northern (4.4%) and least response was from the southern province (3.5%).

Table 1 represents the percentage distribution of various social media sites. Most used social media platform was twitter (98.2%).

Table No.1: % distribution of social media accounts and comparison between gender & social media used

	Gender:						P value
	Male		Female		Total		
Social Media	No.	%	No.	%	No.	%	
Twitter	468	98.7%	1377	98.0%	1845	98.2%	0.304
Instagram	384	81.0%	1270	90.4%	1654	88.0%	0.001*
Facebook	215	45.4%	551	39.2%	766	40.8%	0.019*
You tube	306	64.6%	736	52.4%	1042	55.5%	0.001*

(Table 2) shows the statistics of online orthodontic experience.

Table No.2: Showing the statistics of online orthodontic experience

	Gender:						
	Male			Female		Total	
Shared your experience?	No.		%	No.	%	No.	%
	NO	412	86.9%	1176	83.7%	1588	84.5%
	YES	62	13.1%	229	16.3%	291	15.5%

Significant number of patients said that they do not follow any dental health related accounts (p= 0.001) (Table 3).

Table No.3: Patients following dental health related accounts.

Do you follow any dental health related accounts on social media?	Gender:						P Value
	Male		Female		Total		
	No.	%	No.	%	No.	%	
NO	326	68.8%	747	53.2%	1073	57.1%	0.001*
YES	68	14.3%	371	26.4%	439	23.4%	
Maybe	80	16.9%	287	20.4%	367	19.5%	

85% of the patients said that they followed a dental health related account because the owner was a dentist and almost 6% said that followed the account because of the number of the followers. (Table 4)

Table No.4: Reason behind following the account

Cause to follow	2- Gender:						P value
	Male		Female		Total		
	No.	%	No.	%	No.	%	
No. of followers	50	10.5%	64	4.6%	114	6.1%	P<0.001*
Fol. Comments	131	27.6%	467	33.2%	598	31.8%	0.024*
Before and After	100	21.1%	394	28.0%	494	26.3%	P=0.003*
Owner is Dentist	373	78.7%	1225	87.2%	1598	85.0%	P<0.001*

Table No.5: Patients wanting health providers to communicate with them through social media

Providers – communicate with patient	2- Gender:						P Value
	Male		Female		Total		
	No.	%	No.	%	No.	%	
No	51	10.8%	131	9.3%	182	9.7%	
Yes	423	89.2%	1274	90.7%	1697	90.3%	0.361

Table No.6: Patients respond to the" reasonable prior notice period for changing or cancelling an appointment"

How would you prefer to receive dental information during treatment	Gender						P-Value
	Male		Female		Total		
	No.	%	No.	%	No.	%	
Text	86	18.1%	292	20.8%	378	20.1%	
Photos	131	27.6%	397	28.3%	528	28.1%	0.367
Videos	257	54.2%	716	51.0%	973	51.8%	

Most patients stated that they wanted dental health providers to communicate with them through social media accounts (90.3%) (Table 5).

About half of the patients (51.8%) wanted the information to be viewed to them via videos (Table 6).

DISCUSSION

This article sheds light on the demographic data related to use of social media when it comes to their dental/orthodontic health. It also discusses the impact of social media and its possible role in influencing the general public for trends and tendencies in health care profession.

Since its inception almost a decade ago**, s**ocial media has taken the world by storm. It has totally changed the way the information is processed, shared, perceived and received. It has huge impact on every aspect of life, and health care is one of it. Use of the Internet for health information continues to grow rapidly, but its impact on health care is still unclear. Concerns include whether patients' access to large volumes of information will improve their health; whether the variable quality of the information will have a deleterious effect; and whether the physician-patient relationship will be improved as patients become more equal partners, or be damaged if physicians have difficulty adjusting to a new role[8].

This study was done to assess the impact of social media on the dental health of orthodontic patients in Kingdom of Saudi Arabia. Also, to know how positive or negative that impact is. According to this study, twitter is the strongest and widely used social media tool used by the general public to access the orthodontic information, followed by Instagram, YouTube and face book respectively. The comparison between male and female patients showed that there was no significant difference between the males and females users with twitter. It's an equally popular tool amongst both genders. However, there was significant difference between the males and females in using Instagram, females preferred Instagram more over the males. On the other hand, Facebook and YouTube was more popular in males and the difference was statistically significant. A very small percentage of patients shared their experience online. These findings match with the study done by Henzel et al, in which very small number of patients used the social media sites to post their post treatment experience[5]. This trend highlights that patients in Kingdom are not very open to sharing their own post treatment experiences. This can be attributed to the religious and sociocultural norms. A small percentage of patients followed the dental health related accounts to gather information about orthodontist and orthodontic care. These findings are also consistent with the findings of Henzel et al[5] which concluded that patient preferred to gather treatment related information directly form the orthodontist instead of dental health accounts. Amongst that small percentage, the reason to follow the dental health account was that owner was dentist or orthodontist. Only 6% of the participants stated they followed the account because of the number of followers.

Nowadays the success of an individual or company is measured in terms of his/her Instagram followers or the

subscribers to YouTube channels. It's easier for people to log onto social network site and get the free and easy information, rather to actually go to a place/practice or to make a call, which will cost more money and involves complex logistics[9,10]. These days number of social media followers set the popularity trends for entrepreneurs, fashion houses and brands. The more the number of followers, the more the customers. People of all demographics are embracing these technologies through their computers or smart phones and they are increasingly using the social media for health-related issue[11,12,13]. One would expect the same trends in health care profession. But it seems that patients still prefer the direct contact and communication with their doctors and, the satisfaction they get from face to face contact doesn't match the information available on a health blog or social media site.

Nonetheless, interesting fact of the study was that significant number of participants wanted their orthodontist to communicate with them via social media. This finding is consistent with the latest drifts of how the trends of telemedicine are on a rise[11]. This can be explained by the readiness of information available on internet and also the ease of availability of internet in every nook and corner of world. Social media communication directly from the doctor brings lot of ease to the patients. This means less complex logistics, elimination of need of travelling to doctor's office and waiting to get the information.

Although social media has potential as tool for health education and promotion, still both the service providers i.e. the health care professionals/dentists, as well as consumers i.e. the patients, are a long way from embracing it, as in the other walks of life. Same people who are comfortable to trust a blog for beauty or latest fashion trend, are not when it comes to their health. Going to a dentist/orthodontist still stays as an imperative part of total treatment regime. Even if the use of social media increases over the passage of time, both the provider and consumer should have a prudent approach when it comes to the use of this platform. More studies are required to assess the impact of social media in dental health care in general and orthodontic health care in particular. And also, to quantify the precarious bearing of the information associated with it[14,15].

CONCLUSION

Twitter was the most used social networking site among orthodontic patients, followed by Instagram. The majority of patients have never shared their Orthodontic experience on social networking sites, nor have they followed any dental care during the orthodontic treatment accounts. Most patients may have trust on the information especially if the user presenting the information was a dentist. Most patients would like their healthcare providers to communicate with them providing the information via videos. The majority of orthodontist have not advised their patients to follow any dental healthcare account during orthodontic treatment on social networking sites, yet most patients would like them to.

Recommendations: More studies are required consisting of a larger sample. Also, the need of creating more Social Media accounts to provide dental health information, interact with patients and answer their questions to improve their overall dental health and to meet the rising trends of social media in every walk of life.

Author's Contribution:

Concept & Design of Study:	Rabia Bilal
Drafting:	Rabia Bilal
Data Analysis:	Rabia Bilal
Revisiting Critically:	Rabia Bilal
Final Approval of version:	Rabia Bilal

Conflict of Interest: The study has no conflict of interest to declare by any author.

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Original Article

Longevity and Causes of Failure of Amalgam and Composite Restoration

Causes of Failure of Amalgam

Muhammad Amer Khan[1], Mohammad Adnan Khan[2], Mamoona Shah[3], Shawana[3], Junaid Ahmed[4] and Shehzad Fahad[3]

ABSTRACT

Objective: The objective of this was to determine the longevity and causes of failure of amalgam in patients reporting to tertiary care center.

Study Design: Cross-Sectional Study

Place and Duration of Study: This study was conducted at the Khyber College of Dentistry Peshawar, Bacha Khan Medical College Mardan and Kohat Institute of Dental Sciences on 100 patients for a period of ten months from January 2019 to October 2019.

Materials and Methods: Patients with faulty amalgam or composite restorations, placed at least 6 months before the time of examination, and needing replacement their tooth restorations on esthetic or functional ground were included in this study. Patients with limited mouth opening, below 10 year of age, mental and psychiatric disorder were excluded. Teeth were examined under mirrors and explorers. Proximal restorations were evaluated with dental flosses. Evaluation was also done using periapical and bite-wing radiographs when required. We ask for reasons for replacement which are; endodontic treatment/pain, caries, fracture of tooth, fracture of restoration, extraction of adjacent tooth, and insufficient approximal contact. The operator experience and duration of restoration were also recorded. Data analysis was done in SPSS 20. Data stratification was done by using Chi-Square test. A P-value of less than or equal to 0.05 was considered significant.

Results: The mean age of the participants was 29.98±8.84 years. The males were 62(62%) and females were 38(38%). The most common location of restorations was mandibular molars (n=49, 49%) followed by mandibular anterior teeth (n=18, 18%). The frequency of failed restoration was found in 28(28%) cases. The most common cause of amalgam and composite failure was combined endodontic failure and fracture of the restored teeth (n=9, 9%) followed by fracture of restoration itself (n=8, 8%) and need for root canal treatment (n=6, 6%). The most common longevity of restoration was of 2-5 years duration (n=49, 49%) followed by 6-8 years (n=17, 17%) and 1-2 years (n=16, 16%). Most commonly failed restorations were those placed by technicians (n=8, 53.30%), student in institute (n=3, 37.50%) and general dental practitioners (n=14, 25.5%). The failure for specialist (2-year degree) was 14.3% (n=1) and specialist (4-year degree) was 13.30% (n=2) and they were statistically significant (P=0.109).

Conclusion: The amalgam and composite restorations needed to be replaced due to endodontic failure, fracture of tooth, fracture of restoration itself, secondary caries, and insufficient proximal contact. The clinicians need to be vigilant to combat these issues in their practices.

Key Words: Amalgam, composite, restoration, causes of failure, reason for replacement

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INTRODUCTION

Many alterations have been happened in the application of restorative dental materials during the last three decades. For instance there an increasing trend in the importance of aesthetic restoration of posterior teeth.[1] Though the aesthetic perspective is now giving importance in restorative dentistry recently; nevertheless, longevity of fillings should be the most important criteria in the selection of material.[2] In dental practice, the major concern is failure of amalgam and composite restorations and it is estimated that replacement of restorations due to failure is approximately 60% of overall operative procedure.[2] Though amalgam fillings still have the greater durability in term of function[3] but there is concern about its application in recently because of the incorporation of mercury in its composition.[4] The

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mercury is adding in order to make the material plastic, moldable and useable in direct restoration.[5] Additionally, more tooth preparation is required enhancing large restoration retention, make amalgam restoration questionable for conservative dental practice. That's the reason that the composite restoration has been increasing worldwide for as a direct restoration in posterior teeth.[6, 7]

In a study of 7 year follow up on 1748 restorations found that overall failure was 10.1%. The amalgam restoration's survival rate was 94.4% while for composite it was 85.5%. The main reason for failure in both amalgam and composite fillings was secondary caries. For composite the relative risk due to secondary caries was 3.5 times more.[8] Another study assessed the most common reasons for replacing amalgam in vital as well root canal treated teeth. They reported that cusp fracture and recurrent caries was common reason for amalgam restoration replacement.[9]

In dental practice the major concern is the failure of dental restorations. Majority of operative work is comprised of replacement of failed direct restorations. Dental professionals should knowledgeable of the durability of direct restorations, and potential causes for its failure. So, the objective of this was to determine the longevity and causes of failure of amalgam in patients reporting to tertiary care center.

MATERIALS AND METHODS

This cross-sectional study was carried out after the obtaining the approval from hospital ethical review committee in Khyber College of Dentistry Peshawar, Bacha khan medical college Mardan and Kohat Institute of dental sciences. This study included 100 patients (100 restored teeth). These patients were selected consecutively from patients referring to the Department of Operative Dentistry, from outpatient department of these hospitals form January 2019 to October 2019. Verbal informed consent was taken from each patient after full explanation the detail and purpose the research.

Patients with faulty amalgam or composite restorations, placed at least 6 months before the time of examination, and needing replacement their tooth restorations on esthetic or functional ground were included in this study. Patients with limited mouth opening, below 10-year age, mental and psychiatric disorder were excluded after history and intra-oral examination.

Teeth with restoration were dried with air spray and examined under mirrors and explorers. Proximal restorations were evaluated with dental flosses. Evaluation of the restored dentition was also done using periapical and bite-wing radiographs when required. Patients were asked when the restorations had been placed.

We used closed ended questions proforma design after studying previous literature.[9] We ask for reasons for replacement which are; endodontic treatment/pain, caries, fracture of tooth, fracture of restoration, extraction of adjacent tooth, and insufficient approximal contact. The operator experience and duration of restoration were also recorded.

Data analysis was done in SPSS version 20. Frequencies and percentages for the reasons for failure of the restorations (amalgam and composite) and duration were computed. Data stratification was done by gender, age and operator experience using Chi-Square test. A P-value of less than or equal to 0.05 was considered significant.

RESULTS

The mean age of the participants was 29.98±8.84 years. The age was ranging from 18 to 60 years. Of total hundred restorations/cases the maximum number of cases (n=65, 65%) were age 18 to 30 years followed by age group 31 to 40 years (n=26, 26%). The males were 62(62%) and females were 38(38%). Amalgam restorations were found in 47(47%) and composite were in 53(53%) cases. The most common location of restorations was mandibular molars (n=49, 49%) followed by mandibular anterior teeth (n=18, 18%).

Table No.1: Distribution of age, gender, material, location of restoration and failure of restoration categories

Parameter	Category	Frequency	Percent
Age	18-30	65	65
	31-40	26	26
	41-50	5	5
	51-60	4	4
	Total	100	100
Gender	Male	62	62
	Female	38	38
	Total	100	100
Material	Amalgam	47	47
	Composite	53	53
	Total	100	100
Location of restoration	Lower anterior	18	18
	upper anterior	12	12
	Lower molar	49	49
	Upper molar	8	8
	Lower premolar	11	11
	upper premolar	2	2
	Total	100	100
Failure of restoration	Yes	28	28.0
	No	72	72.0
	Total	100	100.0

Table No.2: Distribution of causes of restoration failure and Longevity of restoration

Parameter	Category	Frequency	Percent
Causes of restoration failure	No	72	72
	Endodontic treatment/ pain	6	6
	Fracture of tooth	1	1
	Fracture of restoration	8	8
	Insufficient approximal contact	1	1
	Endodontic + restoration fracture	9	9
	both fracture of tooth and restoration	1	1
	Secondary caries	2	2
	Total	100	100
Longevity of restoration	less than 1year	7	7.0
	1-2 years	16	16.0
	2-5 years	49	49.0
	6-8 years	17	17.0
	9-12 years	11	11.0
	Total	100	100.0

In maxilla there were 12(12%) restorations in anteriors and 8 restorations in molars. The frequency of failed restoration was found in 28(28%) cases. The rest of details are shown in table 1.

The most common cause of amalgam and composite failure was combined need for endodontic failure and fracture of restoration (n=9, 9%) followed by fracture of restoration itself (n=8, 8%) and need for root canal treatment (n=6, 6%). Other causes for failure of restoration were secondary caries (n=2, 2%), insufficient approximal contact (n=1,1%), and fracture of tooth (n=1,1%). The most common longevity of restoration was of 2-5 years duration (n=49, 49%) followed by 6-8 years (n=17, 17%) and 1-2 years (n=16, 16%). The maximum longevity of 9 to 12 years was found in 11(11%) cases. Less than one-year duration was found in 7 cases. The details are shown in table 2.

The failure was more in composite (n=20,27.8%) than amalgam (n=9, 19.2%) restorations and the results were statistically significant (P=0.040). Most commonly failed restorations were those placed by technicians (n=8, 53.30%), students in institute (n=3, 37.50%) and general dental practitioners (n=14, 25.5%). The failure for specialist (2 years degree) was 14.3% (n=1) and specialist (4 years degree) was 13.30% (n=2). But these differences were not statistically significant (P=0.109). Similarly, the failure rate among different age groups (P=.249), and in various locations (P=.065) were not statistically significant. The detailed statistics are given in table 3.

Table No.3: Failure of restoration stratified by material, operator experience, Cause of failure age and location of restoration

		Failure of restoration				P-value
		Yes		No		
		N	%	n	%	
material	Amalgam	9	31.03	38	80.90	0.04
	Composite	20	27.8	33	62.2	
Operator experience	General dental practitioner	14	25.50	41	74.50	.109
	Technician	8	53.30	7	46.70	
	Specialist (4-year degree)	2	13.30	13	86.70	
	Specialist (2-year degree)	1	14.30	6	85.70	
	Student in institute	3	37.50	5	62.50	
Cause of failure	No	0	0.00	72	100.00	<0.001
	Endodontic treatment/pain	6	21.40	0	0.00	
	Caries	0	0.00	0	0.00	
	Fracture of tooth	1	3.60	0	0.00	
	Fracture of restoration	8	28.60	0	0.00	
	Extraction of adjacent tooth	0	0.00	0	0.00	
	Insufficient approximal contact	1	3.60	0	0.00	
	Endodontic + restoration fracture	9	32.10	0	0.00	
	both fracture of tooth and restoration	1	3.60	0	0.00	
	Secondary caries	2	7.10	0	0.00	
Age	18-30	21	75.00	44	61.10	.249
	31-40	7	25.00	19	26.40	
	41-50	0	0.00	5	6.90	

	51-60	0	0.00	4	5.60	
Location	Lower anterior	0	0.00	18	25.00	.065[a,]
	upper anterior	5	17.90	7	9.70	
	Lower molar	17	60.70	32	44.40	
	Upper molar	2	7.10	6	8.30	
	Lower premolar	4	14.30	7	9.70	
	upper premolar	0	0.00	2	2.80	

DISCUSSION

This study was conducted to know the longevity and causes of failure of amalgam in patients reporting to tertiary cares. Our findings showed that composite restorations were more than amalgam. Most common site of failure was in mandibular molars. The frequency of failure of amalgam and composite was 28%. The most common cause of amalgam and composite failure was combined endodontic failure and fracture of restoration followed by fracture of restoration itself and need for root canal treatment. Other causes for failure of restoration were secondary caries, insufficient approximal contact, and fracture of tooth. The maximum longevity for direct restoration was 12 years. The failure was more in composite than amalgam filling.

Several factors affecting the performance of direct restorations, including the experience level of the clinician,[10] the type of restorative materials used,[5] the tooth's position in the jaw,[11] the type of tooth,[11] the design of restoration,[12] the size of restoration,[11] the number of restored surfaces and the age of the patient[13].

Our results showed that composite filling were more than amalgam. The reason for this may more use of composite in posterior teeth. While in anterior teeth only composite filling are placed. The other reason for greater number of composite restoration than amalgam may due to concern of mercury toxicity in amalgam filling. It is now gaining popularity to restore posterior teeth with composite resins among practitioners, and there is increasing demand for such esthetic restorations. Certainly, the composite resin is most common esthetic alternative to dental amalgam.[14]

Our study showed that most common site of failure was in mandibular molars. This can be due to reason that mandibular first molar erupt first of all among the permanent teeth at the age of 5 years.[15] At that time children are careless and most of our parents are not aware about oral hygiene of their children, so they are prone to caries and need restoration in order to relieve pain.[16]

The current results showed that the failure more in composite than amalgam filling. The results were statistically significant. A Cochrane review conducted on direct composite resin fillings versus amalgam fillings for permanent or adult posterior teeth in 2014 included seven trials in the systematic review and reported that resin composites lead to higher failure rates and risk of secondary caries than amalgam restoration.[17] These results are in consistent to the current findings.

The causes of amalgam and composite failure was combined need for endodontic failure and fracture of restoration followed by fracture of restoration itself, need for root canal treatment, secondary caries, insufficient approximal contact and fracture of tooth. A study conducted in Pakistan on reasons for the failure of class I and II amalgam restorations showed that common reasons to replace amalgam fillings was secondary caries, followed by inadequate resistance form.[18] These results are similar to our findings as in our study we found that fracture of restorations or restored teeth was in the list of the reason for failure amalgam. These two; fracture of restorations or restored teeth are called inadequate resistance form.

In our study the frequency of failed restorations was 28%. A study conducted by Shah et al.[19] in Pakistan on replacement of amalgam restorations reported that around 47% of the restorations underwent failure. The failure of Shah et al. is higher than our may due to improvement in modern materials and increased knowledge among practitioner as the Shah et al. study was conducted in 2010. Other reason for difference may that we calculated failure for both composite and amalgam while Shah et al. only reported amalgam failure rate.

In previous studies many cause of failure of composite fillings were reported which were secondary caries, occlusal stress risk, socioeconomic factors, experience of clinical operators, cavity designs, and endodontic failure. [10, 12, 20]

However, the current study is cross study and cannot calculate survival of restoration. The survival analysis need follow up studies, so further large scale and longitudinal studies are needed on this subject. We ask the patients about duration of restorations so recall bias can be an issue in this study.

CONCLUSION

The amalgam and composite restorations needed to be replaced due to endodontic failure, fracture of tooth, fracture of restoration itself, secondary caries, and insufficient proximal contact. The clinicians need to be vigilant to combat these issues in their practices.

Author's Contribution:

Concept & Design of Study:	Muhammad Amer Khan
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Revisiting Critically:	Muhammad Amer Khan, Mohammad Adnan Khan
Final Approval of version:	Muhammad Amer Khan

Conflict of Interest: The study has no conflict of interest to declare by any author.

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Original Article

Does Hemostatic Gelatin Foam Packing Produce a Lower Mean Pain Score than Conventional Nasal Packing in Septoplasty? A Comparative Study

Shehzad Ahmed[1], Muhammad Aqil Jilani[2], Tahir Hussain Khan[3] and Jamil Memon[3]

ABSTRACT

Objective: Comparing mean pain score of Haemostatic Gelatin Foam Packing versus conventional packing in patients undergoing septoplasty.

Study Design: Longitudinal Study

Place and Duration of Study: This study was conducted at the ENT department of Dow University of Health Sciences, Karachi for six months from September 2015 to February 2016.

Materials and Methods: After approval, the study was carried out at the ENT department of DUHS. 124 patients with DNS were selected through the non-probability sampling technique. The participants were divided into two groups of 62 each with one receiving the hemostatic gelatin foam packing (Group A) and the other group receiving the conventional nasal packing (Group B) after Septoplasty had been completed. The primary outcome measures will be PS- PIP due to the presence of packs in the nose and PS-PR pain associated with their removal. Data will be analyzed using SPSS with both the groups being compared for means of PS-PIS and PS-PR using Independent samples t-test. P-value < 0.05 will be taken as significant.

Results: A total of 79(63.7%) males and 45(36.3%) females were a part of the study, 35 aged between 18-25 years, 63 aged between 26-30 years, and 26 aged 30 years and above. A significant difference was observed between the mean pain score IN-Situ between Simple Conventional Nasal Pack (Mean: 46.084±10.75575) and Gelatin Nasal Pack (Mean: 30.8548±8.78868) (P-value<0.001). A significant difference was also observed between the mean pain score at removal be Simple Conventional Nasal Pack (Mean: 40.9677±11.55311) and Gelatin Nasal Pack (Mean: 24.6613±13.51616) (P-value<0.001).

Conclusion: After Septoplasty Haemostatic Gelatin Foam packing produces lesser mean pain scores than conventional nasal packs.

Key Words: Haemostatic Gelatin Foam, Conventional Nasal Packs, Septoplasty, Pain

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INTRODUCTION

The nasal septum is a major component of the nose and is crucial in the function and stability of the nasal cavity[1]. However, one of the most well-known pathologies related to the nasal septum is deviated nasal septum (DNS)[2].

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DNS leads to multiple complications such as headaches, sinusitis, epistaxis, and sleep apnea[3]. 80% of the population still suffer from DNS, in one way or another[4]. Septoplasty is a procedure that is performed for the correction of a deviated nasal septum. It is the most frequently performed ear, nose, and throat operation in adults[5]. After every surgical procedure, adequate hemostasis is vital. Therefore, after Septoplasty nasal packing is placed to achieve desirable hemostasis[6]. Nasal packing has been an essential part of the Septoplasty procedure to limit post-operative bleeding. It is also stated that nasal packing can stabilize the cartilaginous septum that remains and minimize any chances of future recurrence of DNS[7]. There are many types of nasal packing that are available such as conventional nasal packs, pre-fabricated nasal tampons, air-filled balloons, and self-resorbable nasal packs[8]. Although nasal packs have a myriad of benefits, they also have their demerits. They create discomfort to the patient along with other complications such as toxic shock syndrome, sleep

difficulties, and infections post-operatively[9-10]. Some even consider not using nasal packs altogether; however, it cannot be avoided in most of the situations and is still used by many surgeons as of now[11]. To overcome the drawbacks of traditional nasal packs and also avoid not placing nasal packs at all, various absorbable materials have been introduced in the market. These include porcine gelatin, antifibrinolytics, hyaluronic acid, and more[12-14]. Although these materials proved to be very effective in eliminating pain during removal and preventing postoperative bleeding, these materials are quite expensive. Therefore, a new material, gelatin foam was introduced into the market which also had hemostatic effects[15]. In our study wed determined if Haemostatic Gelatin Foam Packing produces a lower mean pain score than conventional nasal packing in Septoplasty.

MATERIALS AND METHODS

After the approval of the synopsis from the institutional review board (IRB). A longitudinal study was conducted at the ENT department of Dow University of Health Sciences. The study spanned for the duration of 6 months. 124 patients with DNS were selected for this particular study through consecutive non-probability sampling techniques aged between 18-60 years. The patients before being admitted into the study were informed of their inclusion, were brief about the purpose of the study, and only after seeking verbal and written consent were they included in the study. The participants were divided into two groups of 62 each, with all patients being randomly allocated into the two groups. The random allocation was also concealed from the doctor. Group A will be allocated to receive gelatin foam packs and Group B will receive conventional nasal packs bilaterally. Septoplasty was to be performed by a qualified otolaryngologist. After the surgery, the hemostatic gelatin foam or conventional nasal packing was to be placed bilaterally according to the allocated groups. All the patients were prescribed oral paracetamol for pain relief. The packs will be removed 24 hours after surgery. The primary determinant to be measured will be PS-PIP (Pain score in-site) and PS-PR (Pain score on removal) both of which will be noted on a visual analogue from a scale of 0-100. All the data was recorded and analyzed using the Statistical Package of social sciences (SPSS). Quantitative variables will include Age, PS-PIS and PS-PR. Qualitative variables will include Sex. Both the groups will be compared for means of PS-PIS and PS-PR using Independent samples t-test. P-value < 0.05 will be taken as significant.

RESULTS

Table 1 & Figure 1: Shows the age distribution of patients in the study

Table 2 & Figure 2: Shows the gender distribution of patients in the study

Table 3 & Figure 3: Shows the visual analogues score of patients after septoplasty

Table No.1: Age distribution of patients

Age stratification	Conventional Nasal Pack		Gelatin Nasal pack	
	Frequency	Percent	Frequency	Percent
18-25 years	14	22.6	21	33.9
26-30 years	33	53.2	30	48.4
30 years above	15	24.2	11	17.7
Total	62	100.0	62	100.0

Table No.1: Gender distribution of patients

	Conventional Nasal Pack		Gelatin Nasal pack	
	Frequency	Percent	Frequency	Percent
Male	41	66.1	38	61.3
Female	21	33.9	24	38.7
Total	62	100.0	62	100.0

Table No.3: Visual Analogue Scores of Septoplasty Patients

Pain Score Category	Conventional Nasal Pack		Gelatin Nasal pack	
	Frequency	Percent	Frequency	Percent
Low	1	1.6	9	14.5
Mild	28	45.2	47	75.8
Moderate	29	46.8	5	8.1
High	4	6.5	1	1.6
Total	62	100.0	62	100.0

Table No.4: Comparison of Pain Score IN-Situ

	Nasal Pack Groups	n	Mean	Std. Deviation	P-Value
Pain Score In Situ	Simple Conventional Nasal Pack	62	46.0484	10.75575	< o.oo1
	Gelatin Nasal Pack	62	30.8548	8.78868	

Table No.5: Comparison of Pain Score at removal

	Nasal Pack Groups	n	Mean	Std. Deviation	P-Value
Pain Score at removal	Simple Conventional Nasal Pack	62	40.9677	11.55311	< o.oo1
	Gelatin Nasal Pack	62	24.6613	13.51616	

Table 4 & Figure 4: Shows the comparison of Pain Score IN-Situ

Table 5 & Figure 5: Shows the comparison of Pain Score at removal.

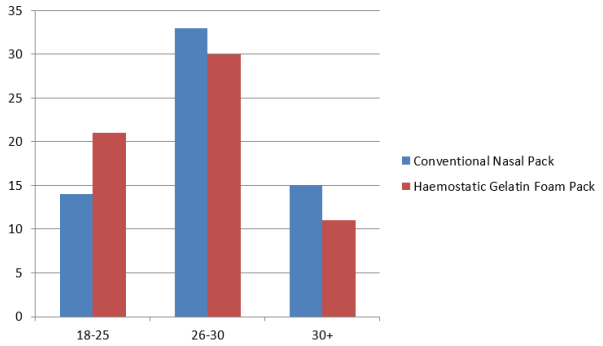

Figure No.1: Age distribution of patients

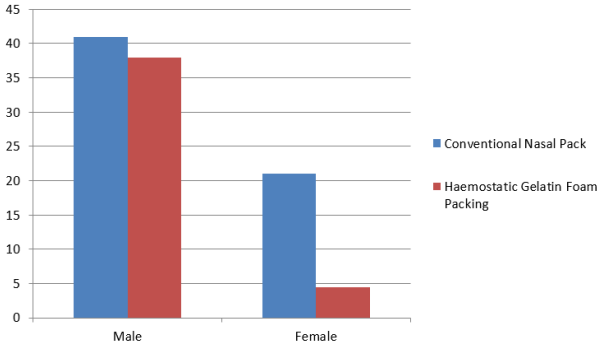

Figure No.2: Gender distribution of patients

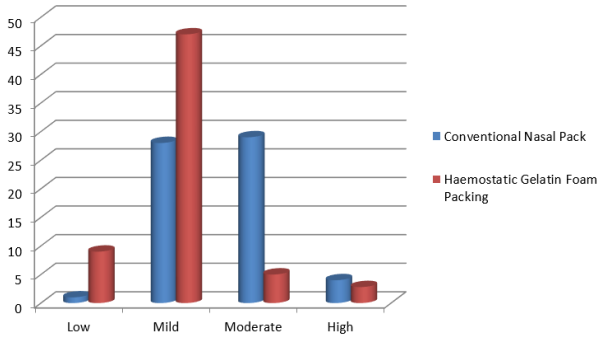

Figure No.3: Visual Analogue score of Septoplasty Patients

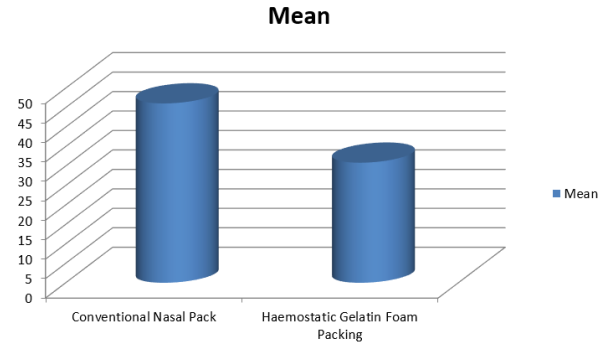

Figure No.4: Comparison of Pain Score IN-Situ

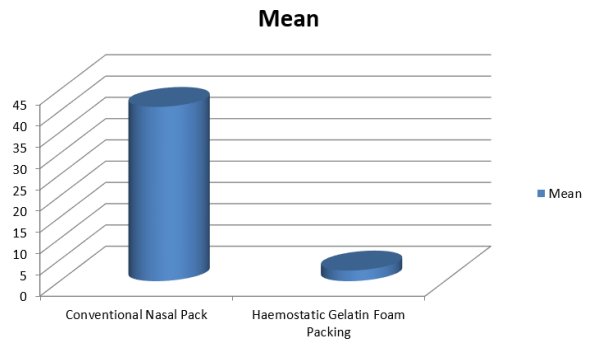

Figure No.5: Comparison of Pain Score at removal

DISCUSSION

Pain is subjective; some experience it to a greater extent than others. The perception of pain is a handicap in researches that study pain as a variable. The importance of nasal packs is well documented in the literature and its advantages are evident. However, its disadvantages one of it being pain has led to many other techniques being adapted. Currently, trans-septal suturing is also gained some favor in the community as it avoids patients' pain and anxiety[16]. However, in Pakistan nasal packing is still being used broadly in the ENT community. Pain relief from nasal packing is still a concern and the search continues to reduce pain when placing nasal packs[17]. Nonsteroidal anti-inflammatory drugs (NSAIDs) can be given to patients to reduce pain after surgery and some also advocate using nasal packs soaked in local anesthesia solutions for relief[18]. Our study evaluated that can gelatin foam be a more effective alternative to the conventional nasal pack in preventing bleeding and hematoma, and also causes lesser pain upon being placed in the nasal cavity and at removal. Studies like this have been conducted in the past before[19]. Our study showed a significant difference (P value= <0.001) when it came to comparing Pain In-site and Pain at removal between gelatin foam and conventional nasal packing. The mean pain score was significantly lower in the hemostatic gelatin foam packing groups showing that it indeed is a better option when it comes to levels of pain. These results are in line with another study conducted by Jawaid et al (2013) in which he showed that significantly less pain occurred on the removal of gelatin foam as compared to traditional nasal pack (P=0.01), with both of the nasal packs being equally effective in reducing post-operative bleeding and hematoma[20]. Valentine et al stated that conventional nasal packs cause patients discomfort, thus absorbable biomaterials should be used[21]. Gelatin foam is cost-effective and as mentioned previously also hemostatic in nature and can be used in surgery. Another comparative study compared gelatin foam to another material FloSeal to show the amount of granulation tissue production, in which FloSeal had a clear trend towards forming more granulation tissue than thrombin-soak gelatin[22]. The use of hemostatic gelatin foam should be done more as we also found no significant crusting and adhesions in the packing. This

along with its low pain scores mean that it is equally effective and can be better tolerated by the patient as well.

CONCLUSION

The Haemostatic gelatin foam packing infect does produce lesser pain scores both IN-site and upon removal compared to conventional nasal packing and thus can be used more widely as a nasal packing agent after Septoplasty.

Author's Contribution:

Concept & Design of Study:	Shehzad Ahmed
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Data Analysis:	Tahir Hussain Khan, Jamil Memon
Revisiting Critically:	Shehzad Ahmed
Final Approval of version:	Shehzad Ahmed, Muhammad Aqil Jilani

Conflict of Interest: The study has no conflict of interest to declare by any author.

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Original Article

Echinococcosis Granulosis in High-Risk Group

Frequency of Echinococcosis Granulosis in High-Risk Group, Experience in District Mardan, Khyber Pakhtunkhwa

Ziauddin[1], Shah Zeb[2], Arif Khan[3], Sajjid Ali[3], Sumbal Hussain[4] and Sheema Khan[2]

ABSTRACT

Objective: To know the prevalence of Cystic Echinococcosis in high risk population in district Mardan.
Study Design: Prospective study
Place and Duration of Study: This study was conducted at the Department of Medicine, Mardan Medical Complex Mardan and Department of Biotechnology Abdul Wali Khan University, Mardan in Khyber Pakhtunkhwa from January 2021 to March 2021.
Materials and Methods: Mardan is the second biggest district of KP. After informed consent, blood samples were collected from high risk group and were transferred to health Biotechnology laboratory Abdul Wali Khan University. Serological identification was performed by Elisa method. Results were calculated according to the formula; Sample O.D / cut off serum O.D x 10.
Results: Total of 80 blood samples were enrolled, out of which 07(8.75%) were found positive for Cystic Echinococcosis. Maximum samples (20%) were reported from Takht Bhai region. Most effected (42.85%) age group was 31-45 years.
Conclusion: Strategies to create awareness and effective preventive and treatment programmes against this disease are needed.
Key Words: Cystic Echinococcosis, E. granulosis, ELISA, Mardan, Khyber Pakhtunkhwa

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INTRODUCTION

Cystic Echinococcosis (CE) or hydatid cyst disease is a parasitic disease. CE is also known by name of Hydatid cyst and also by Hydatidosis. It is caused by the metacestode of Echinococcus granulosis. It is a zoonotic infection and the cause of human infection in eggs of E. granulosis when humans unintentionally eat the eggs of tapeworm[1].

CE is a zoonotic infection that affects and damages ani mals and humans' vital organs, especially the liver and lungs. The main cause of the infectious disease is E. gra nulosis[2]

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It silently destroys the health of humans and animals and produces major public and economic loss around the globe especially in those areas and regions where dogs and animals are raised in number and share human life activities[3-6] Two distinct mammalian hosts are needed for the life cycle of the echinococcosis.

Definitive hosts such as foxes, dogs, and wolves and others are intermediate hosts including herbivores like as hoarse, sheep cattle and hardly humans.[7] The regions where the hydatid cyst disease is endemic include, Mediterranean, Northern China, North Africa, Australia, Turkey, Indian subcontinent, South America and New Zealand,[8]

The disease observed in human and mammalian tissues, particularly in the liver and lungs, causes echinococcos is.[9] Other mammalian organs effected include pancreas, heart, spleen, brain[10,-12]. The cycle of E. granulosis is naturally a dog or sheep cycle in which an infected dog implies contamination of a sheep through its feces. In the parasitic natural life cycle, humans are not a part, in the life cycle of parasite; humans unintentionally take the place of the sheep through the close interaction of the infected dog.[13] Human beings are usually dead ends for the parasite[14]. Various risk factors are involved in causing the infection. These include poor open slaughter house practices, abundance of stray dogs, contaminated vegetables and other foodstuffs available in the market and poor healthcare facilities.[15] Defensive approaches would, therefore, include health education,

reduced interactions with dogs and sheeps and effective removal of their wastes.[16] The inaccessibility of clean drinkable water and the close communication of human beings with sheep and dogs make Pakistan an endemic region to this disease.[17]

To recognize distinct parasite genotypes, molecular characterization of Echinococcosis granulosis is necessary. Genotyping enables to manage their life cycle and transmissions[18]. Ten distinct strains of this parasite are reported worldwide. All strains are disease-causing agents, excluding G4 strain. Most prevalent and main causative agent of the infection in both humans and livestock is E. granulosis sensustricto (G1-3) across the globe. In Pakistan, the G3 and G6 strains of the parasite have been reported in Punjab and Khyber Pakhtunkhwa provinces while in Indian occupied Kashmir the G1 and G3 strains have been reported.[19-21] Discussing characteristics are antigenicity, sensitivity to chemotherapeutic agents, transmission dynamics, and patterns of pathology life-cycle, development rate and host specificity.[22] For the diagnostic reagents, vaccine development and impacting of drugs on the control and epidemiology of echinococcosis may have important implications for these characteristics.[23] Certainly, Echinococcus species individually keeps a specific genetic identity with host-adapted that infrequently overlaps in some geographical areas.[22] Different serological methods are being used for the diagnosis and analysis of hydatid cyst disease such as latex agglutination, hemagglutination, ELISA, skin test and immune electrophoresis.[24] Previously no such studies were done in KPK. Aim of our study is to find out the prevalence of hydatid cyst disease in high risk population of KPK using ELISA technique.

MATERIALS AND METHODS

This prospective was conducted at department of Medicine, Mardan medical complex and department of Pathology, Abdul Wali Khan University, Mardan in Khyber Pakhtunkhwa from Ist January 2021 to 31Ist March 2021. A total of 80 blood samples were collected from high-risk population. After collection, samples were transferred to the health biotechnology laboratory of Abdul Wali Khan University Mardan KPK for further processing using stranded protocols.

Patients of all age and of either gender were included in the study. Data was collected using a structured data collection proforma. Data was entered and analyzed using statistical package for social sciences (SPSS) Version 22. Our study was approved by ethical committee of Mardan Medical Complex.

Serological identification for the detection of Echinococcus granulosis in the high-risk groups was done through ELISA method. All the samples for hydatid Cyst infection were processed according to the manufacturer's instructions (Vircell" Hydatidosis Elisa IgG 96, Germany). Samples were run along with positive and negative controls.

We adopted the following procedure**:**

- Incubation was done at 37℃
- The temperature of ingredients was lower down to room temperature.
- Besides, labeling was based on a sample set, including positive negative cut off serum for the estimation of plate validity.
- Initially 100 µl of serum diluent of the kit was added followed by the addition of 5 µl serum sample and shaking in plate shaker.
- Plates were sealed using the sealing sheet supplied in kit followed by incubation at 37℃ up to 45min.
- After completion of incubation the liquid content was aspirated completely and the wells were washed five times by pouring 300µl washing solution in each well.
- After performing washing 100µl IgG solution of the kit was added and the plate was further incubated for 30min at 37℃
- Furthermore, after incubation liquid was aspirated and 100µl substrate was added on the spot, the plate was again incubated for 20min at room temperature the plate was protected from light.
- The incubation period was followed by the addition of 50µl stopping solution to each well provided in the kit and was read under ELISA reader at 450nm

RESULTS

Results were calculated according to the formula, (Sample O.D/ cut off serum O.D) × 10, from the reading taken by ELISA reader from the ELISA plate. Figure 1 shows the positive and negative samples general outcomes.

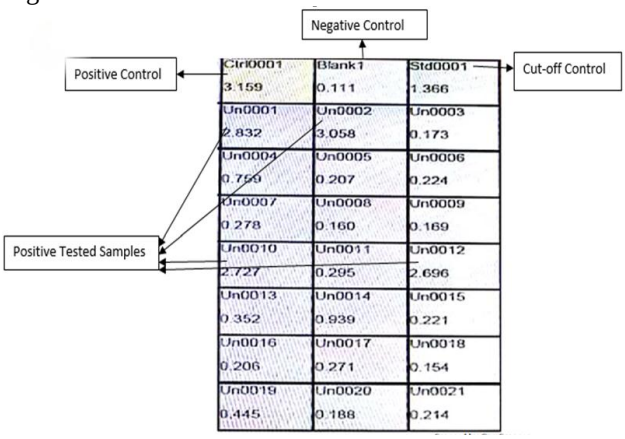

Figure No.1: Figure displaying the samples read by ELISA

Ctrl 0001 designated the positive control, Blank 1 represents Negative control and cut-off control designated for Std 0001. The positive tests are the samples Un 0001, Un 0002, Un 0010, and Un 0012.

Out of 80 samples 07(8.75%) were found positive for Cystic Echinococcosis as shown in figure 2.

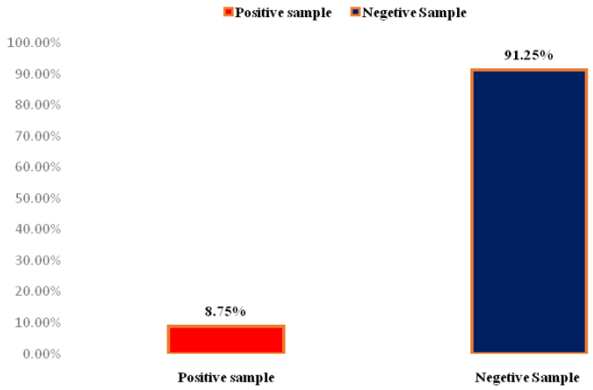

Figure 2: Showing positive and negative samples

Maximum number of samples were from Takht Bahi region of district Mardan, On the other hand less number of samples were collected from Shankar area, as shown in figure 3.

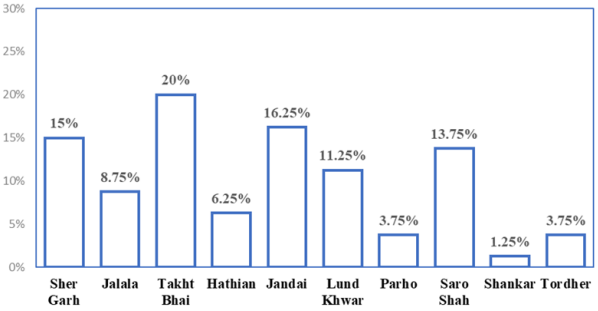

Figure No.3: Showing Area-wise collection of samples

As far as age is concerned, age of the study participants ranged from 01 to 60 years. 21.25% of blood samples were collected from patients with age of 1-15 years, 38.75% from age of 16-30 years. While 28.75% and 11.25% of the samples were collected from patients with age in range of 31-45 years and 46-60 years respectively.

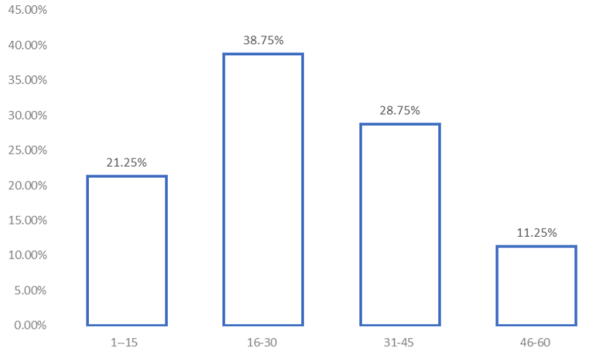

Figure 4: Showing Age-wise distribution of samples

Maximum number of samples (42.85%) were found positive between the age of 31 to 45 years. One sample (14.28%) was tested positive in each age group of 01-15 years and 46 -60 years. Patients in age group of 16-30 years had 02(28.56%) samples tested positive for Cystic Echinococcosis.

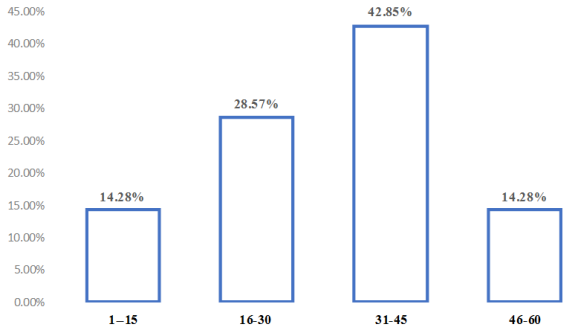

Figure No.5: Showing the percent of positive samples age-wise.

DISCUSSION

Echinococcosis soundlessly destroys the livestock industry and human health. Echinococcosis is a problem for livestock and public health, affecting distinct countries' economies. The previous retrospective study and genotyping in Pakistan and India showed that this disease in these nations is widespread and prevalent.[25] It is mentioned in tropical countries as a neglected tropical disease[26]. E. granulosis is identified as widespread throughout the country, according to the literature, "camel-dog" and "sheep-dog" are strains that infect humans[12,27]. There are Several reports on molecular detection of E. granulosis genotypes are available in domestic animals.[24,28,30] Three genotypes of E. granulosis were reported in different organisms.

In Khyber Pakhtunkhwa, there is no previously published research study on the retrospective and genotypical characterization of hydatid cyst. To avoid its life cycle, it was important to approximate the disease burden. This is the first research of its kind that was conducted in KP.

A total of 80 blood samples were collected from the high risk group. We found 07 samples as positive. Our study demonstrated that most morbidity of CE was in the age of 31to 45 years.

Khan D et al and Pal R along with his colleagues in their research work showed the incidence of CE in cattle as 5.5 to9.6%, 12.3% in buffalo,8.3% in sheep and 7.5% in goats.[31,32]

Several investigators reported the occurrence of hydatidosis in Pakistan. Iqbal Z and his co researchers studied the existence of cyst in different animals slaughtered at Faisalabad abattoir and reported 14.8% sheep, goats 5.9%, buffaloes 49% and cattle 33% infected with the disease.[33] Pal R in his research work reported the existence of hydatidosis in sheep 5.3%, goats 1.79% and cattle 31.5% Rawalpindi abattoir individually.[32]

The molecular characterization of echinococcus species in all areas of Pakistan requires large-scale surveillance.

This type of large-scale study will surely help to estimate the disease burden in Pakistan. It is the need of the hour to create awareness about this disease in the rural population of Pakistan. Necessary prevention, control measures, diagnosis, and treatment are required to improve public health and reduce economic loss.

CONCLUSION

It is concluded from our study that E. granulosis is an important source of economic loss in our community. All over the country molecular characterization of Echinococcosis species needs extensive surveillance. Moreover, large-scale studies will help to evaluate the disease burden in Pakistan.

Author's Contribution:

Concept & Design of Study:	Ziauddin
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Data Analysis:	Arif Khan, Sumbal Hussain
Revisiting Critically:	Ziauddin, Sajjad Ali
Final Approval of version:	Ziauddin

Conflict of Interest: The study has no conflict of interest to declare by any author.

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Original Article

Pattern of ABO and Rh Blood Groups Distribution Among COVID-19 Patients

Shabana Asif[1], Aashi Ahmed[2] and Nadia Nisar[2]

ABSTRACT

Objective: This study was conducted to find out the pattern of blood group distribution among Covid-19 patients in this part of world.

Study Design: cross-sectional study

Place and Duration of Study: This study was conducted at the department of Pathology, Margalla Hospital Taxila from April to June during first phase of Corona followed by second wave in October to December 2020.

Materials and Methods: In this study, 3936 participants were included using non-purposive consecutive sampling technique, who were tested for COVID 19 by real-time reverse RT-PCR. Data was analyzed using SPSS version 26. Frequencies for different blood groups were calculated. Cross tabulation was done for RT-PCR positive and negative blood groups and chi square test of significance was applied.

Results: Out of 3936, 436 (11.1%) tested positive by RT-PCR. Majority of males tested positive (64%, p=.001). Most frequent blood group among covid patients was B (38.7%, p= .001), followed by O (29.3%), A (22.7%) and AB (9.1%). Out of total 436, 399 (91.5%) were Rh positives.

Conclusion: Blood group B and Rh positives were more frequent among study population; however, it doesn't conclude that these blood groups increase susceptibility to covid infection.

Key Words: SARS-COV-2, COVID- 19, ABO blood groups, Rh blood groups

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INTRODUCTION

Outbreak of Zoonotic origin viral infection (SARS-CoV-2), caused by novel corona virus occurred in Wuhan, China in December 2019. Leading to unexplained pneumonia, this infection was declared a pandemic and Global Health Emergency by World Health Organization (WHO) on 11th March, 2020.[1] The novelty of this virus and lack of literature has led to uncertainty in multiple aspects of this disease.[2] Association of Covid-19 infection with various biological markers including blood group antigens is among them. International society of blood transfusion has recognized 34 human blood group systems among which ABO and Rh blood group antigens are commonly investigated.[3] Difference in blood group antigens expressions can increase or decrease host susceptibility to various bacterial and viral agents[4].

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Blood group antigens mainly serve as a receptor or co-receptor for infectious agents and many blood group antigens facilitate adhesion, intracellular uptake and signal transduction through organization of microdomains.[5] Previous studies have shown susceptibility of ABO blood groups to bacteria like helicobacter pylori and viruses such as Hepatitis B, Norwalk virus and SARS corona Virus.[6,7] In this ongoing pandemic people more susceptible of acquiring this infection should be identified so in future certain characteristics are kept in mind while diagnosing the illness.[8] Risk of acquiring COVID-19 infection is equal among people with different blood group types.[9] However, a study from Wuhan, China showed that odds of having SARS-COV-2 infection was more common among A while less among O blood group of ABO system. Zietz and Tatonetti found that blood type A was correlated with a higher odds of testing positive for disease while Rh (D) positive blood groups were associated with increased infection and death following infection.[10] Another study also showed higher risk of acquiring SARS-COV-2 with blood group A and lower risk with O group as compared to non-O groups.[11] Regarding RH factor, Rh (–) blood group is found to be protective and the Rh (+) blood group is susceptible to Covid 19 significantly.[12]

We undertook this study to understand the pattern of SARS-COV-2 among ABO blood group in our part of the world. In this study we observed the blood groups in SARS-COV-2 infected population and compared

them against the ABO blood of SARS-COV-2 negative population. The aim is to identify increased susceptibility of acquiring COVID-19 infection among certain blood groups. So that high-risk blood groups are identified as markers of acquiring infection and are dealt accordingly in future for better control and elimination of this public health disease.

MATERIALS AND METHODS

This was a cross-sectional study carried out in the department of Pathology, Margalla hospital Taxila from April to June during first phase of Corona followed by second wave in October to December 2020, after approval of Ethical Review Committee of the hospital. Patients of all age groups irrespective of their gender were included after informed consent. The confidentiality of the patients was preserved. Non-purposive consecutive sampling technique was used. All persons who were screened for COVID 19 by real-time reverse transcriptase polymerase-chain-reaction test (RT-PCR) were included in the study. Sample size calculated for total population with a margin of error of .05% was 430. Study variables (ABO, Rh blood groups, gender, indication of test and test results were obtained from Hospital data record (HMIS). Nasopharyngeal swabs were collected from all persons by trained lab technician after wearing proper PPEs using minitip swab with a flexible shaft (wire or plastic) through the nostril parallel to the palate until resistance encountered after tilting the head back to 70 degrees, till it reached the depth, equal to distance from nostrils to outer opening of the ear. Then by gently rubbing and rolling the swab to absorb secretions. Swabs were placed immediately into a sterile transport tube containing 2-3mL of viral transport medium (VTM), followed by labelling each specimen container with the patient's ID number and the date. These samples were then transported to tertiary care center for performance of RT-PCR, in a thermopole container containing ice packs maintaining temperature to 2-8 Celsius.

RESULTS

Total 3936 participants were tested for COVID-19 using RT-PCR either because of having symptoms or for preventive screening. Out of 3936, 436 (11.1%) tested positive for PCR, whereas 3500 (88.9%) tested negative. Overall test positivity was 11%. Male participants were 2835 (72%), whereas females were 1101(28%).

Table No.1: Gender distribution among PCR Positive and Negatives

Gender	RT-PCR Result		p -Value
	Positive	Negative	
Male	280 (64%)	2555 (73%)	.001*
Female	156 (35.7%)	945 (27%)	
Total	436	3500	

Statistically significant association was observed between gender and RT-PCR positivity status

The mean age of participants was 37.12 (SD=14.83). Minimum age was 2 months and maximum was 86 years. A statistically significant association was observed between age categories and study groups.

Table No.2: Age distribution of the study participants

Age categories	Study participants		Total	P Value
	PCR Positive	PCR negative		
0 -18 years	68	395	463	.001*
19-60 years	349	2995	3344	
≥61 years	19	110	129	
Total	436	3500	3936	

*Statistically significant at .05

Regarding distribution of blood groups, majority of patients (158) having positive PCR had B+, followed by O+ (117). Statistically significant association was found to exist between blood groups and PCR positive and negatives.

Table No.3: Frequency of ABO blood groups among study groups

Blood Groups	Study Participants		P Value
	PCR Positive	PCR Negative	
A	99 (22.7%)	813 (23.2%)	.001*
AB	40 (9.1%)	353 (10%)	
B	169(38.7%)	1279(36.5%)	
O	128(29.3%)	1055(30.1%)	

Table No.4: Frequency of and Rh blood groups among study groups.

Rh+ Blood Groups (n=3551)	PCR Positives	PCR Negatives	Rh- Blood Groups (n=385)	PCR Positive	PCR Negative	P Value
A+	89(2.5%)	742 (20.8%)	A-	10(2.5%)	71(18.4%)	.87
AB+	35 (.98%)	309 (8.7%)	AB-	5 (1.2%)	44 (11.4%)	.57
B+	158 (4.4%)	1168 (32.8%)	B-	11(2.8%)	111 (28.8%)	.40
O+	117 (3.2%)	933 (26.2%)	O-	11(2.8%)	122 (31.6%)	.19
Total	399 (11.2%)	3152 (88.7%)	Total	37(9.6%)	348 (90.3%)	.57

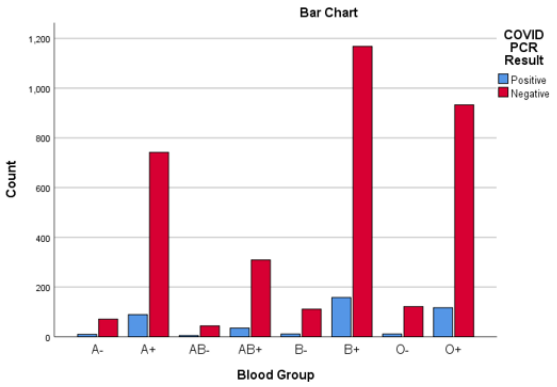

Figure No.1: Distribution of blood groups among RT-PCR Positives and Negatives

DISCUSSION

Since COVID-19 is an emerging virus, number of studies have been conducted to establish an association between ABO blood groups to SARSCoV-2 infection causing COVID-19 disease and it was found that blood group O was less frequent among severely ill patients, while Blood group A was found to be most vulnerable.[13]

Results of our study showed that maximum covid patients had blood group B (38.7%), followed by O (29.3%), A (22.7%) and AB (9.1%). These findings are inconsistent with findings of study conducted at Wuhan that showed maximum patients had blood group A (37.7%), followed by blood group B (26.5%), O (25.8%) and AB (10%).This distribution of blood groups among covid patients at Wuhan was similar to that found among general population of Wuhan.[14]

Angileri F et al, reported significantly low frequency of B and O blood groups 927 (52.2%) among COVID-19 patients as compared to group A and AB 848(47.8%) collectively. Where A was significantly more frequent 670 (37.7%) as compared to AB 178 (10%).[15] This distribution is evident from findings of current study. More than half of covid-19 patients had blood group O and B (68% collectively), with majority of having blood group B 169 (38.7%).

Regarding pattern of RH positives and negatives among Covid-19 patients, frequencies of B+, O+, A+ and AB+ were (4.4%), (3.2%). (2.5%) and (.98%). Whereas the frequencies of B-, O-, A- and AB- were (2.8%), (2.8%), (2.5%) and (1.2%) respectively. These findings contradict the results of study conducted by Saify et al, showing distribution of O+, A+, B+, AB+ as (25.25), (29.24), (17.61), and (9.30%) respectively and frequencies of O-, A-, B- and AB- as (7.31%), (7.97%) (2.66%) and (0.66%) respectively.[16]

Frequency of blood groups among 11,468 COVID-19 patients reported in a study conducted at USA showed that blood group O was most frequent (48.1%), followed by A (39.6%), B (9%) and AB (3.2%).[17] Same pattern of blood groups distribution was observed between hospitalized O(49.2%), A(38.6%), B(8.8%), AB(3.4%) and non-hospitalized O(47.9%), A(39.9%), B(9.1%), AB(3.1) covid-19 patients in that study. Whereas in our study blood group O (29.3%) was second most frequent after blood group B (38.7%), followed by A (22.7%) and AB (9.1%).

Ad'hiah et al demonstrated pattern of blood group distribution among covid patients (n=300) in Iraqi an population. No significant difference was observed to occur between distribution of A (28.7%), B (26.7%), O (025.1%) and AB (19.6%). These findings are not aligned with results of present study. A statistically significant difference was observed among COVID-19 PCR positive and negative groups, secondly the most frequent blood group in present study was B (38.7%).[18] This difference might be attributed to demographic variations among two populations.

Findings of this study are consistent with results of another study conducted by Rahim F et al, that showed proportion of blood type-B was significantly higher among COVID-19 group (35.9% vs 31.9%, p=0.009). 93.3% were having Rh Positive blood types in COVID-19 group. This finding is aligned with results of present study (91.5% RH positives).[19] This similarity is likely due to ethnically homogenous samples in both studies.

Despite of a significant difference in distribution of blood groups among Covid-19 PCR positive and negatives, our data does not support any correlation between COVID-19 and blood groups, in contrast to previous studies that shows diverse association of ABO blood group to SARSCoV-2 infection causing COVID-19 disease. The influence of blood group antigens on body's immunity still needs further research for better understanding.

CONCLUSION

Blood group B and Rh positives were more frequent among study population; however, it doesn't conclude that these blood groups increase susceptibility to covid infection.

Author's Contribution:

Concept & Design of Study:	Shabana Asif
Drafting:	Aashi Ahmed
Data Analysis:	Nadia Nisar
Revisiting Critically:	Shabana Asif
Final Approval of version:	Shabana Asif

Conflict of Interest: The study has no conflict of interest to declare by any author.

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Original Article

Inguinal Hernia-Hernioplasty

Inguinal Hernia: Compare the Laparoscopic Trans-Abdominal Pre-Peritoneal Hernioplasty with the Gold Standard Open Tension-Free Lichtenstein's Hernioplasty

Rahmat Ullah Shah[1], Sadia Shah[2], Gul Sharif[1], Adnan Badar[3], Haroon Muhammad[1] and Shabir Ahmad[1]

ABSTRACT

Objective: To compare laparoscopic trans-abdominal pre-peritoneal hernioplasty with open Lichtenstein's hernioplasty.

Study Design: Prospective study

Place and Duration of Study: This study was conducted at the Department of Surgery, MTI, Lady Reading Hospital, Peshawar from 1st January 2019 to 31st December, 2019.

Materials and Methods: Seventy patients with primary, unilateral inguinal hernia which were randomly divided into two equal groups. Group-A patients had laparoscopic trans-abdominal pre-peritoneal repair while Group-B patients underwent open Lichtenstein's repair. Both groups were compared for mean operative time, intra- & post-operative complications including pain & development of recurrent hernia, in-hospital stay and time taken to resume daily activities.

Results: The mean taken time for repair was greater in laparoscopic trans-abdominal pre-peritoneal (72.4±6.09 minutes) than Lichtenstein's repair (53±6.97 minutes) (p-value<0.001). Postoperative complications, such as wound infections, seroma formation and urinary retention were more common in Lichtenstein's group. The mean pain score was significantly less for laparoscopic trans-abdominal pre-peritoneal hernioplasty than Lichtenstein's group especially on post-operative day 7 (p-value<0.001). The mean in-hospital stay was 2±1.5 days in both groups. The time taken to resume daily activities was shorter after laparoscopic trans-abdominal pre-peritoneal repair than Lichtenstein's repair (p<0.001).

Conclusion: Though mean operative time was more in laparoscopic trans-abdominal pre-peritoneal repair, there were no significant difference in complications rate, but patients who underwent trans-abdominal pre-peritoneal repair had significantly less post-operative pain with shorter in-hospital stay and resume their routine activities earlier when compared to Lichtenstein's group.

Key Words: Inguinal hernia, Laparoscopic trans-abdominal pre-peritoneal hernioplasty, Lichtenstein tension-free hernioplasty

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INTRODUCTION

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Inguinal hernioplasty is among the commonest surgeries carried out by surgeons globally. Surgery for inguinal hernia has evolved greatly especially in the recent past but still there is controversy about its ideal surgical procedure.[1,2]

Annually around seventy thousand procedures are carried out for repairing hernias in USA. There is an improvement in outcome of surgical repair because of better technique, use of synthetic meshes and understanding the finer anatomical details.[3] The surgeon's skills and potential plus patient's desire are the main driving forces behind the technique used for surgical repair ofhernia.[4]

Repair of inguinal hernia with mesh, either laparoscopically or by open technique is the norm now-a-days.[5] Currently open mesh hernioplasty introduced

by Lichtenstein, is regarded as the gold-standard procedure for inguinal hernia.[6] For primary, unilateral hernia, various guidelines recommend Lichtenstein's repair and Laparoscopic hernioplasty.[7,8]

Laparoscopic mesh repair has many benefits including reduced post-operative pain, shorter in-hospital period plus the added capability of visualizing and repairing hernia on opposite site.[5] Lengthy duration of surgery, more postoperative complications and requiring skilful expertise are the major constraints of hernia repair done laparoscopically.[9-11]

The objective of this study was to compare the outcomes of laparoscopic trans-abdominal preperitoneal repair with Lichtenstein repair in terms of mean operative time, intra- and post-operative complications including pain and development of recurrent hernia, in-hospital stay and time taken to resume daily activities.

MATERIALS AND METHODS

This prospective study was carried out in Department of Surgery, MTI Lady Reading Hospital Peshawar from 1st January 2019 to 31st December, 2019. A total of 70 patients aged ≥18 years presenting with primary, unilateral inguinal hernia were included. Patients with large scrotal/bilateral/recurrent hernia or those having hydrocele/varicocele along with hernia were excluded. Also, patients having hernia with complications like incarceration, strangulation, or obstruction were put in the exclusion criteria. The patients were randomly divided in two equal groups of 35. Patients' demographics, history/examination findings and drug history were noted and necessary work up like full blood picture and abdominopelvic sonographic studies were carried out on initial visit. Patients in group-A had laparoscopic trans-abdominal preperitoneal (TAPP) mesh repair under general anaesthesia while those in group-B, operated by open Lichtenstein technique mostly received regional/spinal anaesthesia. All patients received perioperative broad-spectrum antibiotics as per hospital protocol and intravenous non-steroidal anti-inflammatory drugs (Ketorolac) every 8 hours for 1 day and then switched to oral medications. The following intra- and postoperative variables were noted; mean operative-time, intra- and postoperative complications including pain and development of recurrent hernia, in-hospital stay, and time taken to resume routine daily activity.

The data was entered and analyzed through SPSS-25. Visual analogue pain scale was used for assessing post-operative pain. The t-test was used for comparing the mean of two groups and $p<.05$ was considered significant.

RESULTS

All the patients were males (100%), having age ranging from 18-70 years and mean age of 44.51±11.56 years in TAPP repair while 47.97±11.05 years for Lichtenstein's repair. Patients were operated in either group, had unilateral inguinal hernia. 64.28 percent (45 patients) had right inguinal hernia while 35.7 percent (25 patients) had hernia on left side.22 patients (31.4%) had direct while 48 patients (68.57%) had indirect hernia. Among patients having direct hernia 9 patients had laparoscopic while 13 patients had open repair (Table I). The mean duration of surgery for open and laparoscopic TAPP repairs was 53±6.97 and 72.4±6.09 minutes respectively (p-value<0.001), while the mean length of hospital stay was 2±1.5 days in both groups.

None of the patients in both groups experienced any intraoperative complication such as bleeding or injury to the spermatic cord/bowel/bladder. Postoperative wound infection developed in 5 cases (14.3 percent) whereas seroma formation was noted in 6 cases (17.1 percent) of group-B/open repair. While in group-A/laparoscopic TAPP only one patient (2.8%) had wound infection while 4 cases (11.4 percent) had seroma formation. Urinary retention was recorded in 7 cases (20 percent) from group-B. Group-A patients did not suffer from retention as they were already catheterized during surgery. All patients were followed up at 1 month, 6 months and 1 year and none of them has recurrent or port-site hernia. There was no significant difference in post-operative complications in both groups (Table 2)

Using visual analogue scale, mean pain score was recorded for every patient on postoperative day, 0, 3 and 7. When the two groups were compared, the mean score was not different significantly on postoperative day 0 [5.8±1.5 in TAPP group vs 6.5±2.4 in open group (p=0.21)], however this difference was remarkable on postoperative day 3 [4.1±1.5 vs 4.9±1.7 (p=0.04)] and on postoperative day 7 [1.5±1.1 vs 2.9±1.3 (p=<0.001)] (Table 3). Similarly, the time taken to resume daily activities was lesser in TAPP group, 5±1.5 days as compared to 8.5±2 days in open hernia repair group [p<0.001] (Table 4).

Table No.1: Distribution of hernia (n=70)

Group	Right sided hernia (n=45)				Left sided hernia (n=25)			
	Direct		Indirect		Direct		Indirect	
	No.	%	No.	%	No.	%	No.	%
TAPP	7	15.55	17	37.77	2	8.0	6	24.0
Open	9	20.0	12	26.66	4	16.0	13	52.0

Table No.2: Intra- and post-operative complications (n=70)

Complication	TAPP (n=35)		Open (n=35)		p-value
	No.	%	No.	%	
Wound infection	1	2.8	5	14.3	0.08
Seroma formation	4	11.4	6	17.1	0.49
Urinary retention	-	-	7	20.0	-
Bleeding	-	-	-	-	-
Injury to spermatic cord/ bladder/bowel	-	-	-	-	-
Recurrent hernia (at 1 year)	-	-	-	-	-

Table No.3: Pain score using visual analogue score

Type of hernia repair	Pain score		
	POD 0	POD 3	POD 7
TAPP	5.8±2.3	4.1±1.5	1.5±1.1
Open	6.5±2.4	4.9±1.7	2.9±1.3
P-value	0.21	0.04	<0.001

Table No.4: Resumption of normal daily activities

Type of hernia repair	No. of Days
TAPP	5±1.5
Open	8.5±2
P-value	<0.001

DISCUSSION

In the present study, there was no statistically significant difference in age of patients in both groups (p=0.02), with mean age of 44.51±11.56 years in TAPP repair and 47.97±11.05 years for Lichtenstein's repair. Similarly, other authors also did not report any significant difference in age in their studies when comparing laparoscopic with open hernia repair.[9,10,12]

In our study all patient operated had unilateral inguinal hernia, 64.28 percent (45 patients) had right inguinal hernia while 35.7 percent (25 patients) had hernia on left side. 22 patients (31.4%) had direct while 48 patients (68.57%) had indirect hernia. Saeed et al[13] and Alam et al[14] have also reported similar results.

The mean duration of surgery for open and laparoscopic TAPP repairs was 53±6.97 and 72.4±6.09 minutes respectively (p-value<0.001). Hamza et al[9], Rathod et al[11] and Memon et al[15], all reported that mean time taken by laparoscopic hernioplasty was greater when compared to Lichtenstein's hernioplasty.

Many prospective studies and Cochrane reviews report a higher rate of visceral and vascular complications in patients who underwent laparoscopic repair.[16-20] In comparison we did not encounter any intraoperative complication such as bleeding from injury to spermatic/epigastric vessels or visceral injury to the bowel/urinary bladder or spermatic cord in either group. Wound infection developed in 5 cases (14.3 percent) whereas seroma formation was noted in 6 cases (17.1 percent) of open repair. While in laparoscopic TAPP only one patient (2.8%) had wound infection and 4 cases (11.4 percent) developed seroma. Urinary retention was recorded in 7 cases (20 percent) from group-B. In comparison, group-A patients had no such issue as they were already catheterized during surgery. All patients of this study were followed up at 1 month, 6 months and 1 year and none of them has recurrent or port-site hernia. Higher p-value suggests that there was no significant difference in post-operative complications in both groups. Sudarshan et al[10] also noted similar incidence of complications in their study.

Using visual analogue scale for pain scoring, when the two groups were compared, the mean score was not different significantly on POD-0 [5.8±1.5 in TAPP group vs 6.5±2.4 in open group (p=0.21)], however this difference was remarkable on POD-3 [4.1±1.5 vs 4.9±1.7 (p=0.04)]and on POD-7 [1.5±1.1 vs 2.9±1.3 (p=<0.001)]. Sudarshan et al[10] also observed in their study that laparoscopic group had less post-operative pain.

Various studies report differently on length of hospital stay when comparing laparoscopic hernia repair with open repair.[10,21] The mean stay in our study was same in both groups i.e., 2±1.5 days.

The time taken to resume daily activities was significantly different between laparoscopic TAPP group and Lichtenstein's repair group i.e., 5±1.5 days as compared to 8.5±2 days (p<0.001). Ugraiah et al[1]and Rathod et al[11] also demonstrated similar results in their studies.

In view of our results, it is noteworthy that with adaptation of laparoscopic technique, one can achieve all the benefits of minimally invasive surgery in hernia repair without any significant increase in post-operative complications. However, there were certain limitations to this study such as a) shorter duration, b) it didn't explore the long-term results or recurrences and c) exclusion of bilateral/recurrent/complicated hernias.

CONCLUSION

Though mean operative time was more in laparoscopic TAPP repair, there were no significant difference in complications rate, but patients who underwent TAPP repair had significantly less post-operative pain with shorter in-hospital stay and resume their routine activities earlier when compared to Lichtenstein's group.

Author's Contribution:

Concept & Design of Study:	Rahmat Ullah Shah
Drafting:	Sadia Shah, Gul Sharif
Data Analysis:	Adnan Badar, Haroon Muhammad, Shabir Ahmad
Revisiting Critically:	Rahmat Ullah Shah,

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Conflict of Interest: The study has no conflict of interest to declare by any author.

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Original Article

Efficacy of Atorvastatin (40mg) in Reducing Proteinuria in Chronic Kidney Disease (CKD) Patients

Nafidullah Khan[1], Raza Muhammad Khan[1], Iftikhar Ali Khan[2], Bughdad Khan[2], Haider Ali Khan[3] and Muhammad Nadeen Khan[4]

ABSTRACT

Objective: his study was planned to determine the efficacy of atorvastatin 40mg in reducing proteinuria in Chronic Kidney Disease patients, in our population at district Bannu and adjacent areas.

Study Design: Cross-Sectional, Descriptive

Place and Duration of Study: This study was conducted at the Department of Medicine/Nephrology, DHQ Teaching Hospital (DHDTH) Bannu, Khyber Pakhtunkhwa. Study was carried out for a period of 12 months, from July 2020 to June 2021.

Materials and Methods: The study was conducted on 246 patients presented to Department of Medicine/Nephrology, DHQ Teaching Hospital (DHDTH) Bannu, Khyber Pakhtunkhwa, who were having Hyperlipidemia (cholesterol>6mmol/L=232mg/dl, LDL-chol>2mmol/L=78mg/dl, TGs>1.9mmol/L=170mg/dl) and some CDK component (based on Proteinuria ie urinary protein excretion of > 150 mg per day). They were started on atorvastatin in the dose of 40mg once daily for hyperlipidemia for three months, and called for follow up after 3 months, to look for proteinuria.

Results: Treating dyslipidemia with atorvastatin 40mg/day not only reduced the risk of cardiovascular events but also aided in preventing the further deterioration of renal function in CKD cases. Our results revealed that atorvastatin in the dose of 40mg once daily for three months significantly reduced serum lipids and proteinuria in CKD patients.

Conclusion: In the light of above discussed evidences, it is concluded that atorvastatin 40mg once daily can be used in CKD patients to reduce hyperlipidemia and proteinuria. However, more detailed research is required in future to evaluate the dose dependent effect of atorvastatin in reducing proteinuria and to compare the efficacy of different statins in reducing the proteinuria in CKD patients.

Key Words: Atorvastatin, Proteinuria, Chronic Kidney Disease (CKD), Bannu

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INTRODUCTION

Chronic Kidney Disease (CKD) is considered as a silent global epidemic. It has been associated with cardiovascular events. Hyperlipidemia is also a main risk factor for cardiovascular diseases and development of proteinuria and impaired renal function. The patients of CKD should be evaluated for dyslipidemia.

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Treating dyslipidemia not only reduces the risk of cardiovascular events but also aids in preventing the further deterioration of renal function in CKD cases.

CKD (Chronic Kidney Disease) is a global health issue with growing incidence and prevalence, poor outcomes and high cost [1]. Globally the increasing cases of CKD are very alarming and are threatening to reach epidemic proportions over the up-coming decades [2]. The incidence of CKD is increasing globally with annual growth rate of 8%. The epidemiological studies have reported that incidence of CKD is much higher in developing countries than in developed nations. The incidence of CKD is about 6 to 10 times higher in elderly patients aged between 70 to 90 years as compared to adults aged between 30 to 50 years [3].

CKD (Chronic Kidney Disease) is defined as decreased GFR (Glomerular Filtration Rate), increased urinary excretion of albumin, or both [4]. According to KDIGO (Kidney Disease: Improving Global Outcomes), CKD is defined as "Structural or functional abnormalities (markers of renal damage) present for more than 3 months with implications for health and requires one of two criteria to be documented or inferred for more than

3 months; either GFR < 60ml/min/1.73m^2 or markers of kidney damage including albuminuria" [5]. CKD has been classified into 5 stages (stage 1 to 5) depending upon the urinary excretion of proteins and renal function assessed by GFR which is derived from age, gender, race and serum creatinine concentrations. ESRD (End-stage renal disease) is the last or stage-5 of CKD characterized by GFR of < 15ml/min/1.73m [6].

Patients of CKD experience various symptoms both due to the treatment and the disease itself. The most common symptoms of CKD include drowsiness, lack of energy or fatigue, pain, pruritus, bone or joint pain, sleep disturbances, dyspnoea, poor appetite, poor mobility and dry skin etc. [7][8]. Hypertension and Diabetes are the main risk factors that lead to CKD [9]. Unhealthy diet, sedentary life style, obesity, increase age, hyperlipidemia, hyperuricemia and high alcohol consumption increases the risk of CKD [10].

Proteinuria (increase urinary protein excretion of > 150 mg per day [11]) is a hallmark of kidney disease. Besides blood pressure, serum creatinine and urinalysis, estimation of urinary protein excretion plays significant role in diagnosis, monitoring and classification of kidney diseases [12]. Proteinuria in CKD patients, is not only a prognostic tool of progression of CKD, but also a mediator of this disorder, and has been associated with high mortality and morbidity and increase cardiovascular risk in CKD patients [13].

Hyperlipidemia not only increases the risk of cardio-vascular disease but also considered as an independent factor that worsens the CKD. HMG CoA reductase inhibitors (statins e.g.; Atorvastatin) are widely used for the treatment of hyperlipidemia and for prevention of CHD (coronary heart disease). Apart from its lipid lowering effect, it has a protective effect on kidneys, and aids in reducing proteinuria, inflammation and prevents histological alterations of inflammation and fibrosis in the kidney [14].

MATERIALS AND METHODS

Study Design: Cross-Sectional, Descriptive.

Place and Duration of Study: Department of Medicine/Nephrology DHQ Teaching Hospital (DHDTH) Bannu, Khyber Pakhtunkhwa, for a period of 12 months, from July 2020 to June 2021.

Inclusion Criteria:

- Patients with known chronic kidney disease (GFR <60 >15ml/min) for at least three months.
- Patients of both genders and either race.
- Age between 18 to 75 years.
- Both diabetic and non-diabetic CKD patients.
- Patient with Proteinuria in the range of 0.5-3.5 grams protein per gram Creatinine on urinary protein-creatinin ratio (uPCR).

Sample Size: 246 patients, who were having Hyperlipidemia and some CDK component.

Sampling Technique: Consecutive, Non-probability Sampling.

Exclusion Criteria: Those patients who were not filling the inclusion criteria,patients terminally ill, and patients who were not willing to be included in study, on Statins/other drugs decreasing proteinuria, and patients mentally retarded were not included, because they would not benefit from future planned treatment or would give recall bias. If included in the study, these would act as confounders to introduce bias in the study results.

1. Patients already on statins.
2. Patients of acute liver disease. ALT >300 IU/L.
3. Hypersensitivity to statins.
4. Patients on renal replacement therapy.
5. Patients on ACE inhibitors or ARBs for the least 3months.

Data Collecting Procedure: The study was conducted after approval from hospitals ethical and research committee/ board.

All the patients who were meeting the inclusion criteria, as per operational definitions, presented to the Department of Medicine/Nephrology, DHQ Teaching Hospital Bannu, through emergency or OPD, were included in the study. All patients were first counseled by explaining them the study objectives and possible side effects of the drug i.e. atorvastatin. All the queries regarding the study were answered clearly and properly. The purpose and benefits of the study were explained to all patients, and a written informed consent was obtained from all who agreed to participate in the study. Participants were explained in detail how to collect clean catch midstream random urine sample. Participants were ensured that all the information obtained will be kept confidential and will be used for research purpose only.

For all these patients (study population), at first visit, Renal Function Tests, Fasting Lipid Profile (Total cholesterol, LDL-Chol and TGs), and spot urine for Urine protein/creatinine ratio were sent to hospital lab initially to note as base line references, and these were noted on flow sheet as data collection tool having all variables of interest. Then the same investigations repeated from same lab, after the usage of atorvastatin 40mg daily at bedtime for consecutive three months, under the supervision of researcher, and reports were collected by him personally. To ensure follow up after 3months, contact numbers of patients were also noted.

All the patients were categorized in various groups. All the information including name, age, gender, address and lab values (both initial and at 3 months) were recorded in that pre-designed Proforma. Only a complete Proforma was subjected to analysis. Strict exclusion criteria was applied to control confounders and bias in the study results.

Statistical Analysis: Data obtained was entered into SPSS version 23 and analyzed in analytical statistics.

Mean ± SD were calculated for numerical/ quantitative variables like age. Co-relation between proteinuria and other clinical variables was analysed using multiple linear regression. For the comparison of pre and post treatment data, we used paired t-test. P- values of < 0.05 were considered significant. These were stratified among age and gender to see the effect modifiers. All results were presented in the form of tables, charts.

RESULTS

This results are tabulated at table 1&2.

Table 1 represents the association between proteinuria and its determinants from pre-treatment data. Statistical analysis showed that before treatment, LDL and triglycerides were significantly raised along with proteinuria, whereas no association of SBP, DBP and eGFR with proteinuria was observed.

Table 2 represents the efficacy of atorvastatin 40mg/day in treating proteinuria and its determinants (comparison between pre and post treatment data). Statistical analysis showed that atorvastatin 40mg/day, after 3 months of continuous dosing, significantly reduced the proteinuria, total cholesterol, triglycerides and LDL whereas no effect was observed on SBP, DBP and eGFR.

Table No.1: Determinants of Proteinuria from pre-treatment data

	Beta-coefficient	SE	P-value
Systolic BP	.034	.001	.574
Diastolic BP	.113	.001	.077
eGFR	-.117	.002	.062
Total cholesterol	.039	.001	.519
LDL-cholestrol	-.124	.002	.042
HDL-cholestrol	-.296	.002	.000
Triglyceride	.175	.005	.004

Table No.2: Efficacy of Atorvastatin 40mg in treating proteinuria and its determinants

	Pre-treatment		Post-treatment		P-value
	Mean	SD	Mean	SD	
Systolic BP	129.68	9.804	128.456	17.234	0.3
Diastolic BP	84.41	16.96	84.41	16.96	0.16
eGFR	86.709	9.006	87.345	12.777	0.48
Total cholesterol	247.04	17.06	187.63	11.18	0.0001
LDL-cholestrol	174.98	8.52	112.77	11.77	0.0001
HDL-cholestrol	43.35	2.89	42.5	3.27	0.0003
Triglyceride	172.18	6.7	144.44	8	0.0001
Protienuria (g/day)	2	0.22	0.8	0.15	0.0001

Table1: represents the association between proteinuria and its determinants from pre-treatment data. Statistical analysis showed that before treatment, LDL and triglycerides were significantly raised along with proteinuria, whereas no association of SBP, DBP and eGFR with proteinuria was observed.

Table 2: represents the efficacy of atorvastatin 40mg in treating proteinuria and its determinants (comparison between pre and post treatment data). Statistical analysis showed that, atorvastatin 40mg/day, after 3 months of continuous dosing, significantly reduced the proteinuria, total cholesterol, triglycerides and LDL, whereas no effect was observed on SBP, DBP and eGFR.

DISCUSSION

Globally, Chronic Kidney Disease (CKD) is considered as 16th leading cause of death. Timely screening, proper diagnosis and early treatment by health care clinician is necessary to prevent CKD associated complications such as cardio-vascular events, end-stage renal disease and death [15]. Proteinuria is a typical and persistent sign of renal dysfunction in CKD patients. It has been considered as a therapeutic target in delaying the progression of CKD and preventing cardio-vascular mortality in CKD patients [16]. In this study, we have determined the efficacy of atorvastatin; a drug which belongs to HMG CoA reductase inhibitor (anti-hyperlipidemic agent) class, in reducing the proteinuria, in the dose of 40mg once daily, for three consecutive months. According to the results of our study, it has been established that, there is a strong relation between serum cholesterol, triglycerides, LDL and proteinuria. Statistical analysis by linear regression of pre-treatment data showed, increased serum lipids concentration along with proteinuria, in CKD patients. Our study findings also revealed that atorvastatin 40mg once daily for three months is very effective in reducing serum lipids concentration, as well as proteinuria (which is a classical symptom of CKD) in CKD patients.

Increase serum lipids concentration leads to impaired renal function [17]. Abnormal lipo-protein metabolism often accompanies renal disease, and is considered to be involved in the pathogenesis of kidney injury. Hyperlipidemia is a modulator for progression of primary renal diseases. Elevated serum lipoproteins along with proteinuria, increase the rate of loss of renal function by two-folds. One of the mechanism that supports the evidence of hyperlipidemia induced renal injury is that, the serum lipids directly acts on the resident cells of the kidney. The renal tubulo-interstitium and glomerulus is a preferred site for lipid deposition where they interact with the resident cells. Due to the absence of basement membrane that separates mesangium and the capillary stream, and the presence of fenestrated epithelium lining glomerular and peritubular capillaries, lipids easily access these areas and initiates local metabolism. Mesangial cells have been shown to bind and take up native and oxidized LDL cholesterol. Binding of LDL and other

lipids to mesangial cells initiates cellular proliferation, and stimulates the secretion of inflammatory mediators such as prostanoids, interleukin-6, platelet derived growth factor (PDGF), TGF- β 35, 36, 37, 38 leading to initiation of injury process [18].

Treating hyperlipidemia, not only reduces the proteinuria, but also slows down the progression of CKD and its associated complications [19]. Statins (HMG CoA reductase inhibitors) are used as a first line therapy in the management and treatment of dyslipidemia and prevention of atherosclerosis and cardio-vascular diseases. The use of statins in CKD population, not only helps in treating hyperlipidemia and reducing proteinuria, but also delays the progression of CKD and its adverse outcomes [20]. Hence these evidences strongly support our current study findings i.e. atorvastatin 40mg is very effective in reducing proteinuria in CKD patients.

CONCLUSION

In the light of above discussed evidences, it is concluded that atorvastatin 40mg once daily can be used in CKD patients to reduce hyperlipidemia and proteinuria. However, more detailed research is required in future to evaluate the dose dependent effect of atorvastatin in reducing proteinuria and to compare the efficacy of different statins in reducing the proteinuria in CKD patients.

Recommendations: In the view of the above study, we **recommend:** All the health care providers and physicians should be aware of the hidden burden of the hyperlipidemia and proteinuuria, where the patients have no or vague signs symptoms, but having positive lab findings, for early diagnosis and prompt treatment of these, to decrease the disease progression, its complications, burden and their misery.

Hyperlipidemia is a main risk factor for cardiovascular diseases and development of proteinuria and impaired renal function. The patients of CKD should be evaluated for dyslipidemia.

Author's Contribution:

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Original Article

Incidence of Hyponatremia in Neonates Receiving Phototherapy for Neonatal Hyperbilirubinemia

Lubna Riaz[1], Mehwish Asghar[2], Muhammad Anwar[3], Neelam Faryad[1], Shazia Iram[4] and Maria Javed[1]

ABSTRACT

Objective: To determine the incidence of hyponatremia in neonates receiving phototherapy for neonatal unconjugated hyperbilirubinemia.

Study Design: Descriptive case series study.

Place and Duration of Study: This study was conducted at the Department of Paediatrics, Sheikh Zayed Hospital Lahore, and Sir Ganga Ram Hospital Lahore from March 2020 to September 2020.

Materials and Methods: One hundred and eighty neonates and their demographic data were obtained. Blood sample was collected from the neonates included in the study for total bilirubin and serum sodium. Phototherapy was administered by senior consultant having experience more than 5 years after their post- graduation to avoid bias as per operational definition. Serum sodium was checked before phototherapy and at 48 hours of phototherapy.

Results: Seventy-seven (42.78%) were between 0-15 days of life while 103 (57.22%) were between 16-28 days of life with mean age was 15.03±5.78 days. One hundred and six (58.89%) were males and 74 (41.11%) were females. Mean serum sodium levels before treatment were recorded as 143.65±3.87 while 140.72±4.28 after treatment. Hyponatremia in neonates receiving phototherapy for hyperbilirubinemia was recorded as 16 (8.89%).

Conclusion: The frequency of hyponatremia is not much higher in neonates receiving phototherapy but it should also be considered that the previous results are varied.

Key Words: Neonatal hyperbilirubinemia, Phototherapy, Hyponatremia

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INTRODUCTION

Almost all the newborn develops an unconjugated serum bilirubin level more than 30 µmol/L (1.8 mg/dL) during the first week of life.[1] Term neonates have 60% and preterm neonates 80% have neonatal jaundice typically at 2-4 days of life.[2] Incidence of neonatal hyperbilirubinemia varies with ethnicity, race, geography, gender, gestational age, and financial status.[3,4]

Neonatal hyperbilirubinemia can occur either due to physiological cause or pathological cause. Physiological hyperbilirubinemia (unconjugated) reflects a normal transitional phenomenon. It occurs due to increased breakdown of foetal erythrocytes (increased load of bilirubin), decreased capacity of the liver to produce conjugated bilirubin and is exaggerated by breast feeding, dehydration etc.[5] Pathological causes include sepsis, ABO and/or Rh incompatibility, RBC membrane defects, G6PD deficiency, conjugating enzyme deficiencies, increased enterohepatic circulation, hypothyroidism, galactosemia etc.

Neonatal hyperbilirubinemia is treated by phototherapy, pharmacotherapy, and exchange transfusion. Phototherapy is non-invasive procedure use of visible light to transform bilirubin into water soluble isomers without conjugation in the liver.[6] However, various studies have revealed its side effects as diarrhea, feed intolerance, retinal changes, hyperthermia, dehydration, skin rashes, genotoxicity, bronze baby syndrome, electrolyte imbalances.[7] Electrolyte imbalance is a major concern as it leads to increased risk of morbidity and mortality. The relation between hypocalcaemia and phototherapy is well established by various studies, however a little is known about effect of phototherapy on sodium levels.

A study published in 2020 shows incidence of hyponatremia to be 19.3% in term and 29.4% in preterm infants after 48 hours of phototherapy.[8] Another regional study conducted in 2019 in India has shown incidence of hyponatremia to be 13.59% in

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neonates receiving phototherapy which was relatively more in preterm and low birth weight infants as compared to full term and healthy neonates.[9] Hyponatremia in neonates is a significant problem, however, only few studies are conducted to establish its relationship with phototherapy. More regional and international studies should be conducted to know the incidence of hyponatremia in neonates receiving phototherapy. This study will therefore be helpful in recognizing the frequency of sodium imbalance in relation to gestational age, gender and birth weight before and after the phototherapy hence the preventive measures should be applied.

MATERIALS AND METHODS

This descriptive case series study was conducted from 8th March 2020 to 8th September 2020 at Paediatric Medicine Department of Sir Ganga Ram Hospital and Sheikh Zayed Hospital, Lahore. A total of 180 neonates were included in the study by non-probability consecutive sampling technique. We included all the neonates of either gender having unconjugated hyperbilirubinemia as per operational definition and on mother feed or standard formula feed. We excluded all the neonates who developed jaundice on first day of life, jaundice lasting more than 14 days, signs and symptoms of sepsis, ABO/Rh incompatibility, history of birth asphyxia, hypothyroidism, G6PD deficiency, IUGR, obvious congenital malformations, infant of diabetic mother, conjugated hyperbilirubinemia, history of exchange transfusion, mother taking anti-convulsive and/or abnormal electrolyte status (Na < 135 meq/L before the start of phototherapy.

After selection of neonates according to inclusion and exclusion criteria were admitted to Neonatal Unit and filling detail history and examination was done. 2 cc of venous blood samples were collected for serum bilirubin and sodium. They were subjected to standard phototherapy as per operational definition, of wavelength 425-275 nm, at 25-30 cm from the skin after covering eyes and genitalia. After 48 hours of phototherapy sodium level was sent again. Total and direct bilirubin was measured by diazo method and sodium by auto analyzer Erba EM 200 machine.

The data was entered and analyzed through SPSS-20 Data was stratified for age, gender, preterm birth, and low birth weight baby to address effect modifiers. Post stratification Chi-square test was applied taking p-value ≤ 0.05 as significant.

RESULTS

There were 106 (58.89%) males and 74 (41.11%) females with mean age 15.03±5.78 days and gestational age 39.11±4.25 weeks (Table 1). Mean birth weight, serum bilirubin levels and sodium level before and after phototherapy of the patients are shown in Table 2.

There were 16 (8.89%) neonates have hyponatremia and 164 (91.11%) have no hyponatremia (Table 3). There was no significant difference in age, gender and significant difference was found in preterm birth weight (Table 4).

Table No.1: Frequency of age, gender and gestational age (n=180)

Variable	No.	%
Age (days)		
0-15	77	42.78
16-28	103	57.22
Gender		
Male	106	58.89
Female	74	41.11
Gestational age (weeks)		
<37	43	23.89
≥ 37	137	76.11

Table No.2: Mean birth weight, serum bilirubin levelsand sodium level before and after phototherapy of the patients

Variable	Mean±SD
Birth weight (kg)	2.94±1.01
Bilirubin	
Before treatment	17.12±4.87
After treatment	13.48±3.71
Sodium levels	
Before treatment	143.65±3.87
After treatment	140.72±4.28

Table No.3: Frequency of hyponatremia in neonates receiving phototherapy for neonatal hyperbilirubinemia (n=180)

Hyponatremia	No.	%
Yes	16	8.89
No	164	91.11

Table No.4: Comparison of hyponatremia according to age, gender, preterm birth and low birth weight

Variable	Hyponatremia		P value
	Yes	No	
Age (days)			
0-15	7	70	0.95
16-28	9	94	
Gender			
Male	9	97	0.82
Female	7	67	
Preterm birth (weeks)			
<33	11	33	0.000
33-36	5	131	

DISCUSSION

During the first days of life neonatal jaundice can occur which can be treated by phototherapy which plays significant role in prevention and treatment of this condition.[10] It is widely available non-invasive treatment with relatively fewer side effects as compared to other modes of treatment. Electrolyte disturbance is one of the commonest side effects of phototherapy. In

one study hypocalcaemia is one of the major side effects [11] Another study shows that 90% of preterm and 75% of full-term neonates develop low calcium level post phototherapy [12]

In our study, 77 (42.78%) 0-15 days of life 103 (57.22%) were between 16-28 days age with mean age was 15.03±5.78 days, 106 (58.89%) were males and 74 (41.11%) were females. Mean serum sodium levels before treatment were recorded as 143.65±3.87 while 140.72+4.28 after treatment incidence of hyponatremia was recorded as 16 (8.89%).

A study done in 2015, reported the incidence of hyponatremia after phototherapy was 6% which was more in low birth weight (birth weight<2.5kg) babies (17.2%, p<0.001) and preterm neonates (<37 weeks of gestation) (17.6%, p< 0.001) than in normal weight babies (2.6%) and term neonates (3.1%) and in 17.4% babies (p<0.001).[13] Another study reported similar statistics of low sodium level after phototherapy was 6% more in LBW babies 17.2% (p<0.001) and 17.6% in preterm birth (p<0.001)[14] which are consistent with our study findings.

A recent study published in 2019 studied 206 cases, out of which 27 patients (13.6%) developed hyponatremia after phototherapy [9] The low sodium level was more in preterm (18.31%) and low birth weight neonates (18.75%) as compared to term (11.02%) and normal weight neonates (10.32%). The results of this study show significantly higher incidence of hyponatremia as compared to our study.

This study has some limitations as phototherapy is one of the commonest non-invasive measures for the treatment of hyperbilirubinemia. We must need large scale of data in the form of these samples large samples in multiple setups and look for the association of sodium imbalance in these children despite of limitations this study contributes important finding to the limited literature on the outcomes among the newborns.

CONCLUSION

The conclusive finding of our study is that hyponatremia is not much higher in neonates receiving phototherapy, but it should also be considered that the results of previous studies are varied some of them reported the higher incidence of hyponatremia. Serum sodium level must be checked in babies having phototherapy.

Author's Contribution:

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Original Article

Frequency of Newly Diagnosed Diabetes Mellitus as a Comorbidity Among Acute Ischemic Stroke Patients

Syed Yasir Hussain Gilani[1], Saima Bibi[2], Afsheen Siddique[3], Farrukh Addil[2] and Sadia Bibi[4]

ABSTRACT

Objective: The aim of the study was to determine the frequency of newly diagnosed DM and other associated risk factors in patients with AIS.

Study Design: cross sectional study

Place and Duration of Study: This study was conducted at the Department of Medicine of Ayub Teaching Hospital, Abbottabad for a period of one year from January 2018 to December 2018.

Materials and Methods: The sample comprised all AIS patients of both genders between the age group of 30 to 60 years while the patients with known diabetes were excluded. Diabetes was evaluated on the basis of fasting blood sugar (FBS), random blood sugar (RBS) and Glycated hemoglobin (HbA1c) estimates. The history regarding other risk factors was also taken i.e. patients age, weight, body mass index (BMI) and blood pressure (BP) etc. Data was analyzed using SPSS version 22. Chi-square test was applied to investigate the association between diabetic profile and associated risks. A p-value<0.05 was considered significant.

Results: A total of 136 AIS patients with a mean age of 42.58±11.10 years competed the study. Based on HbA1c and FBS levels, 28(20.6%) patients were diagnosed with DM. Moreover, obesity, hypertension and hyperlipidemia were the most frequently reported risk factors among the newly diagnosed diabetic AIS patients (p<0.05).

Conclusion: AIS patients with increased glucose concentrations remain un-diagnosed in a large number of patients. Therefore, initial diabetes screening is recommended for all acute stroke patients, in order to reduce complications and control associated morbidity and mortality.

Key Words: Acute ischemic stroke, Diabetes Mellitus, Hypertension, Obesity, Hyperlipidemia

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INTRODUCTION

Stroke has become a debilitating illness worldwide resulting in increased neurological morbidity and mortality. One of the leading causes of disability and the third commonest cause of death, it reduces the overall mobility among the sufferers[1,2]. Based on the rough estimates, the incidence rate is increasing rapidly among Asian countries.

Although there are a very few local epidemiological studies specifying the stroke incidence rate, Pakistan contributes a significant proportion of this globally devastating burden due to its inadequate resources, financial crisis, declining community health, services and the overall compromised economy of the country[3,4]. A study provided the estimated rate of stroke incidences in Pakistan i.e. 95/100,000cases are reported per year[5,6]. Moreover, ischemic strokes contribute to 87% of all stroke cases observed globally[2].

Diabetes mellitus (DM) and hypertension, are the traditional and well-known predictors and/or risk factors of cardiovascular diseases (CVD), providing predictions for recurrent stroke as well as stroke following transient ischemic attack (TIA)[7-9].Around 90% of the stroke cases are associated with modifiable risk factors including patient's blood pressure (BP), BMI, renal functioning, glucose and lipid profile[10]. Nearly 74% cases are related to the behavioral and lifestyle risk factors like smoking, alcohol consumption, dietary pattern and physical activities etc while air pollution is responsible for the remaining 29% risk ratio[10].

The stroke and diabetes/hypertension burden shows a similar trend. It has been reported that majority of the Pakistani population is suffering from either diabetes or hypertension or both along with a third comorbid i.e. stroke[3,4]. Which unfortunately remains undiagnosed due to lack of personal healthcare, medical checkups, screening unavailability. Even though if successfully

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diagnosed, lack of follow-up visits and decreased treatment compliance are among the other challenges which results in incompetent management of the disease condition[11]. Apart from the above mentioned risks factors, obesity is also among the precipitating factors for acute ischemic stroke (AIS)[11].

Hyperglycemic incidences among the patients with acute stroke either diabetic or non-diabetic contribute to increased risk and complexities as compared to the counterparts without hyperglycemic incidences, indicating glucose intolerance or diabetes among such cases. This comorbid often remains ignored as it is usually thought to be occurring secondary to the physiological stress of acute stroke[8].

Hence, the rapidly increasing ratio of diabetic patients, under-diagnosed silent diabetes cases and the association of diabetes with ischemic stroke prompts the need for diabetes screening of all the AIS patients with hyperglycemia. It is essential to diagnose diabetes among AIS patients as it modulates the overall management of the patients especially in terms of associated comorbidities other than diabetes and associated risk factors including lipids and blood pressure outcomes. Since, there is a paucity of local data regarding un-diagnosed diabetes in stroke patients and associated comorbid conditions, the current study was designed to determine the frequency and association of newly diagnosed diabetes in AIS patients.

MATERIALS AND METHODS

This cross-sectional study was conducted at Department of Medicine, Ayub Teaching Hospital Abbottabad Pakistan over a period of one year from 1st January 2018 to 31st December 2018. The sample size for the study was 140, calculated using the WHO sample size calculator[9] assuming 95% confidence level, 8% anticipated prevalence and 9% absolute precision. Of them 136 completed the study while 4 cases were dropped due to incomplete data records. All patients aged between 30 to 60 years irrespective of gender with diagnosed acute ischemic stroke (AIS) as confirmed by history of loss of function of a part of body and compatible physical and radiological findings (computed tomography scan of brain as loss of grey-white matter differentiation, hypoattenuation of deep nuclei and cortical hypodensity with associated parenchymal swelling with resultant gyral effacement) were included in the study. While patients presented with hemorrhagic stroke, known diabetics with acute ischemic stroke and patients with gestational diabetic history were all excluded.

Based on the inclusion criteria, patients were recruited from medical ward and OPD. After receiving informed consent, the patient's demographics details and clinical records were taken. Moreover, 2 ml blood sample was drawn from each patient for measurement of FBS, RBS and HbA1C levels. Type 2 diabetes was diagnosed on the basis of HbA1C levels, patients were categorized as diabetics (HbA1C>6.5) and non-diabetics (HbA1C<6.5) based on the American Diabetes Association (ADA) Criteria (2016). Height and weight of the patients were recorded to obtain body mass index (BMI). Using BMI patients were further classified as non-obese (<25), overweight (25–30) and obese (>30). Data was recorded using a predesigned structured questionnaire and analyzed using SPSS version 22. Mean and standard deviation were calculated for continuous variables while categorical variables like gender, age groups, BMI groups, diabetes status groups were presented as frequencies and percentages. Significance testing was done using chi-square test where $p<0.05$ was considered significant.

All the patients were managed according to the ethical protocols under the supervision of a consultant physician having at least five years' experience and the study was conducted in accordance to the ethical guidelines after receiving approval from the ethical review board of Ayub Teaching Hospital, Abbottabad(ERB/2019/medicine/233).

RESULTS

Out of 136 AIS patients, 77(56.6%) were males and 59(43.4%) were females with a mean age of 42.58±11. 10 years. The mean FBS (mg/dl), RBS (mg/dl) and HbA1c (%) was also assessed and recorded as 122.70±9.65, 188±7.69 and 6.53±0.47 respectively. Of the 136 AIS patients, 28(20.6%) were diagnosed with newly diagnosed diabetes mellitus (DM).

Table No.1: Baseline characteristics of study population(n=136)

Baseline Characteristics	**n=136**
Mean Age (years)	42.58±11.10
Weight (kg)	89±19.22
Height (m)	1.522±0.3049
BMI (kg/m^2)	27 ±5.41
FBS (mg/dl)	122.70±9.65
RBS (mg/dl)	188±7.69
HbA1c (%)	6.53±0.47
Gender	
Male	77(56.6)
Female	59(43.4)
Associated risk factors	
Diabetes Mellitus	28(20.6)
Obesity	20(14.7)
Hypertension	38(27.9)
Hyperlipidemia	20(14.7)

*Values are given as mean±SD and n(%)

*HbA1c - Glycated hemoglobin; FBS-Fasting Blood Sugar; BMI- Body Mass Index

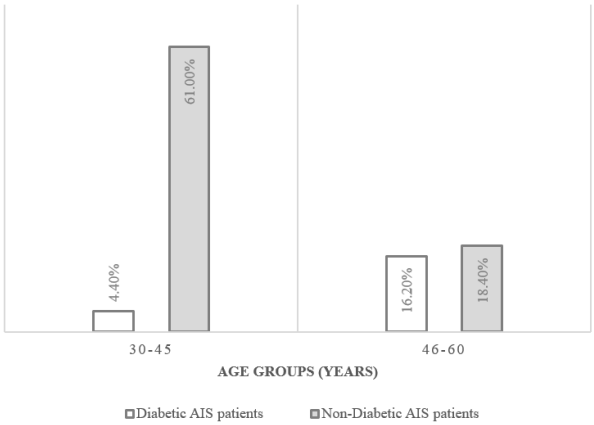

Figure No.1: Age-wise distribution of diabetic and non-diabetic AIS patients

The AIS patients were divided into two categories based on age i.e. 30-45 years and 46-60 years. 4.40% and 16.20% AIS patients between the age group of 30-45 years and 46-60 years were diabetic respectively ($p<0.05$).

The results showed that obesity, hypertension and hyperlipidemia were significantly associated with diabetic profile ($p<0.05$). Increased prevalence of the mentioned three risk factors was observed among diabetic AIS patients as compared to non-diabetic AIS patients.

Table No.2: Association of risk factors with diabetic status of the AIS patients

Risk Factors	Diabetic AIS patients	Non-Diabetic AIS patients	p-value
Obesity	13(9.6)	7(5.1)	<0.05
Hyperlipidemia	13(9.6)	7(5.1)	<0.05
Hypertension	28(20.6)	10(7.4)	<0.05

*Values are given as n(%)
*p<0.05 is considered significant
*AIS- Acute Ischemic Stroke

DISCUSSION

AIS, is a complex disease with multifactorial etiologies, indistinguishable and heterogeneous pathophysiological presentations resulting in severe disabilities and high mortality rates. Substantial contribution from other comorbidities further increase the disease complications and associated risks which in turn requires altered management and treatment according to the primary and secondary disease as well for effective control. Out of total 136 AIS patients presented to the study setting, 28(20.6%) cases were diagnosed with DM(Table 1). Consistent with our findings, a local study reported 50(20%) newly diagnosed DM-AIS cases with an average FBS level 148±10 mg/dl[13]. Furthermore, the vast data from the FIN MONICA and FIN STROKE registers also suggested that one-fourth of AIS patients are affected by diabetes i.e. 1103/4390 (25%) AIS patients were diagnosed with DM[14].

It is evident that of all the unmodifiable risk factors associated with AIS, age is the most significant constant risk in the general population[15]. In support, our results also indicated higher diabetes incidence rate among the older age group (46-60 years) (Figure 1). Besides this, common modifiable risk factors including hypertension, obesity and hyperlipidemia were significantly associated with diabetes profile and were more frequently reported comorbidities among diabetic AIS patients enrolled in the study (Table 1 & 2). In support, international data also recognized the association between stroke and this comorbid conditions [16-18]. Furthermore, a local study conducted by Zahra et al reported increased frequency of comorbidities among diabetics i.e. hypertension (71 DM cases vs 26 Non- DM cases) and hyperlipidemia (21 DM cases vs 14 Non- DM cases)[13].

Hence, the fact cannot be denied that these risk factors are interrelated and have significant effects on each other and on the diabetic profile of AIS patients as well. Obesity was more common among 46 to 60 years of AIS patients i.e. 18(13.2%) as compared to those in between 30 to 45 years of age, finding were statistically significant ($p<0.05$) and same was in the case of hypertension and hyperlipidemia ($p<0.05$).

The current study has several limitations, although the studies discussed major risk factors associated with DM among AIS patients but the common CVD associated risks and lifestyle factors were all subsided. Unlike other studies, no records of atrial fibrillation, myocardial infarction and CHD were maintained. The complications associated with each of the reported risk factors were not considered. With limited facilities and rapidly increasing disease burden, the current situation is terribly alarming indicating 1 case in every 5 AIS patient with associated diabetes profile. The condition is worsening due to the lack of knowledge and patient's un-awareness. And if not diagnosed and treated early, this morbidity and associated comorbidities will accelerate the economic burden of the country. Physicians are recommended to be will equipped with all recent knowledge and should be able to instruct the patient regarding their disease state. Follow-up visits must be considered to track the glucose levels among these patients.

CONCLUSION

Our study results were comparable to several national and international studies and hence it can be concluded from our findings that the frequency of newly diagnosed diabetes is high among patients with AIS. Patients presented with ischemic stroke must be screened for DM and other potential risk factors including obesity, hypertension, hyperlipidemia, smoking and lifestyle factors in order to avoid

complexities. Further, multicenter descriptive studies including diverse population are required for better understanding of the disease and its associated complexities.

Author's Contribution:

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Conflict of Interest: The study has no conflict of interest to declare by any author.

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Original Article

LVH among Non-Diabetics Pre Dialysis

Left Ventricular Hypertrophy among Non-Diabetics Pre Dialysis Patients with Chronic Kidney Disease in Local Population

Samiullah Khan[1], Sunehra Iqbal[2], Muhammad Niaz Khan[3], Muhammad Nadeem Khan[1], Amirullah[2] and Saadullah Shah[1]

ABSTRACT

Objective: To determine the frequency of left ventricular hypertrophy among non-diabetics pre dialysis patients with chronic kidney disease.

Study Design: Descriptive cross-sectional study.

Place and Duration of Study: This study was conducted at the DHQ Teaching Hospital Bannu from September 2017 to August 2018.

Materials and Methods: Patients with CKD were selected for study from out patients department of Nephrology under informed written consent. They were interviewed through a pre-designed research proforma. Base line BP, HR, height, Serum creatinine and RBS were recorded. Echocardiography was performed to detect and define LVH. Data was analyzed using SPSS version 16.

Results: A total of 931 CKD patients were screened to select 116 non diabetic patients. Mean age of 54.76 ±1.60 years. Male were 57.8%. Mean LVMI HR, SBP, DBP were121.89 ±31.06 gm/m^2, 76.16 ± 12.04, 146.81±30.08 & 87.41 ±14.89, respectively. Both Systolic (r=0.534, p<0.0001) and diastolic BP (r=0.339, p< 0.0001) were significantly correlated to LVMI. Frequency of LVH was 73.27% (85) with almost similar distribution among Male 45 (52.94%) vs. Female 40 (47.05%). Majority 37.06% (43) were having Mild LVH. Hypertension was found in 69% (80). Patients with Mild LVH, Mod LVH & Severe LVH were having 76.7% (n, 33), 90% (n, 9), 90.6% (n, 29) hypertension. Of the 80 (69%) hypertensive patients, 09 (7.8%) had normal LVMI.

Conclusion: Left ventricular hypertrophy is frequently present among non-diabetics predialysis patients with chronic kidney disease.

Key Words: Left Ventricular Hypertrophy, CKD, Predialysis, Cardiovascular Diseases, Non Diabetic

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INTRODUCTION

Chronic kidney disease is an international pandemic. About 1.8 million people are currently treated with renal replacement therapy (RRT) worldwide.[1] More than 10% of United States population is estimated to have CKD. The percentage is even higher for diabetic and hypertensive and among adults elder than 65 years.[2,1]

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Developing countries are facing a silent epidemic of CKD. Data from community-based studies in Pakistan reveal the overall CKD prevalence of 12.5% (95% CI).[3] Cardiovascular diseases are one of the most frequent complications of CKD. These include abnormalities of left ventricular structure and function including LVH, CAD and valvular dysfunctions. Uremic environment is the strongest risk factor leading to these complications in addition to other risk factors. Diabetes and hypertension are among the most common causes of CKD and CVD, thus compound the cardiovascular effects of CKD.[4]

LVH is the most important of all CKD associated cardiovascular diseases. In non-dialysis dependent CKD patients, LVH is one of the strongest predictors of progression to dialysis dependency[5] and increased mortality.[6] The clinical consequences of LVH include both systolic and diastolic cardiac dysfunction, CAD and predisposition to ventricular arrhythmias and sudden cardiac death.[7]

Many factors have been described as having association with CKD associated LVH. These include traditional

risk factors such as hypertension, inadequate dialysis dose, volume status and Anemia.[8] Diabetes mellitus is independently associated with LVH in a multi-ethnic sample. The presence of DM increased the risk of LV hypertrophy by about 1.5-fold. After adjusting for several potential confounders, multivariate logistic regression analyses showed significant association of LVH in non-diabetic male CKD patients.[9] For the same reason extensive research is being focused internationally on LVH in CKD.

This study aims to determine the frequency and severity of LVH in our local CKD Predialysis non diabetic population and thus pave the way for more research to enhance our understanding of this phenomenon. On the basis of the results of this study regular Echo-cardiographic screening of LVH can be suggested in CKD patients and hence to reduce morbidity and mortality by timely interventions.

MATERIALS AND METHODS

This hospital based cross-sectional study was carried out at Nephrology department in DHQ Teaching Hospital Bannu from September 2017 to August 2018. We evaluated non diabetic CKD patients, who were not on hemodialysis, from out patients department. Individual consent was obtained, following approval from the hospital ethical committee. Data was collected on preformed proforma.

The variables recorded were pertinent clinical history, CVD risk factors like HTN and DM. Base line heart rate, blood pressure, height, serum creatinine and RBS were measured. These patients then underwent transthoracic echocardiography to detect LVH.

Sampling: Sample size was 116 keeping 74%[7] frequency of LVH, 95% confidence interval and 8% margin of error using WHO sample size calculations. It was Consecutive non-probability sampling.

Inclusion criteria:

All patients (Age ≥18 years of either genders) with CKD not yet initiated on hemodialysis

Exclusion criteria:

Maintenance hemodialysis, volume overload status (confounding factor[10]) and DM.

LVH was calculated as Left Ventricular Mass Index (LVMI= LVM/Height) corrected for height. LVM was calculated by Echocardiography using Devereux's adjusted Formula through automated in built software. The severity of LVH was graded as per American society of Echocardiography criteria[11] as shown in table 1.

Chronic Kidney Diseases: It was defined as abnormalities of kidney structure or function, present for >3 months with either following;

1. Evidence of decreased GFR (GFR <60 ml/min/1.73 m^2)
2. History of CKD Albuminuria (≥30 mg/24 hours)
3. Abnormalities detected by histology
4. Structural abnormalities detected by imaging

Diabetes Mellitus: Patients were considered as diabetics if they self-reported diabetesor those with Random Blood sugar ≥ 200 mg/d and or FBS≥126 mg/dl.

Hypertension: it was defined as SBP ≥ 140 mmHg and or DBP≥90 mmHg pressure.

RESULTS

A total of 931 CKD patients were screened to select 116 non diabetic, who were not on hemodialysis, and satisfying the inclusion and exclusion criteria. Mean age was 54.76 ±1.6 (18-94 yr) and majorities were in 4th to 6th decade of life. Male (n, 67) to female (n, 49) ratio was 1.3 to 1 (Table 3). The Mean LVMI was 121.89±31.06 gm/m^2 (Table 2). Frequency of LVH was 73.27% (n, 85) with almost similar distribution among Male 45 (52.94%) vs. Female 40 (47.05%) patients [Table 3].The most frequent age group having LVH for both male 21 (18.1%) and female 21 (18.1%) was ≥55 years. Frequency of LVH in male vs. female (p=0.43) is shown in Table 3.

When LVH was sub-classified on the basis of severity, majority 37.1% (n, 43) were having Mild LVH while Mod and Severe LVH was 8.6% (n, 10) and 27.6% (n, 32), respectively (Figure 1).

Hypertension was found in 69% (n, 80), with the mean HR, systolic and diastolic BP were 76.16 ±12.04, 146.81±30.08 & 87.41 ±14.89, respectively [Table 2]. There were statistically no significant difference (p=0.62) between male 38.8% (n, 45) and female 30.2% (n, 35) distribution within hypertension prevalence.

Of the 80 (69%) hypertensive patients, 09 (7.8%) had normal LVMI, while out of 36(31%) Normotensive patients, 22(19%) had Normal LVMI, while 10 (8.6%) had Mild, 1(0.9%) Moderate, and 3 (2.6%) had Severe LVH (Table 4).

It was found that Hypertension was progressively more frequently present with worsening LVH severity. Patients with Mild LVH, Mod LVH & Severe LVH were having 76.7% (n, 33), 90% (n, 9), 90.6% (n, 29) hypertension [Table 4].Both Systolic (r=0.534, p<0.0001) and diastolic BP (r=0.339, p< 0.0001) were significantly correlated to LVMI. (Table 4).

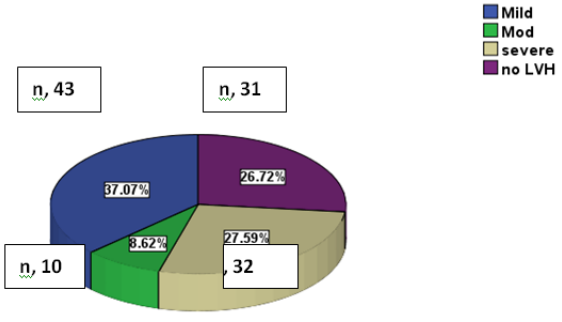

Figure No.1: LVH categories by severity

Table No. 1: Severity of LVH

	Women				Men			
Lvmi	Refrence range	Mild LVH	Moderate LVH	Severe LVH	Refrence range	Mild LVH	Moderate LVH	Severe LVH
LV mass/height(g/m)	41-99	100-115	116-128	≥129	52-126	127-144	145-162	≥163

Table No. 2: Statistical Means for Different Quantitative Variables

Statistics								
		Age	**Heart Rate**	**Systolic BP**	**Diastolic BP**	**Serum Creatinine (mg/dl)**	**Random Blood Sugar**	**Left Ventricular Mass Index**
N	**Valid**	116	116	116	116	116	116	116
	Missing	0	0	0	0	0	0	0
Mean		54.7672	76.1638	146.8103	87.4138	2.4466	123.1810	121.8991
Median		57.0000	71.0000	145.0000	90.0000	2.2000	124.5000	124.5000
Mode		61.00	68.00	145.00	90.00	1.80[a]	90.00	134.00
Std. Deviation		1.60669E1	12.04697	30.08970	14.89795	.82877	26.92456	31.06995
Range		76.00	48.00	150.00	80.00	3.00	158.00	169.00
Minimum		18.00	62.00	80.00	50.00	1.40	12.00	11.00
Maximum		94.00	110.00	230.00	130.00	4.40	170.00	180.00

a. Multiple modes exist. The smallest value is shown

Table No. 3: LVH categories by severity* hypertension cross tabulation

			Hypertension		**Total**
			Hypertensive	**Normotensive**	
LVH Categories by Severity	**Mild**	Count	33	10	43
		% within LVH by Severity	76.7%	23.3%	100.0%
		% within HTN	41.2%	27.8%	37.1%
		% of Total	28.4%	8.6%	37.1%
	Mod	Count	9	1	10
		% within LVH by Severity	90.0%	10.0%	100.0%
		% within HTN	11.2%	2.8%	8.6%
		% of Total	7.8%	.9%	8.6%
	severe	Count	29	3	32
		% within LVH by Severity	90.6%	9.4%	100.0%
		% within HTN	36.2%	8.3%	27.6%
		% of Total	25.0%	2.6%	27.6%
	No	Count	9	22	31
		% within LVH by Severity	29.0%	71.0%	100.0%
		% within HTN	11.2%	61.1%	26.7%
		% of Total	7.8%	19.0%	26.7%
Total		Count	80	36	116
		% within LVH by Severity	69.0%	31.0%	100.0%
		% within HTN	100.0%	100.0%	100.0%
		% of Total	69.0%	31.0%	100.0%

Table No. 4: Person Correlation of LVMI to Systolic & Diastolic BP

Correlations				
		Left Ventricular Mass Index	Systolic BP	Diastolic BP
Left Ventricular Mass Index	Pearson Correlation	1	.534**	.399**
	Sig. (2-tailed)		.000	.000
	N	116	116	116
Systolic BP	Pearson Correlation	.534**	1	.742**
	Sig. (2-tailed)	.000		.000
	N	116	116	116
Diastolic BP	Pearson Correlation	.399**	.742**	1
	Sig. (2-tailed)	.000	.000	
	N	116	116	116

DISCUSSION

Cardiovascular complications are the leading cause of death in patients with end-stage renal disease (ESRD), accounting for 43-52% of deaths in these patients. LVH is a frequent occurrence in patients with CKD and is an important adverse prognostic indicator.[12,13]

In the present study frequency of LVH was 74.14% with mean LVMI of 121.89 ±31.06 gm/m^2. Most of the studies show prevalence 40-80% of this cardiac geometric anomaly in the pre-dialysis patients.[14,15] Paoletti et al[7] demonstrated about similar LVH prevalence of 74% in 244 similar cohort of patients but higher mean LVMI of 160 ±50 gm/m^2. This higher LVMI could be because more than half of his patients were suffering from stages 3 to 5 CKD.

Advancing age was related directly to the increasing prevalence of LVH. The most frequent age group having LVH for both male 21 (18.1%) and female 21 (18.1%) was those with age equal or more than 55 years. Paoletti et al showed that age was directly related (P0.0013) to the LVMI.[7]

Gender has no significant effect (p=0.43) on LVH within age group with almost similar distribution of LVH among male 43.10% vs. female 31.03% patients in the present study. Zheni et al showed higher prevalence 81.9% of LVH in non-diabetics CKD patients before starting renal replacement therapy with only 22% of whom were women.[12]

When LVH was sub-classified on the basis of severity, the highest percentage of the patients 46.51% (n, 40) were having Mild LVH. This could possibly because of two reasons. First the prevalence of advance stage CKD patients, containing higher prevalence of LVH, are usually already on hemodialysis which were excluded from this study. Secondly there is low prevalence of advance CKD in population. Previously it was reported that the prevalence of LVH increased with progressive renal decline: 26.7% of patients with creatinine clearance (Ccr) greater than 50 mL/min had LVH and 45.2% of patients with severe renal impairment (Ccr<25 L/min) had LVH (P = 0.05).[16]

We observed that the prevalence of hypertension is 56.89% of the total CKD patients with the mean systolic and diastolic Blood Pressure of 146.81±30.08 & 87.41 ±14.89, respectively. Bregman et al[14] determined almost similar mean systolic & diastolic BP 143 ±27 and 83±16. Moreover LVH was significantly (p=0.0056) more prevalent in hypertensive than normotensive patients. Hypertension is thought to be the commonest factor responsible for LVH. Almost similar frequency of LVH 53.6% in hypertensive CKD patients was reported previously.[17]

Cardiovascular disease is still the major cause of death in end stage CKD[7]with a mortality rate approximately 10 to 30 times greater than that of the general population.[18] Heart disease or failure is the reason of morbidity and mortality in these population and advanced cardiomyopathy is caused by left ventricular hypertrophy.[19]

In a recent study by Covic et al, 86.4% of dialysis dependent patients had LVH at baseline. Serial echocardiography during follow up showed that LVH strongly correlated with hemoglobin level, Systolic BP, Pulse Pressure, serum phosphate, and serum calcium level. These patients were then managed according to Kidney Disease Quality Initiative and European Best Practice Guidelines. They achieved 62.1% regression in LVMI, over more than 12 months period of guideline implementation.[20]

This and other studies suggest that control of Risk factors causing LVH can result in regression of LVH and therefore its consequences.

CONCLUSION

This study has demonstrated that left ventricular hypertrophy is frequently present among non-diabetics' pre dialysis dependent chronic kidney disease patients.

Recommendations: On the basis of the results of this study regular Echocardiographic screening of LVH is suggested in all CKD patients. It is now clear some of its determinants are reversible factors. Thus, early detection can lead to preventive measures for LVH which will further help to bring down CVS mortality and morbidity in CKD patients.

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Final Approval of version:	Samiullah Khan

Conflict of Interest: The study has no conflict of interest to declare by any author.

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Original Article

Acute Kidney Injury in Patients Hospitalized with COVID-19 in a Tertiary Care Hospital of Islamabad

Acute Kidney Injury with COVID-19

Muhammad Sajid Rafiq Abbasi[1], Maryam Masud[2], Khawar Sultan[4], Uzma Rehman[2], Sajid Nasim[3] and Rukhsana Manzoor[1]

ABSTRACT

Objective: This study is conducted to find out prevalence, risk factor and outcome of acute kidney injury (AKI) in patients admitted with COVID-19 in Pakistani population.

Study Design: Retrospective, Observational Study

Place and Duration of Study: This study was conducted at the PAF hospital Islamabad from April, 2020 to December, 2020.

Materials and Methods: It involved a review of data from electronic hospital records of patients who were aged18 years or older with laboratory-confirmed COVID-19. We describe the frequency of AKI and, AKI recovery, dialysis requirement and adjusted odds ratios (aORs) with mortality.

Results: Total 191 COVID-19 patients were enrolled, AKI occurred in total 38 (19.8%) patients and out of them 8(4.2%) patients had severe AKI and required dialysis. Regarding AKI staging, stage 1 was present among 18 (9.4%) patients, 06 (3.1%) had stage 2 and 14 (7.3%) had stage 3 AKI. The patients in ICU developed AKI more frequently stage 1 15.4%, stage 2, 7.7%, and stage 3 by 13.5% respectively. Patients with AKI were more likely to have admission in ICU, requirement for mechanical ventilation and requirement for inotropic support. Mortality was very high among patient with AKI 60.5% as compared to patient with no AKI 13.7%.

Conclusion: We found in our study that AKI is a relatively common complication observed among patients hospitalized with COVID-19. It is linked to poor outcome and high mortality.

Key Words: COVID-19, AKI, Dialysis

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INTRODUCTION

Coronavirus Disease 2019 (COVID-19) is caused by the severe acute respiratory coronavirus-2 (SARS CoV-2). It causes acute respiratory illness and first case was reported in Wuhan city of China in December 2019[1]. In January 2020 first case of COVID-19 was reported in Washington USA[2]. COVID-19 was declared as pandemic by World Health Organisation on March 11,2020[3]. After that sharp rise in cases was observed and then it became epicentre of the disease[2,4]. Similar to the observations earlier in China and Italy, a lot of patients with COVID-19 required hospitalization, intensive care admissions and respiratory support worldwide[5,6].

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Along with other clinical presentations, high number of patients presented with acute kidney injury (AKI). Early reports from Italy and China showed that prevalence of AKI had range of 0.5% to 29%[7-13]. US data from Seattle Hospital showed 19% prevalence AKI in ICU admitted patients[14]. Recent study from China utilizing autopsy data showed there was evidence of SARS-CoV-2 causing direct endothelial invasion and tubular damage to the kidneys[15].

Pakistan is one of those countries with high COVID-19 infection rate. But literature on AKI in COVID in Pakistani population is limited. Purpose of this study is to find out prevalence of AKI in patients admitted with COVOD-19, their risk factors and outcome.

MATERIALS AND METHODS

This retrospective cross sectional study was done April 1, 2020 to December 1, 2020 in Pakistan Air Force Hospital Islamabad after approval from institutional ethical review board. Patients were selected according to following criteria;

Inclusion Criteria: Admitted patients of either gender with age≥ 18 years who were confirmed COVID positive by PCR were included in this study.

Exclusion Criteria: We excluded patients with known ESRD prior to admission and patients who were hospitalized for 48 hours.

Data Collection: Data of selected patients was obtained from electronic data system of hospital. Demographics included age, sex, was recorded. Vital signs and laboratory values were obtained.

Definitions of Outcomes: The primary end point was AKI , which is defined as per Kidney Disease Improving Global Outcomes (KDIGO) criteria; a rise in the serum creatinine of 0.3 mg/dl over a 48-hour period or 50% increase in baseline creatinine[16]. AKI stages were defined according to KDIGO; stage 1 as an increase in serum creatinine of ≥0.3 mg/dl or increase to ≥1.5–1.9 times baseline serum creatinine, stage 2 as an increase to >2–2.9 times from baseline serum creatinine, and stage 3 as an increase to more than three times baseline serum creatinine or a peak serum creatinine ≥4.0 mg/dl or if the patient received dialysis during admission.

Other end point was in hospital mortality.

Statistical Analysis: As the data was not normally distributed (supplement table I) checked using Shapiro-Wilk test so, baseline characteristics were reported as medians and interquartile ranges (IQRs) for continuous variables. Categorical variables were reported as frequencies and percentages. We used M Whitney U /Kruskal-Wallis (non-parametric) tests for continuous variables and chi-squared test for categorical variables. For survival analysis, Kaplan-Meier survival curves was generated, and comparison was done using the log-rank test. Logistic regression models were used to estimate the adjusted odds ratio (aOR) for AKI in patients. SPSS version 23.0 was used for statistical analysis. P-value<0.05 was taken as statistically significant.

RESULTS

Incidence and severity of AKI

Total 191 COVID-19 patients were enrolled, AKI occurred in total 38 (19.8%) patients. Out of them 8(4.2%) patients had severe AKI and required dialysis. Regarding AKI staging, stage 1 was present among 18 (9.4%) patients, 06 (3.1%) had stage 2 and 14 (7.3%) had stage 3 AKI. The patients in ICU developed AKI more frequently stage 1 15.4%, stage 27.7%, and stage 3 by 13.5% respectively (table II).

AKI and Outcome

Patients with AKI were more likely to have admission in ICU, requirement for mechanical ventilation and inotropic support. Mortality was very high among patient with AKI 60.5% as compared to patient with no AKI 13.7% .The results of the Kaplan-Meier survival analysis stratified with AKI are shown in figure II. The curves indicate that the survival among AKI patients is lower than that of the no AKI patients and log-rank test statistics is also statistically significant (p=0.002).

There were 191 COVID-19 patients included in the study with median (IQR) age of 62 (41-83) years, the median (IQR) length of hospital stay was 8 (2-14) days, the median (IQR) creatinine on admission and discharge was 1.07 (0.69-1.45) mg/dL and 1.00 (0.59-1.41) mg/dL respectively, the median (IQR) eGFR on admission and discharge was 66 (31-101) mg/dL and 74 (36-112) mg/dL respectively.

Table No.1: Patient Characteristics of all and those with and without AKI

Patient Characteristics		All (n=191)	AKI (n=38)	No AKI (n=153)	p-value[a,b]
Age (years), median (IQR)		62 (41-83)	67.5 (47.75-87.25)	61.0 (38.5-83.5)	0.009*
Length of Stay (days), median (IQR)		8 (2-14)	8 (1.5-17.5)	7 (1.5-12.5)	0.070
Creatinine admission (mg/dL), median (IQR)		1.07 (0.69-1.45)	1.22 (0.18-2.26)	1.06 (0.71-1.41)	0.04*
Creatinine Discharge (mg/dL), median (IQR)		1.00 (0.59-1.41)	1.98 (0.85-4.81)	0.93 (0.61-1.25)	<0.001*
eGFR admission (mg/dL), median (IQR)		66 (31-101)	52 (2.75-106.75)	68 (37-99)	0.002*
eGFR Discharge (mg/dL), median (IQR)		74 (36-112)	28.5 (20.25-77.25)	80 (49-111)	<0.001*
Specific Gravity		1.02 (1.01-1.03)	1.02 (1.01-1.03)	1.02 (1.01-1.03)	0.024*
White Blood Cells/L, median (IQR)		4.0 (0-8)	6.0 (0-12)	4.0 (1-7)	<0.001*
ALC admission (mg/dL), median (IQR)		1120 (82-2158)	938.5 (307.25-2184.25)	1173 (166-2180)	0.280
ALC Discharge (mg/dL), median (IQR)		1260 (324-2196)	1000 (134-1866)	1320 (367-2273)	0.095
Sex	Male (%)	112 (58.6)	18 (47.4)	94 (61.4)	0.115
	Female (%)	79 (41.4)	20 (52.6)	59 (38.6)	
ICU Admission		52 (27.2)	19 (50.0)	33 (21.6)	<0.001*
Inotropes (%)		20 (10.5)	10 (26.3)	10 (6.5)	0.001*
ACEIsARBs (%)		37 (19.4)	08 (21.1)	29 (19.0)	0.770
Dialysis (%)		08 (4.2)	08 (21.0)	0 (0)	<0.001*
Hematuria (%)		10 (5.2)	09 (23.7)	01 (0.7)	<0.001*
Proteinuria (%)		27 (14.1)	17 (44.7)	10 (6.5)	<0.001*
Leukocyturia (%)		55 (28.8)	22 (57.9)	33 (21.6)	<0.001*
Death (%)		44 (23)	23 (60.5)	21 (13.7)	<0.001*

*=p-value <0.05; a=Mann Whitney U test for continuous variables; b=Chi-square test for categorical variables

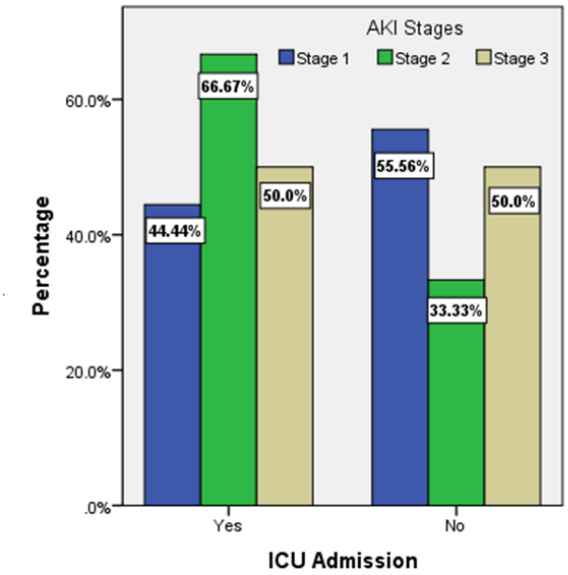

Figure No.1: Graphical Presentation of AKI stages with ICU admissions

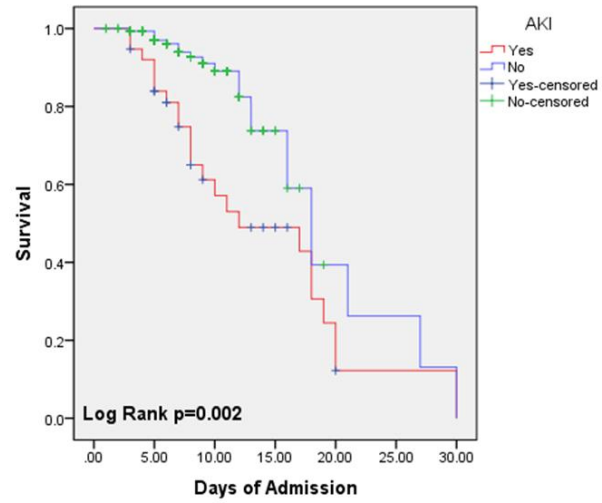

Figure No.2: Survival Probability of AKI cases as compared to no AKI Patients

Regarding protein presence, 1+ protein was found in 21 (11%), 2+ were present in 06 (3.1%). Regarding categorical variables, there were 112 (58.6%) males and remaining 79 (41.4%) were females; 134 (70.2%) were having comorbidities and amongst them major proportion 22 (11.5%) of the patients had hypertension, 17 (8.9%) had hypertension along with diabetes mellitus followed by 14 (7.3%) had hypertension, diabetes mellitus and ischemic heart disease and 11 (5.8%) had obstructive sleep apnea (OSA). There were 52 (27.2%) patients admitted in the ICU, 57 (29.8%) were admitted in HDU and remaining 82 (42.9%) patients were admitted in the ward. O_2 supplementation was invasive in 07 (3.7%), non-invasive among 123 (64.4%) and 61 (31.9%) did not need any supplementation and regarding outcome of patients, 44 (23%) had died.

Regarding gender, females (52.6%) had AKI and among males (47.4%), statistical significance of AKI vs no AKI was found with ICU admissions (p<0.001), inotropes (p=0.001), dialysis (p<0.001), hematuria (p<0.001), proteinuria (p<0.001), Leukocyturia (p<0.001) and death (p<0.001). (Table 1).

The ICU admissions were seen regarding AKI stages as 44.4% having stage 1, 66.67% having stage 2 and 50% having stage 3 were admitted in ICU (Figure I).

Regarding gender, 11.4% females had AKI stage 3, 10.1% had stage 1 AKI and 3.8% had stage 2 AKI and among males, 8.9% had AKI stage 1, 4.5% had stage 3 AKI and 2.7% had stage 2 AKI, statistical significance of various AKI stages was found with ICU admissions (p=0.004), inotropes (p<0.001), dialysis (p<0.001), hematuria (p<0.001), proteinuria (p<0.001), Leukocyturia (p<0.001) and death (p<0.001). (Table 2)

Table No.2: Patient Characteristics of Patients with no AKI and AKI Stages

Patient Characteristics	No AKI (n=153)	Stage 1 (n=18)	Stage 2 (n=6)	Stage 3 (n=14)	p-value[a, b]
Age (years), median (IQR)	61.0 (38.5-83.5)	67 (41.5-92.5)	62.5 (40.25-84.75)	70 (54.25-85.75)	0.048*
Length of Stay (days), median (IQR)	7 (1.5-12.5)	8 (0.75-15.25)	16 (0.75-30.75)	8 (0.75-16.75)	0.174
Creatinine admission (mg/dL), median (IQR)	1.06 (0.71-1.41)	1.04 (0.45-1.63)	0.91 (0.25-1.57)	3.62 (1.32-11.6)	0.002*
Creatinine Discharge (mg/dL), median (IQR)	0.93 (0.61-1.25)	1.45 (0.44-2.46)	1.73 (0.12-3.34)	4.8 (0.04-9.56)	<0.001*
eGFR admission (mg/dL), median (IQR)	68 (37-99)	60 (9.75-110.25)	67.5 (18.5-116.5)	15 (30-62.25)	0.002*
eGFR Discharge (mg/dL), median (IQR)	80 (49-111)	49.5 (1.75-97.25)	34 (17-85)	9.5 (1.75-17.25)	<0.001*
Specific Gravity	1.02 (1.01-1.03)	1.02 (1.01-1.03)	1.01 (1.0-1.03)	1.02 (1.01-1.03)	0.060
White Blood Cells/L, median (IQR)	4.0 (1-7)	5.0 (1-9)	9 (20.5-38.5)	6.0 (2-13)	<0.001*
ALC admission (mg/dL), median (IQR)	1173 (166-2180)	1502.5 (251.5-2753.5)	1166 (857.5-2189.5)	624.5 (67.5-1181.5)	0.029*
ALC Discharge (mg/dL), median (IQR)	1320 (367-2273)	1521.5 (594.25-2448.7	911 (502.5-1319.5	837.5 (283.25-1391.7	0.066

			5)	)	5)	
Sex (%)	Male	94 (83.9)	10 (8.9)	03 (2.7)	05 (4.5)	0.292
	Female	59 (74.7)	08 (10.1)	03 (3.8)	09 (11.4)	
ICU Admission		33 (63.5)	08 (15.4)	04 (7.7)	07 (13.5)	0.004*
Inotropes (%)		10 (50)	03 (15)	03 (15)	04 (20)	<0.001*
ACEIsARBs (%)		29 (78.4)	02 (5.4)	01 (2.7)	05 (13.5)	0.394
Dialysis (%)		01 (12.5)	00 (00)	00 (00)	07 (87.5)	<0.001*
Hematuria (%)		01 (10)	03 (30)	02 (20)	04 (40)	<0.001*
Proteinuria (%)		10 (37)	04 (14.8)	03 (11.1)	10 (37)	<0.001*
Leukocyturia (%)		33 (60)	09 (16.4)	04 (7.3)	09 (16.4)	<0.001*
Death (%)		21 (47.7)	10 (22.7)	05 (11.4)	08 (18.2)	<0.001*

Table No.3: Adjusted and Unadjusted OR for AKI presence in patients

Variables	Unadjusted OR	Adjusted OR	p-value
ICU Admission	3.64 (1.729-7.648)	0.46 (0.114-1.88)	0.282
Proteinuria	11.58 (4.68-28.63)	3.10 (0.832-11.54)	0.092
Leukocyturia	5.0 (2.36-10.59)	1.59 (0.562-4.50)	0.382
Hematuria	47.17 (5.75-386.69)	10.74 (1.03-111.91)	0.047*
Dialysis	34.32 (4.08-288.99)	18.17 (1.57-210.40)	0.020*
Inotropes	5.11 (1.94-13.41)	2.39 (0.62-9.24)	0.206
Outcome	9.64 (4.34-21.38)	6.98 (1.76-27.71)	0.006*

*p<0.05; OR=Odds Ratio

DISCUSSION

AKI is frequently observed in covid-19 and carries poor outcome. In our study AKI occurred in total 38 (19.8%) patients and out of them 8(4.2%) patients had severe AKI and required dialysis. Regarding AKI staging, stage 1 was present among 18 (9.4%) patients, 06 (3.1%) had stage 2 and 14 (7.3%) had stage 3 AKI. The patients in ICU developed AKI more frequently stage 1 15.4%, stage 2, 7.7%, and stage 3 by 13.5% respectively. It was higher from what was reported from Singapore which showed incidence of AKI was 8.1%, out of them , (68%) were at AKI stage 1 ,(16%), were at in stage 2 and (16%) stage 3. It further showed that AKI was associated with high mortality[17]. Data from Mexico showed prevalence more than our data and there prevalence of AKI was 58.6%. In-hospital mortality was significantly higher in patients those patients who had stage AKI stage 3 and AKI stage 2 (68.7%) or those who required dialysis compared with those with AKI stage 1[18]. These findings were similar to our study.

One large study from US done on 22,122 patients from different hospitals showed incidence of AKI among Covid-19 patients to 30.6%. and dialysis requiring AKI 8.5%[19]. These findings were very much comparable to our findings. Another study of 3993 patients from USA showed very high prevalence of AKI (46%) of which 19% required dialysis. The proportion of stages were as follows stage 1,2 and 3 AKI were were 39%, 19%, and 42%, respectively. 24% of COVID-19 patients were admitted to ICUand (76%) of them experienced AKI. In hospital mortality was 50% in patients with AKI as compared to 8% without AKI[20]. This study showed high prevalence of AKI among US population. One multicenter study of US population published of almost 6,000 patients showed almost similar results. AKI was found in (36.6%) of patients. The peak stages of AKI were stage 1 in 46.5%, stage 2 in 22.4% and stage 3 in 31.1%. Out of these patients, 14.3% required renal replacement therapy. AKI was primarily seen in patients on mechanical ventilation[21].

The variations in the prevalence of AKI in COVID-19 if different countries and regions may be partly explained by the fact that they these studies use different inclusion criteria. Second different ethnic, demographic groups and presence of comorbid also play a major role in the outcome of the disease. That may be the reason few studies have very high prevalence and few have very low prevalence of AKI.

CONCLUSION

We found in our study that AKI is a relatively common complication observed among patients hospitalized with COVID-19. It is linked to poor outcome and high mortality.

Author's Contribution:

Concept & Design of Study:	Muhammad Sajid Rafiq Abbasi
Drafting:	Maryam Masud, Khawar Sultan
Data Analysis:	Uzma Rehman, Sajid Nasim, Rukhsana Manzoor
Revisiting Critically:	Muhammad Sajid Rafiq Abbasi, Maryam Masud
Final Approval of version:	Muhammad Sajid Rafiq Abbasi

Conflict of Interest: The study has no conflict of interest to declare by any author.

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Original Article

Analysis of Depression and Anxiety Prior and After Coronary Artery Bypass Graft Surgery and their Association with Age

Shafqat Hussain and Muhammad Moeen

ABSTRACT

Objective: The objective of this study is to demonstrate the anxiety and depression scores pre and post-Coronary after bypass graft surgery and the effect of age in changing disorder scores.

Study Design: A Comparative Analytical Study

Place and Duration of Study: This study was conducted at the department of Cardiac Surgery in Ch.Pervaiz Elahi Institute of Cardiology Multan from June 2020 to June 2021.

Materials and Methods: A total of 50 patients participated in the study and were divided into 4 distinct age groups. The patients were required to fill HADS 2 days before and 10 days after the surgery and then anxiety and depression scores were analyzed on the basis of answers given by patients in the questionnaire. The difference between pre and post-surgery was calculated and the increased scores were evaluated. Spearman correlation between age and difference scores was calculated to assess the effect of age on depression and anxiety scores. McNemar tests and ANOVA procedure were also conducted with 'age group' as a factor.

Results: The number of patients who filled the HADS reduced after the surgery irrespective of the anxiety and depression scores before surgery. After analysis, it was discovered that 30% of patients prior while 20.5% after the surgery were anxious, while 22.7% were depressed before surgery and 13.6% after surgery. The depression score also reduced after surgery but the number of high scorers remained the same. A negative co-relation between age and anxiety was calculated (Spearman rho = -.200; p = 0.02) but not with depression (Spearman rho = -.111; p = 0.19).Younger patients showed a significant decline in anxiety after the surgery but had high anxiety scores before surgery ($p<0.05$), this decline was not seen in depression scores.

Conclusion: As the results reflect, the patients are more mentally stressed before surgery and this disorder must be treated. Younger patients showed reduced symptoms after the surgery and fewer symptoms change is observed in elderly patients.

Key Words: Anxiety, depression, Coronary artery bypass graft, Coronary artery disease, aging disorders.

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INTRODUCTION

Almost 20-45% of people with coronary heart disease have been diagnosed with depression [1]Similarly, anxiety has also been found to be prevalent in 20-55% of such patients[2]. These incidences of these mental disorders were also observed in patients who opted for CABG surgery[3]. Depression is perceived as a significant risk factor in the deposition of arteriosclerotic plagues in coronary arteries[4].

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The pathological relationship between the two diseases can be attributed to hypercortisolaemia related factors, including insulin resistance, or due to sympathetic vagal dys-balance caused by irregular blood pressure, unhealthy lifestyle, or smoking habits[5]. Depression not only contributes to primarily causing coronary heart disease but can also appear during secondary and tertiary preventive techniques: Physical and psychosocial morbidity is increased by presurgical depression and postsurgical depression after 6 months and 5 years CABG-surgery[6]; preoperative depression can be an important indicator of mortality in one month following the surgery[7]; depressed patients undergoing CABG surgery are expected to have diminished functionality and health status benefits within 6 months following the surgery[8], and depression appearing after the incidence of myocardial infarction (MI) reduces the probability of secondary CHD prevention after four months of MI[9].

Depressed patients with MI have more health costs than non-depressed patients. According to Canadian research, depressed myocardial patients have 41% more medical

costs in the first year after myocardial infarction than MI patients who are not depressed[10].

On the contrary, anxiety doesn't independently contribute to the occurrence of MI. While Depression increases the likelihood of postsurgical morbidity and mortality, anxiety can only pose such risk if it appears as acute preoperative anxiety whereas trait anxiety hasn't yet proved to be fatal[11]. However, anxiety disorders do increase the chances of sudden cardiac death. This phenomenon is due to pathophysiologically ventricular arrhythmias[12].

In the present time, elderly patients opt more for CABG surgery as compared to the last 10 years. Every year in the UK, 25 000 people undergo CABG surgery, and among them, 1/4th of the patients are above the age of 70 and 8% of them are above the age of 75[13]. Elderly people have a great risk of perioperative mortality. Among various mortality-causing factors, age is considered a significant risk factor[14]. Elderly people are affected by depression the most when compared with other physical disorders[15]. The effect of age on depression and anxiety has been discussed in previous studies.[16]

The objective of this study is to demonstrate the anxiety and depression scores pre and post-CABG surgery and the effect of age in changing disorder scores**.**

MATERIALS AND METHODS

Cardiac Surgery in Ch.Pervaiz Elahi Institute of Cardiology Multan from June 2020 to June 2021. The patients gave their written consent to become part of the survey. All the patients who were included in the study were conscious, had no neurological deficits, were admitted to the hospital on a weekday, had no acute coronary syndrome, didn't have dementia, and didn't undergo CABG surgery in an emergency. The levels of depression and anxiety were noted 2 days before the CABG surgery and also 10 days following the surgery. All the participants of the study were divided into four groups based on their age by means of quartile prior to the conduction of the study. The age groups were: 30-35 years (n=10), 36- 46 (n=10), 47-60 (n=15), 61-72 (n=15).

The patients were administered to specially developed, self-report questionnaire for patients with physical illness, "Hospital Anxiety and Depression Scale" (HADS) to measure depression and anxiety levels in patients[17]. The questionnaire included 14 questions, 7 to analyze depression and the other 7 to examine anxiety. The questions were related to symptoms of these disorders in the past week. Four multiple options were given to select the one option that best described the symptom and were different for every question. The values obtained by HADS could be analyzed in two ways. Firstly, the scores were simply counted to know the number of symptoms of the disorders. On the other hand, the scores obtained were used to classify patients with increased and non-elevated depression and anxiety levels. According to previous studies[18], it was observed that the average score for elevated anxiety and depression is 8[19]. The sensitivity for this cut-off is 0.70 and specificity is 0.90[19].

Statistical Analysis: All statistical analysis was carried out using SPSS (version 18). The McNemar test was used to analyze the significance of the difference in the proportion of patients with high anxiety and depression levels before and after the CABG surgery. The difference in values and anxiety were found out by using the principle of subtraction: values of variables 10 days after the surgery were subtracted from the respective values 2 days before the surgery. A positive result demonstrated a higher pre-surgical level while the negative results showed an elevated post-surgical level of the studied variables. Spearman rho correlations were developed between patient's age and the difference of the analyzed variables in the HADS to ascertain the relationship between age and depression and anxiety, respectively. Mean along with standard deviation was calculated for all the categorical data. Additionally, ANOVA analysis was conducted to detect an association between "age" and pre and post-surgical variables (time). The "Fishers Least Significant Differences" test (LSD) was used to test the significance of this interaction. A p-value less than 0.05 were considered statistically significant.

RESULTS

A total of 50 patients were included in the study, out of which two patients (4.0%) were not able to fill the HADS after 10 days of CABG surgery as they had suffered medical problems after the surgery. However, there was no proof that these medical problems were age-dependent although the patients who suffered them were more than the age of 70 (Table 1).

The percentage of patients filling the HADS varied with ages (Table 1). This difference remained insignificant prior to the surgery(Fisher's exact=0.10). Whereas, 10 days following the surgery, significant difference was observed (Chi-square = 14.5, df = 2; $p < 0.001$). As the age group increased, the number of patients filling HADS decreased. However, statistically significant difference was found only when the age group 30-35 years was compared with 61-72 years group (Chi-square = 10.2; df = 1; $p < 0.001$) and age group "30–35 years" with age group "47– 60 years" (Chi-square = 3.6; df = 1; $p = 0.01$).

Data analysis for anxiety demonstrated that 30% of patients prior while 20.5% after the surgery were anxious, whereas 10.6% of these patients had high levels of anxiety both before and after the surgery. Similarly, 22.7%, 13.6%, and 6.4% of patients were depressed at prior, after, and at both times of the surgery, respectively. However, the percentage changes for both disorders were not significant according to the McNemar Test.

Moreover, a significant correlation relation between change in anxiety and age was observed (Spearman rho = -.200; $p = 0.02$), but age did not have any significant

effect on change in depression scores (Spearman rho = -.111; p = 0.19). This indicated that younger patients have a large difference between levels of anxiety before and after the surgery. The same results were obtained through ANOVA analysis. The study proved a significant interaction between the factors "age group" and "time" for anxiety (F(2, 92) = 2.87; p = 0.02), and a significant effect for the factor "time" (F(1, 93) = 9.85; p = 0.001). The anxiety scores were significantly reduced 10 days after surgery when compared with the values of 2 days before surgery. These changes were, however, age-dependent as LSD posthoc test indicated significant changes only in the youngest age group, 30-35 years (Table 2). The results of this test are also supported by the nonparametric McNemar test, the youngest age group showed diminished anxiety. (McNemar = 4.01; df = 1; p = 0.02).

Table No.1: Percentage of a medical complication that detained patients from editing the HADS and proportion of HADS completed divided into age groups (N = 50)

Age groups (years)	Percentage of medical complications	Percentage of HADS filled in two days before CABG surgery	Percentage of HADS filled in ten days after CABG surgery
30-35 (10)	2.0%	100%	85.5%
36-46 (10)	6.0%	92%	82%
47-60 (15)	4.5%	96.7%	66.3%
61-72 (15)	12.7%	84.5%	52%
Total	6.3&	93.3%	71.45%

Table No.2: Mean values and Standard Deviation (SD) of anxiety and depression two days before and ten days after CABG surgery divided into four age groups (N=50)

Age group (years, N)	Anxiety two days before CABG surgery (mean, SD)	Anxiety ten days after CABG surgery (mean, SD)	Depression two days before CABG surgery (mean, SD)	Depression ten days after CABG surgery (mean, SD)
30-35 (10)	8.55 (5.51)	5.01 (4.5)	7.25 (5.22)	5.74 (4.45)
36-46 (10)	5.83 (2.58)	5.25 (3.28)	5.02 (3.82)	4.82 (4.34)
47-60 (15)	7.10 (3.5)	7.07 (4.25)	6.44 (4.75)	5.55 (4.24)
61-72 (13)	6.75 (4.85)	5.44 (4.07)	5.88 (2.75)	5.45 (4.94)

Table No.3: Number and percentages [%] of high-scorers in anxiety and depression (HADS value ≥ 8) two days before and ten days after CABG surgery divided into four age groups (N=50)

Age groups (years, N)	Anxiety high-scorers 2 days before CABG surgery	Anxiety high-scorers 10 days after the CABG surgery	Depression high-scorers 2 days before CABG surgery	Depression high-scorers 10 days after CABG surgery
30-35 (10)	7 (70%)	5(50%)	6(60%)	3(30%)
36-46 (10)	5(50%)	3(30%)	3(30%)	4(40%)
47-60 (15)	6(40%)	4(26.7%)	4(26.7%)	3(20%)
61-72 (13)	4(30.8%)	6(46.1%)	6(46.1%)	5(38.5%)

On the other hand,depression scores do reduce after surgery but the number of high-scorers does not reduce with time (Table 3 represents number of high scorers). Whereas, significant correlation was found between depression and factor “time” ($p<0.05$).

DISCUSSION

The effect of age was seen on the completion of HADS after the surgery and not before it. But it is to be noted that this inability to complete HADS was not because of the medical complications the patients faced after the surgery. It may be due to weakness after the surgery, physical impairment, or the research may affect the mental status of elderly patients. HADS also addressed the psychological concerns of the participants. Most of the old patients avoid answering questions related to this due to which it was unable to know about their mental comorbidity. It was initially assumed that the patients who were anxious or depressed before the surgery, will not fill the HADS after surgery. But this assumption was proved wrong after analyzing the data as no relation could be seen between anxiety and depression score before surgery and incompletion of HADS after surgery. The results of the study are also congruent to clinical practices.

The decline in anxiety and depression scores suggests that the patients were under mental stress before the surgery. Our results are consistent with the other literature studies[20]. Also, anxiety and depression scores are inversely proportional to age. By studying this relation and the results of the ANOVA procedure, it was revealed that younger patients have a greater decline in scores before and after surgery.

The varying pattern of changing disorders score with age may be due to some reasons. Patients, both young and old, may think about death before surgery because it is a common complication in CABG surgery. The

elderly patients look forward to the relief after the surgery than the strain imposed on CHD. On the other hand, young patients, suffer fewer symptoms of CHD. The pattern may also be because elderly patients often think about death and the stimulus if death is not new to them so they are less anxious at the thought of it. But young patients are not so sure of their death and often estimate their age. So, they are more afraid of the loss and experience anxiety at the thought of losing all those years of their life. One of the elderly patients of our study revealed that old people suffer CHD for many years of their life so they are used to the feeling of being sick so the stimulus is not new to them.

Unexpectedly, only 6.4% of patients had increased depression scores both before and after surgery. Due to the longitudinal design of our study, such a low score was obtained. While other studies on this subject only measure scores at the one-time point.

CONCLUSION

As the results reflect, the patients are more mentally stressed before surgery and this disorder must be treated. Younger patients showed reduced symptoms after the surgery and fewer symptoms change is observed in elderly patients.

Author's Contribution:

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Data Analysis:	Muhammad Moeen
Revisiting Critically:	Shafqat Hussain, Muhammad Moeen
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Conflict of Interest: The study has no conflict of interest to declare by any author.

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Original Article

Frequency of Subclinical Hypothyroidism in Patients with Acute Decompensated Heart Failure

Subclinical Hypothyroidism with Heart Failure

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ABSTRACT

Objective: To Determine the frequency of subclinical hypothyroidism in acute decompensated heart failure patients.
Study Design: Descriptive Cross-Sectional Study
Place and Duration of Study: This study was conducted at the Cardiology Department, DHQ Teaching Hospital, Bannu over a period of 12 months from August 2018 to July 2019.
Materials and Methods: One hundred and seventy-eight (n=178) adult patients above eighteen years of age admitted to cardiology department with acute decompensated heart failure (ADHF) were enrolled in the study. All the patients were evaluated for subclinical hypothyroidism (SH) through lab investigations and frequency of SH was estimated.
Results: A Total of 178 patients with ADHF were evaluated for SH, out of which 61.8% (n=110) were male and 38.2% (n=68) were females. Mean age of patients was 54.4±12.3 years. The mean TSH, Free T4 and LVEF (%) were 3.6± 2.91, 1.3±0.3 and 35.9±4.8, respectively. Subclinical hypothyroidism was present in 25.8% (n=46) of patients. The most frequent 28.9% (n=26) age group was 18-50 yrs. and majority of them were female 26.5% (n=18) patients. SH was more frequently 28.7% (n=39) found in patients having LVEF <35% with no statistical significance (p=0.12).
Conclusion: Subclinical hypothyroidism was frequently (almost 1/4th) determined in patients admitted with acute decompensated heart failure. We recommend screening of all the patients presenting with ADHF on routine basis.
Key Words: Acute decompensated heart failure (ADHF), sub clinical hypothyroidism (SH)

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INTRODUCTION

Acute decompensated cardiac failure is a frequently observed phenomenon in patients presenting with acute respiratory embarrassment and characterized by sudden onset shortness of breath due to filling of pulmonary interstitial and alveolar spaces with fluid.[1] Thyroxine is a hormone produced by thyroid gland having a prominent role in controlling heart rate, systemic vascular resistance and contractility. Hyperactive functioning or hypoactive thyroid gland can lead to potentiation of heart failure (HF) manifestations.[2]

It has recently been reported that subclinical hypothyroidism is associated with atherosclerosis,[3] development of HF,[4] and cardiovascular death.[5] Though it is less symptomatic and not associated with mobility problems,[6] but seems to be associated with cardiac function, exercise capacity, and hemodynamic parameters. However, little is known about the clinical effect of sub-hypo on HF patients.

Hayashi T, et al observed 21% subclinical hypothyroidism in patients admitted with heart failure, 2% subclinical hyperthyroidism, and 35% had low-T3 syndrome. Furthermore, there was poor survival rate with escalated risk of cardiac events amongst subclinical hypothyroid patients.[7] Khan MA, et al reported 9.42% Subclinical hypothyroidism in Pakistan[8].

It was also observed in a study that levothyroxine replacement therapy in patients who do not have accompanying heart failure decreases systemic vascular resistance and mortality; increases cardiac contractile force and hence stroke volume.[9] However, the effect of subclinical hypothyroidism on heart failure prognosis is yet to be determined and whether treatment with thyroxine in SH having heart failure improves the

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prognosis is still controversial and needs further research.[10]

In a recent study, no benefit in terms of cardiac events, quality of life and mortality following levothyroxine therapy reported in elderly patients.[11] Frey et al. reported that about 4.6% heart failure patients had evidence of SH but treatment of subclinical hypothyroidism with thyroxin did not lessen cardiac hospitalization or death.[12]

Several studies have shown that subclinical hypothyroidism affects the prognosis in heart failure patients, and evidence is in favor of screening for subclinical hypothyroidism in these patients at presentation.[1,12]

Hence, our study is structured to estimate frequency of SH in patients presenting with ADHF in our local population. Currently, it is not suggested to perform routine screening for subclinical hypothyroidism in acute heart failure patients. If we find a frequent number of patients with SH in our ADHF population, screening of all the patients presenting with ADHF would be recommended on routine basis**.**

MATERIALS AND METHODS

This is descriptive cross-sectional study conducted at cardiology department, DHQ Teaching Hospital, Bannu from 17th august 2018 to 16th July 2019. One hundred and seventy-eight (n=178) adult patients over 18 years of age admitted to cardiology department with acute decompensated heart failure were enrolled in the study. Sample size was calculated using WHO Sample Size Calculator taking 95% confidence interval. Non-probability Consecutive sampling technique was used. Patients included in the study were having acute decompensated heart failure aged 18 to 70 years and of both genders. Patients excluded from the study were those taking levothyroxine, amiodarone, anti-thyroid medication, patients with a history of radioiodine therapy, pregnant and lactating women.

Hospital ethics committee granted approval for the study. Informed written consent was obtained by all the participants. After enrollment, details of illness and demographic profile of the patients were recorded. Biochemical measurements (TSH and Serum free T4) were done at the time of presentation. The researcher maintained data quality and compliance to the study protocol conducted all the study procedures and data collection. All the obtained data was recorded on the Performa. Data was analyzed through SPSS version 19.0. The numerical data like age, BMI (calculated as defined in operational definitions), LVEF, TSH and FT4 were presented as mean and standard deviation while the categorical data like gender, comorbidities (hypertension, diabetes, dyslipidemia and atrial fibrillation) and subclinical hypothyroidism were expressed as frequency and percentage. Effect modifiers like age, gender, BMI (calculated as defined in operational definitions), comorbidities (hypertension, diabetes, dyslipidemia & atrial fibrillation) and LVEF were controlled by stratification. Post stratification chi square test was applied and *P*-value $\leq$ 0.05 considered as significant.

RESULTS

A Total one hundred and seventy-eight (n=178) patients were evaluated as a diagnosed cases of acute decompensated heart failure (ADHF) for this study on predesign research proforma. Mean age was 54.4 ±12.3 (18 to 70) years. Male (61.8%) to female (38.2%) ratio was 1.6. The mean TSH, Free T4 and LVEF (%) were 3.6± 2.91, 1.3±0.3 and 35.9±4.8, respectively. Demographic, anthropometrics, clinical and laboratory parameters are tabulated in table 01.

Table No.1: Distribution of demographic, anthropometric, clinical and laboratory parameters

Variables	Mean	Std. Deviation
Age (years)	54.4	12.3
Lvef (%)	35.9	4.8
Height (meters)	1.8	0.1
Weight (kg)	74.1	10.3
Bmi (kg/m^2)	22. 5	4.1
Ft4 (ng/dl))	1.3	0.3
Tsh (miu/l))	3.6	2.9

Frequency of subclinical hypothyroidism was 25.8% (n=46) and the most frequent 28.9% (n=26) age group was 18-50 yrs. and majority of them were female 26.5% (n=18) patients. Sub clinical hypothyroidism was more frequently 28.7% (n=39) present with patients having LVEF <35% though it was not statistically significant (p=0.12) Frequency of age groups, baseline LVEF, BMI and subclinical hypothyroidism is illustrated in Figure 01. The most frequent risk factor for heart failure was HTN 26.4% (n=32). Frequency of Risk factors like hypertension, diabetes, dyslipidemia and atrial fibrillation are described in table 2.

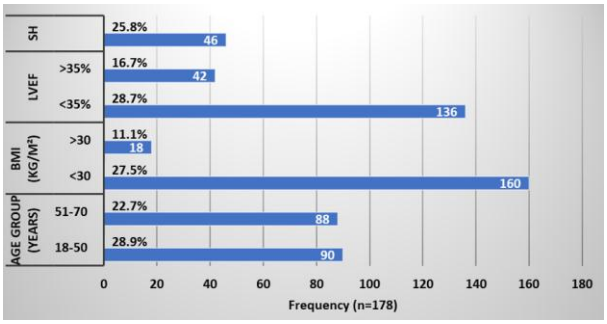

Figure No.1: Frequency of age groups, BMI, LVEF and Subclinical hypothyroidism

There was no statistical significant difference in frequency of SH across different effect modifiers (P>0.05 in all cases) as outlined in table 3.

Abbreviations; BMI: Body Mass Index, LVEF: Left Ventricular Ejection Fraction, SH: Subclinical hypothyroidism

Table No.2: Frequency of different comorbidities and their stratification with Subclinical hypothyroidism

Comorbidities		Subclinical hypothyroidism		Total	P-value chi-Square
		Present	Absent		
Hypertension	Present	32	14	46	0.789
		26.4%	24.6%	25.8%	
	Absent	89	43	132	
		73.6%	75.4%	74.2%	
	Total	121	57	178	
		100.0%	100.0%	100.0%	
Diabetes	Present	19	27	46	0.895
		25.3%	26.2%	25.8%	
	Absent	56	76	132	
		74.7%	73.8%	74.2%	
	Total	75	103	178	
		100.0%	100.0%	100.0%	
Dyslipidemia	Present	10	36	46	0.586
		22.7%	26.9%	25.8%	
	Absent	34	98	132	
		77.3%	73.1%	74.2%	
	Total	44	134	178	
		100.0%	100.0%	100.0%	
Atrial fibrillation	Present	27	19	46	0.750
		25.0%	27.1%	25.8%	
	Absent	81	51	132	
		75.0%	72.9%	74.2%	
	Total	108	70	178	
		100.0%	100.0%	100.0%	

Table No.3: Subclinical hypothyroidism (stratification with respect to age, gender, BMI and LVEF)

Demographic, Anthropometrics, clinical parameter		Subclinical Hypothyroidism		Total	p-value chi-square
		present	absent		
Age Groups (years)	18-50 (years)	26	64	90	0.348
		28.9%	71.1%	100.0%	
	51-70 (years)	20	68	88	
		22.7%	77.3%	100.0%	
Gender	Male	28	82	110	0.880
		25.5%	74.5%	100.0%	
	Female	18	50	68	
		26.5%	73.5%	100%	
BMI	<30 kg/m^2	44	116	160	0.132
		27.5%	72.5%	100%	
	>30 kg/m^2	02	16	18	
		11.1%	88.9%	100%	
LVEF	<35%	39	97	136	0.120
		28.7%	71.3%	100%	
	>35%	07	35	42	
		16.7%	83.3%	100%	

DISCUSSION

Hypothyroidism is a commonly encountered clinical condition with variable prevalence.[13] Effect of thyroid hormones on heart contractility, coronary vessels and the prognosis of SH in heart failure patients has recently been a topic of discussion and research. Symptomatic SH patients suffer from reduced exercise tolerance, and delay in relaxation phase of left ventricle might gravely hamper filling phase of ventricle during exercise leading to left ventricular systolic dysfunction.[14] Several studies have also shown that subclinical hypothyroidism affects the prognosis in heart failure patients, and evidence is in favor of screening for subclinical hypothyroidism in these patients at presentation.[1,9] Our results showed that there were 25.8% (n=46/178) of patients in the study sample who were diagnosed with SH as per our operational definition. The most frequent 28.9% (n=26) age group was18-50 yrs with little female 26.5% (n=18) vs 25.5% (n=28), predominance thought insignificant (p=0.88).

There was no statistical significant difference in frequency of SH across different effect modifiers like gender, age, BMI, baseline LVEF and baseline comorbidities (P>0.05 in all cases).

Our results are similar with other studies on the subject**.** In a recent study, Hayashi T, et al assessed the prevalence and prognostic effect of subclinical hypothyroidism in acute decompensated cardiac failure patients. According to their findings, about 69% patients admitted with ADHF were euthyroid, 21% were having evidence of subclinical hypothyroidism and 35% had low T3 syndrome. Survival rate was reported as poor along with increased frequency of cardiovascular events.[10]

In a local study, Ullah A, et al found that about 3.98 % adult patients aged more than 15 years admitted with congestive heart failure had subclinical hypothyroidism with males affected predominantly and those with age < 60 years.[15]

According to a study conducted by Mahal S and her colleagues, exceptionally high percentage (51%) of patients admitted with ADHF had biochemical SH with history of repeated admissions in 31% of cases (P < .001). There was no significant increase in SH patients in terms of morbidity and mortality.[16] Although we did

not assess the effect of SH on patient's outcome in the present study due to time constraints, yet we suggest future studies in this direction. According to another study, 8.1% patients with ADHF suffered from subclinical hypothyroidism and 2.6% from subclinical hyperthyroidism.[17] Nanchen D, et al reported the occurrence of subclinical hypothyroidism in ADHF around 1.4%.[18]

Several studies have demonstrated that levothyroxine therapy in elderly patients with SH can improve left ventricular function and reduce the rate of hospitalizations in these patients.[19-23] We recommended further clinical trials to evaluate the role of levothyroxine in CHF patients on rate of hospitalizations and mortality in our population.

CONCLUSION

Sub clinical hypothyroidism was frequently observed in patients admitted with acute decompensated heart failure.

Recommendation: We recommend further multicenter research trial to confirm it on large number of patients so that routine screening SH in patients presenting with ADHF could be suggested.

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Original Article

Emotive Elements before Elective Obstetric Surgery from Patient Standpoint: A Comparative Study

Choice of Veginal Birth or C-Section of Pregnant Women

Bushra Zulfiqar, Kausar Parveen and Shagufta Perveen

ABSTRACT

Objective: To observe the emotional state of the pregnant women while making the choice of veginal birth or elective caesarean section cesarean section.

Study Design: Cross sectional study

Place and Duration of Study: This study was conducted at the Gyne and Obs, Al-Tibri Medical College and Hospital, Karachi between the duration of November 2020 to April 2021.

Materials and Methods: A total of 100 pregnant women were included in this study and the all the patient were providing with survey questioner with self-explanatory and open ended questions 42 responses were received including 30 male and 12 female nursing students. A survey of 28 close- and open ended questions was developed after extensive literature review.

Results: Among 100 patients average 45.86% experienced difficulties during house work, TV watching and other activities after surgery. Average 72.67% of the total 100 patients were furious of the surgery and responses, majority of students were male 71% and 29% were afraid of losing fetus, uterus and death. Only 33.33% female were expressive regarding their feared and reservation regarding the surgery. 68%, 36% and 10% observed to be distressed, sad and happy respectively.

Conclusion: It has been observed that the most the pregnant women have very odd fear while and most the patient were very distress and doubtful for the procedure outcomes. Very few were relaxed and happy.

Key Words: Elective surgery, caesarean section, vaginal birth, pregnant.

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INTRODUCTION

Having child is the most important feeling and most delicate experience for almost every woman. Various factors influence the decision of the child birth. In a systematic review there are four crucial factors are reported for the women's child birth experience that are Personal Expectation, attitude and support of the caretakers and relationship between caretaker and patient[1]. "Patient choice" is very much prevailed in obstetricians and gynecologist[2]. Caesarian section rate is highly increasing day by day because of the maternal consent towards worthless or unnecessary caesarian delivery of baby without medical reasons[3,4].

Previous child birth experience effects very much while women decides for the caesarian delivery negative pervious child birth experiences is highly associated with the request of caesarian section[2,5,6]. Negative child experience also develops child birth fear and study suggested that this is not only the factor which compels the women to go for elective caesarian delivery[7]. Child birth fear is a multifarious feeling of anguish which stretched from worries to anxiety which ultimate effects the everyday life till the birth time[8]. In Finland, Sweden and UK 22 percent of the elective caesarian section were because of the childbirth fear[9]. Emergency caesarian and instrumental child birth are also highly associated with the childbirth fear[21]. In western countries the pregnant women got the right to choose the elective caesarian surgery but as per the legislation the caesarian surgery is not the option they can chose for them self. Studies suggested that the mother choice is really hard to evaluate due to several co-founding factors.[10,11]

The Aim of this study is to evaluate the mental state and emotional status of the pregnant female which are going towards the elective surgery. This study can help will help the medical health care worker working in maternity homes and midwives to deal with the pregnant patient. The odd results can help in suggesting the counselling sessions to the patients.

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MATERIALS AND METHODS

After IRB approval, this cross sectional study carried out at Al-Tibri Medical College and Hospital, Gyne & Ops ward. 100 pregnant women were enrolled after taking proper informed consent they were provided a survey questioner, contains self-explanatory and open-ended question to assess the emotional state of the patient toward the upcoming elective surgery. And the responses of the patients were recorded as the frequency basis.

RESULTS

Among 100 pregnant women 92 and 98 percent women faced difficulty in house hold working and walking (Table 1)

The least fear of losing fetus during surgery and dying due to spinal anesthesia was observed in pregnant women (Table 2)

48 percent women were afraid but they accepted the facts while on other hand 20 percent of the women were not afraid and accepted the facts while 32 percent of the women were very much afraid (Table 3)

Only 10 percent patients were happy while going towards the elective surgery (Table 4)

Table No.1: Frequency of faced difficulties as a Result of Elective Surgery

	Yes	No	Frequency
Housework activities	92	8	**92**
Walking	98	2	**98**
Others	28	72	**28**
n= 100			

Table No.2: Frequency of Fear and Acceptance of Elective Surgery

	Yes	No	Frequency
of surgical procedure	82	18	82
of losing Uterus	34	66	34
of Losing Fetus	18	82	18
of dying during surgery	48	52	48
of dying due to general anesthesia	38	62	38
of dying due to spinal anesthesia	23	77	23
of expected next surgery	78	24	78
n=100			

Table No.3: Frequency of consternation in pregnant women / Declaring

	Yes	No	Frequency
very much afraid, but accepted the fact	32	68	32
somewhat afraid, but accepted the fact	48	52	48
not afraid and accepted the fact	20	80	20
n=100			

Overall 45% faced difficulties after the caesarian surgery, 72% have fear but accepted the fact and only 33% were showed consternation while going towards the elective (Table 5).

Table No.4: Feelings of pregnant women towards undergoing Elective Surgery

	Yes	No	Frequency
Distress	68	32	68
Doubt as to the outcome of the surgery	28	72	28
Sadness	36	64	36
Happiness	10	90	10

Table No.5: Difficulties, fear and acceptance etc. among pregnant women

Difficulties	45.86%
Fear & Acceptance	72.67%
Consternation	33.33%

DISCUSSION

This study suggested that the most of the women faced difficulties in fulfilling their chores and walking. It is because of the surgical cut/wound and immune responses which body takes against any surgery processes. It is evident that the postoperative duration eventually effects the women's experience due to the physical restriction and pain[12,13]. In our sample there is great percentages of the pregnant women were observed having the fear of losing their fetus and dying due to spinal anesthesia. It may be due to the lack of awareness regarding the basic medical knowledge and procedures. No evident study was found during the literature survey in this regards. A study reported 14 percent birth related fear[14] but in our study 48 percent fear was observed. Multiple studies suggest that the birth related fear is a strongest factor which contributes in elective cesarean surgery[15-18]. The most important factor which tends women to go for elective ops surgery is childbirth related fear. Constant counselling reflects significant effect in decision making for pregnant women. It is reported in the literature that the fear of pain is directly allied with the childbirth related fear[19]. Gynecological information of all the aspects of the caesarean section is vital for the women who opt caesarean section where no medical symptoms are present. A Study reported that 41 percent women were furious about the surgery but didn't express, similarly in this study 33 percent women were constraining about their fear regarding the upcoming cesarean surgery (ref). It was observed in this study that overall only 10 percent of patients were happy going towards the elective caesarian surgery which is because of the social culture of the Pakistan and attitude of the midwives and nurse of the medical centers.

One of the limitation of the study was small size of the women undergoing caesarean surgeries that is why it is

hard to make it generalize the finding. More longitudinal research needs to be done for better picture of the finding in the aspect with a lager sample size.

CONCLUSION

In a nutshell the finding of the study is that there multiple confounding factors which can effects the emotional state of the pregnant women. Most of them were furious about the process and very few were happy with the caesarean surgery procedure.

Author's Contribution:

Concept & Design of Study:	Bushra Zulfiqar
Drafting:	Kausar Parveen
Data Analysis:	Shagufta Parveen
Revisiting Critically:	Bushra Zulfiqar,
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Original Article

Patterns of Interface Dermatosis - A Comparative Analysis of Clinical and Histopathological Features

Momina Khadija Abbasi[1], Shameela Majeed[1], Nabeela Naeem[1], Amatul Naval[1], Mehak Ali[1] and Mehreen Fatima[2]

ABSTRACT

Objective: To analyze the frequency of various histopathological patterns of interface dermatitis and to compare the clinical and histopathological diagnosis.

Study Design: Comparative, cross-sectional study

Place and Duration of Study: This study was conducted at the Histopathology Department, AMC (Army Medical College Rawalpindi), National University of Sciences & Technology (NUST) Islamabad and Combined Military Hospital (C.M.H) Rawalpindi, Military Hospital (MH) Rawalpindi, from December 2018 to December 2019.

Materials and Methods: Skin biopsies of the clinically diagnosed cases of interface dermatitis/lichenoid dermatitis were collected over a period of one year and were categorised on the bases of intensity and type of interface inflammation, prominent histopathological features and then compared with the clinical features.

Results: A total of 115 samples were collected from the patients who were clinically diagnosed with interface dermatitis or had a previous history of interface dermatitis and presented with a new skin lesion. Histopathology confirmed interface dermatitis in 97 cases. Lichen planus (58.8%) was found to be the most common cell rich type. Erythema multiforme (50%) was the most common cell poor variant and amid the sub-epidermal blistering disorders, bullous pemphigoid (62.5%) was the most frequent blistering disorder showing interface dermatitis.

Conclusion: Interface dermatitis is a clinically diverse entity and clinicopathological correlation helps in differentiating diseases showing interface dermatitis and arriving at an accurate diagnosis.

Key Words: Dermo-epidermal junction, interface dermatitis, lichenoid dermatitis, vacuolar alteration

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INTRODUCTION

Skin is a large organ that not only acts as a barrier to the factors affecting internally and externally but also manifests many of the clinical signs of internal diseases[1]. A number of skin diseases are categorized as superficial inflammatory dermatosis based upon the pattern of tissue reaction and inflammation [2]. One of the categories of the superficial inflammatory dermatosis includes a group of clinically diverse and least known inflammatory skin disease known as interface dermatitis/lichenoid tissue reaction which is characterized by a particular set of histopathological elements [3].

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Diagnosis of interphase dermatitis/lichenoid tissue reaction may present a problem due to variations in clinical and histopathological patterns. In interface dermatitis the principal pathology involves the muddling of dermo-epidermal junction by inflammatory cells comprising mainly of lymphocytes[4]. A number of diseases depending on type, distribution and density of inflammatory cells at the dermoepidermal junction are included in interface dermatitis however they occasionally present the same clinical picture. Thus in order to initiate appropriate therapy the differentiation of one from the other becomes necessary. Clinicopathological correlation is crucial to speculate the sequence and the ideal treatment of the disease. Clinicopathological correlation of lichen planus, a prototypic disease of interphase dermatitis/lichenoid tissue reaction showed that the diagnostic accuracy rate increases by hundred percent when confirmed histopathologically [5,6].

Various histological patterns are seen in interphase dermatitis such as mild or dense inflammatory infiltrate comprising mainly of mononuclear cells, basal cell degeneration causing hydropic change, apoptosis leading to formation of civatte or colloid bodies and pigmentary incontinence due to damage to basal keratinocytes and melanocytes.

Lymphocytic rich Lichenoid Tissue Reaction/Interface Dermatitis

1. Discoid lupus erythematosus (LE)
2. Fixed drug eruption
3. Keratosis lichenoides chronica
4. Lichen nitidus
5. Lichen planus
6. Lichen striatus
7. Lichenoid drug reactions
8. Lichenoid and granulomatous dermatitis
9. Lichenoid mycosis fungoides [7]

Lymphocyte-Poor Tissue Reaction/Interface Dermatitis

1. Acute graft-versus-host skin disease
2. Autoimmune connective tissue skin diseases
3. Acute cutaneous LE
4. Subacute cutaneous LE
5. Dermatomyositis
6. Mixed connective tissue disease
7. Erythema multiforme
8. Erythema multiforme minor
9. Erythema multiform major (Stevens Johnson Syndrome)
10. Interface dermatitis of HIV infection
11. Morbilliform exanthems
12. Virus-induced
13. Drug-induced
14. Paraneoplastic pemphigus
15. Pityriasis lichenoides Chronica [8]

Granulocyte subepidermal blistering disorders showing interface dermatitis

Cell Rich

1. Eosinophil predominate
2. Bullous pemphigoid
3. Neutrophil predominate
4. Dermatitis Herpetiformis
5. Epidermolysis bullosa Acqusita
6. Mixed neutophil and eosinophil
7. Linear IgA disease
8. Bullous SLE

Cell Poor

1. Epidermolysis bullosa hereditary
2. Diabetic Blister
3. Porphyrias
4. Blister in comatosed patients [2]

The statistics of histopathological patterns of interface dermatitis have not been well documented in our setup. The purpose of designing this study is to address this particular problem precisely.

MATERIALS AND METHODS

The study was undertaken at the department of histopathology of Army Medical College RWP. The department of dermatology, Combined Military Hospital and Military Hospital Rawalpindi collaborated in executing the study. The study was conducted during 12 months time from December 2018 to December 2019. A detailed medical history was obtained from all the participants of the study. Elliptical full thickness skin biopsy was taken. The prominent histopathological features were included in the diagnostic, intensity of interface inflammation and then clinical features were compared with the results afterwards.

RESULTS

The present study includes one hundred and sixteen patients and the average age was 38 years (SD $\pm$ 19.68) with minimum age of one year and 85 years as maximum age. Majority of patients were male (74.1%) while 25.9% were female. Out of 115 patients, 81 (69.8%) were diagnosed as interface dermatitis both clinically and histopathologically. Sixteen cases (13.8%) were considered negative clinically for interface dermatitis but on histopathological examination they were confirmed to have interface dermatitis. Eighteen (15.5%) cases were identified with interface dermatitis clinically only while on histopathological examination they were diagnosed with diseases other than interface dermatitis**.** According to histopathological diagnosis, majority of patients; 67 (57.8%) out of 115, were diagnosed as cases of lymphocyte rich IFD. Lymphocytic poor IFD was seen in 21 (18.1%) patients. Granulocyte blistering disorders showing interface dermatitis was confirmed in 9 (7.8%) cases. Nineteen (16.4%) patients were corroborated with diseases which differed from interface dermatitis. The most prevalent disease was found to be lichen planus (figA) rich variant (59.7%).

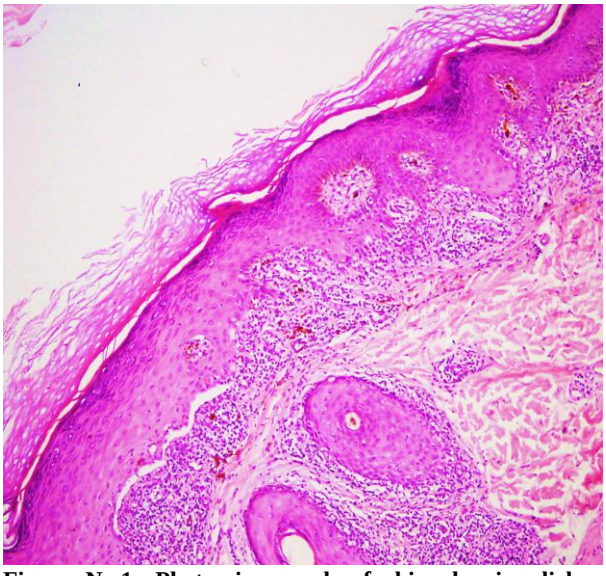

Figure No.1: Photomicrograph of skin showing lichen planus with hyperkeratosis, prominent granular cell layer, Max Joseph space, band like inflammatory infiltrate and pigmentary incontinence (H&E x 100)

Erythema multiforme was the most common lymphocytic poor variant (47.6%) and bullous pemphigoid was the most common granulocyte

blistering disorder (55.6%) showing interface dermatitis.

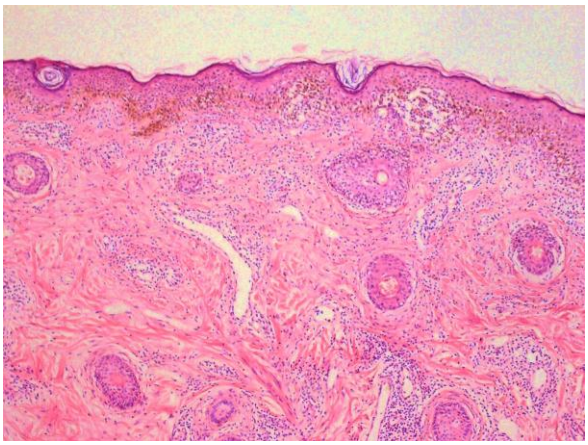

Figure 2: Photomicrograph of skin showing DLE, presenting with follicular plugging, basal layer vacuolation, pigmentary incontinence, dermoepidermal junctional infiltrate, dermal lymphocytic infiltrate and patchy perivascular infiltrate (H&E x 40)

Table No.1: Description of different types of diseases (n = 97)

Disease	Frequency	%tage
Lymphocyte Rich IFD (n = 67)		
Lichen Planus	40	59.6
Lichen Striatus	7	10.4
Lichen Nitidus	6	9
DLE	6	9
PLEVA	4	6
Lichenoid Drug Reaction	3	4.5
Lichenoid Graft Vs Host Disease	1	1.5
Lymphocyte Poor IFD (n = 21)		
Erythema Multiforme	10	47.6
PLC	9	42.9
Autoimmune Connective Tissue Skin Diseases	2	9.5
IFD Granulocytic Blistering Disorder (n = 9)		
Bullous Pemphigoid	5	55.6
Dermatitis Herpetiformis	1	11.1
Epidermolysis Bullosa Acquista	1	11.1
Linear IGA Disease	1	11.1
Porphyrias	1	11.1

Hyperkeratosis, hypergranulosis, acanthosis, and basal cell vacuolation were found to be the most common changes in the epidermis whereas pigmentary incontinence, band like infiltrate at the dermoepidermal junction and perivascular inflammatory infiltrate were the most common dermal features (figure No.2)

DISCUSSION

The range of age of patients in the present study was 1-85 years, however the majority of cases belonged in the range of 31 years to 40 years (20.6%) followed by 21-30 (18.9%) and 41-50 years which are consistent with the results of another study conducted by [9]., 2013. Our results are in conflict with a couple of studies in which majority of the cases belonged to fifth decade of life [10].

With regards to the gender distribution, most of the cases in our present study showed male dominance with 74.1% and female patients being 25.9%, the ratio of male to female was 3: 1. These findings differ from the study conducted by Hedge and Khadikar, 2014 showing female preponderance with (57.6%) among all cases of Interface dermatitis with the male and female ratio was 1:1.3.[11]

In the study under discussion, the most frequent clinical features were itching, papule and plaque formation, hyper and hypopigmentation, scaling, lichenification and bullae formation. These findings are also corroborated by other studies.[12]

The most consistent and uniform histological finding was basal cell vacuolation followed by lymphocytic inflammatory infiltrate, pigmentry incontinence, band-like infiltrate at the dermoepidermal junction. There was a consistent presentation of Civatte bodies. These findings are in harmony with the study carried out by Alsaad[2]. The most persistent secondary epidermal changes seen in addition to the primary histopathological features comprised of hyperkeratosis, acanthosis, parakaratosis, papillomatosis, spongiosis, hypergranulosis and follicular plugging whereas the least observed features were sub-epidermal blisters, Max-Joseph spaces and horn cyst.

This study, subdivides the cases diagnosed with IFD into three categories; cell rich; cell poor IFD and blistering disorders showing IFD. This study is supported by the classification presented by Crowson who classified IFD on the basis of cell poor and cell rich inflammatory process or type of cellular infiltrate [8].

Amongst ninety seven cases that were confirmed histopathologically as IFD, forty were of the Lichen planus type. The most frequent sub group was cell rich IFD (57.8%) followed by cell poor IFD (18.1%) and granulocyte blistering disorders showing interface dermatitis (7.8%). These results were parallel with a study concluding that the most reliable tool for the identification of underlying cause in lichenoid reactions was histopathological examination with the most common prototype being Lichen planus [10].

Dense inflammatory infiltrate characterises cell rich IFD. Basal cell vacuolation, making unclear the dermal/

epidermal junction by a band like inflammatory infiltrate, pigmentary incontinence and dense perivascular and interstitial lymphocytic infiltrate. Lichen planus and its variants are the prototype of this group according to Sehgal [3]. In the present study, amongst the cases labeled as cell rich IFD, lichen planus (59.7%) was found to be the most prevalent type of disease followed by lichen striatus (10.4%), lichen nitidus (9%), DLE (9%), PLEVA (6%), LDR (4.5%) and one case of graft versus host disease.

The prototypic cell-poor interface dermatitis is erythema multiform. Cell poor interface dermatitis shows basal cell vacuolation accompanied by sparse superficial perivascular infiltration of inflammatory cells. In the epidermis Lymphocytic exocytosis is found with civatte bodies [8]. In the present study 47.6% cases of cell poor interface dermatitis, were of erythema multiforme followed by 42.9% cases of pityriasis lichenoid chronica and two cases of connective tissue disease. The common histopathological features (cell poor IFD) seen in epidermis are apoptotic keratinocytes, spongioses, basal cell vacuolation and rarely epidermal necrosis along with subepidermal clefts. In the dermis lymphohistiocytic infiltrate along with scattered eosinophils and few neutrophils are seen.

Sub-epidermal blistering disorders with interface dermatitis are characterised by clefting at the dermoepidermal junction leading to subepidermal blisters in the skin. One of the commonest blistering autoimmune skin disorders is bullous pemphigoid as shown in a study of Bernard and Charneux, 2011.[13] The present study is in agreement with these findings showing bullous pemphigoid as the most frequent blistering disorder (55.6%) followed by each case of dermatitis herpetiformis, epidermolysis bullosa acquista and linear IgA disease exhibiting basal cell degeneration, mixed inflammatory infiltrate comprising of neutrophils and eosinophils in the dermis and basket weave pattern in the epidermis.

CONCLUSION

Interface dermatitis is a diverse clinicopathological entity affecting the basal cells, the papillary dermis and the dermo-epidermal junction. Lichen planus was found to be the most prevalent variant of interface dermatitis. The clinical correlation should be considered with all the specimens submitted for histopathological examination as the diagnostic accuracy is increased by correlating clinical and histopathological findings enabling accurate diagnosis leading to better prognosis and patient care. The clinical and histopathological disparity was seen maximum in cell rich IFD (lichen planus) and minimally in granulocyte blistering disorders showing IFD. Thus clinicopathological correlation is more required in cases diagnosed with lichen planus.

Author's Contribution:

Concept & Design of Study:	Momina Khadija Abbasi
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Conflict of Interest: The study has no conflict of interest to declare by any author.

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Original Article

Clinical Features and Incidence of Heart Failure among Patients with Preserved Ejection Fraction

Heart Failure with Ejection Fraction

Kashif Ali Hashmi, Khawar Abbas, Hafiz Muhammad Rizwan Amjad, Muhammad Zohaib Zahoor, Muhammad Amir Shahzad and Raheel Iqbal

ABSTRACT

Objective: To evaluate the clinical characteristics and incidence of HFpEF cohort in Pakistan as inadequate information is accessible regarding this enormously heterogeneous syndrome.

Study Design: A cross-sectional study

Place and Duration of Study: This study was conducted at the Cardiology Department of Chaudhary Pervaiz Elahi Institute of Cardiology, Multan, Pakistan for one-year duration from May 2020 to May 2021.

Materials and Methods: 108 patients with heart failure were registered in the analsyis to calculate the prevalence of HFpEF. Clinical presentation and Comorbidities among 25 patients for HFpEF were evaluated. Rendering to the guidelines of European Society of Cardiology (ESC) Guidelines: HFpEF was diagnosed among patients. There were 68 males and 40 females.

Results: Among 25 (23.1%) patients: HFpEF was analyzed (CI 95%, 15.3%-30.4%, respectively). 64.0 years was the mean age of the subjects. The patients of 60 to 79 years of age were the most common affected age group. Most of the individuals (63%) were men. Many individuals had a wide range of risk factors and comorbidities. The greatest communal risk factor was hypertension among 76% of the patients. There were 64% of dyslipidemia and 52% of diabetes cases. Coronary artery disease was among 32% of cases. 28% of cases had CKD. The atrial fibrillation was observed among 24% of patients, from which arrhythmia was most common. 64.3% have increased weight ratio with obesity. It was institute that 52% had anemia. NYHA IV in decompensated stage was noticed in 74.10% of patients. The most common complaint (100%) was dyspnea, and the most common sign was the bilateral lung base crepitations (92%).

Conclusion: The results of the studies revealed the description of HFPEF among the Pakistani population, but further epidemiologic trainings are required.

Key Words: clinical presentation, comorbidities, HFpEF

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INTRODUCTION

Heart failure (HF) is an escalating epidemic with high frequency and prevalence that is the leading cause of the morbidity, mortality and impairment of quality of life[1-2]. In 2014, there were almost 2.6 billion persons worldwide with heart failure[3-4]. Although, no information is accessible on the prevalence and incidence of heart failure in Pakistan, but life expectancy has augmented in Pakistan, lifestyle changes have occurred, and there may be increasing stress in treating heart disorders such as MI, valvular disease and arrhythmias subsidizing to the growing load of heart failure in Pakistan.

In current era, HFpEF has been progressively documented as a multifaceted pathophysiological entity[5-6]. In a previous study, the pervasiveness of HFpEFin in the Europe and USA increased from 39% to 55% of altogether cases of heart failure[7-8]. The prevalence of HFpEF is increasing by 1% compared to HFrEF, as suggested by the latest data from this year[9]. In Japanese Cardiac Registry of Heart Failure in Cardiology, the incidence of HFpEF was 26%1[10-11]. HFpEF occurs in elderly patients, especially women, with small heart with atrophy and a high incidence of diabetes, atrial fibrillation and hypertension but evidence suggests that HFpEF individuals have diverse levels of related comorbidities. The prevalence of HFpEF and patient characteristics may vary geographically. Therefore, we wanted to calculate the

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incidence of HFpEF patients in our community and evaluate their clinical characteristics.

MATERIALS AND METHODS

This cross-sectional study was held in patients from the Cardiology Department of Chaudhary Pervaiz Elahi Institute of Cardiology, Multan, Pakistan for one-year duration from May 2020 to May 2021. 124 patients with heart failure participated in the study. Rendering to the guidelines of European Society of Cardiology (ESC) Guidelines: HFpEF was diagnosed among patients. Acute coronary syndrome, Acute myocardial infarction, congenital heart disease, severe valvular heart disease, pacemakers and prosthetic valves and individuals with poor echo window were rejected.

Methodology: The criteria of selection were documented within 72 hours of hospitalization. Selected subjects were informed about the research purpose, demographic statistics were documented and written consent was obtained.

Based on the ECG findings, three categories of the patients were made: HFrEF, HFmrEF, and HFpEF. The percentage and frequency of HFpEF were analyzed.

The clinical data, cardiovascular risk factors, related disorders and detailed clinical history was taken. Patients' symptoms were classified conferring to the classification of NYHA. An appropriate general physical evaluation was performed.

Data was collected from important laboratory tests such as ECG, Doppler echocardiography and chest radiography. In significant cases, blood samples were approved on day 1 for BNP testing for relevant patients.

Statistical analysis: All analyzes were accomplished using the Microsoft Office 2011 in EXCEL data sheet. Continuous variables were accessible as mean ± standard deviation (SD). Categorical variables are documented as percentages and counts.

RESULTS

Among 25 (23.1%) patients: HFpEF was analyzed (CI 95%, 15.3%-30.4%, respectively). 64.0 years was the mean age of the subjects. The patients of 60 to 79 years of age were the most common affected age group. Most of the individuals (63%) were men. Many individuals had a wide range of risk factors and comorbidities. The greatest communal risk factor was hypertension among 76% of the patients. There were 64% of dyslipidemia and 52% of diabetes cases. coronary artery disease was among 32% of cases. 28% of cases had CKD. The atrial fibrillation was observed among 24% of patients, from which arrhythmia was most common. 64.3% have increased weight ratio with obesity. It was institute that 52% had anemia. NYHA IV in decompensated stage was noticed in 74.10% of patients. Figure 1 shows the population BMI distribution.

6 (24%) smoked cigarettes and ischemic stroke was noticed in 1 (4%) of cases. Table II lists the main comorbidities.

Table No.1: Shows the incidence of patients with HFpEF

HF subtype	Frequency	Percentage	95% CI
HFpEF	25	23.1	15.3 –30.4

Table No.2: Shows the different co-morbidities among patients

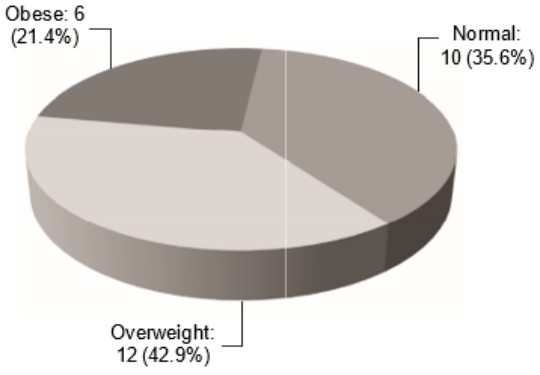
Comorbidities & risk factors	n (%)
Dyslipidemia	16 (64)
Hypertension	19 (76)
CAD	8 (32)
DM	13 (52)
Atrial fibrillation	6 (24)
CKD	7 (28)
Stroke	1 (4)
Smoker	6 (24)

The most common complaint (100%) was dyspnea, and the most common sign was the bilateral lung base crepitations (92%). (Fig. 2). The fatigue was found in 20 patients (80%) and palpitations among 12 (48%).

21 cases (84%) have tachypnea, and 16 cases (64%) were found with high systolic blood pressure. The table-3 shows the usual signs of the study group.

Table No.3: Shows the findings of Physical examination among studied population

Examination findings	Result
Respiratory rate, mean (SD), range	17.86 (4.2), 14-28
Pulse b/m, mean (SD), range	90.03 (13.2), 75-115
DBP mmHg, mean (SD), range	89.0 (14.5), 65-115
SBP mmHg, mean (SD), range	149.33 (18.8), 115-175
Leg oedema, n (%)	8 (32)
Anemia, n (%)	13 (52)
Bilateral basal creps, n (%)	23 (92)
Raised JVP, n (%)	2 (8)



n = number of study population

Figure No.1: Pie diagram showing the distribution of BMI

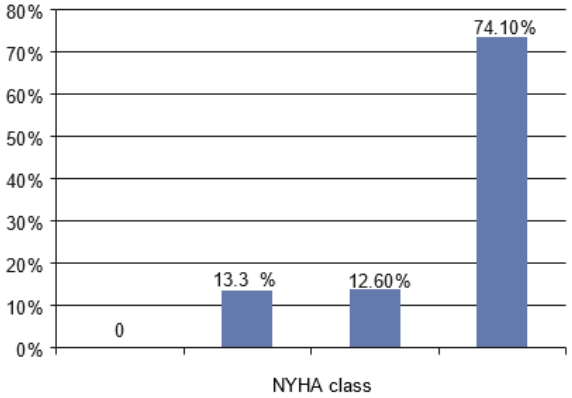


Figure No.2: Presentation of study population according to NYHA class (n = 25)

DISCUSSION

The characteristics and frequency of HFpEF patients changed significantly because of the consistency of diagnostic criteria and the heterogeneity of the syndrome itself. As far as we know, conferring to the 2016 European Society of Cardiology (ESC) Heart Failure; this is the first study to use the diagnostic criteria for HFpEF in Pakistan[12-13].

In this study, the incidence of HFpEF was 25 (23.1%), which is nearly comparable to the results of cardiology in the Japanese Cardiac Registry (JCARE-CARD) where the incidence of HFpEF was 26%. In the US and Europe, HFpEF accounted for 39% to 55% of all cases of heart failure in previous studies as well as in recent large studies. The Organized Program and database of Decompensated Heart Failure National Registry (ADHERE) to start Treatment for Live saving modalities in admitted patients with HF, the incidence of HFpEF was 51.1% and 52.5%, respectively; however, equally of these records had a lesser ejection fraction (≥ 40%) as in criteria of inclusion[14-15]. Differences in the incidence of HFpEF may be more stringent inclusion criteria for this study compared to previous studies, and there may also be absence of knowledge of HFpEF amongst reference physicians[16]. 64.0 years was the mean age of the subjects. These subjects were young than OPTIMIZE-HF registry 75.6 (13.1) mean (SD) age and ADHERE 73.9 (13.2) mean (SD) age[17-18].

Mostly of the subjects (64.3%) have increased weight with obesity, with Preserved Cardiac Function; Treatment of Heart Failure by Aldosterone Antagonist as in TOPCAT study[19-20]. Most patients with HFpEF had different comorbidities in our analysis. In 76% of patients have hypertension which is a communal risk factor. Earlier research has found that hypertension ranges from 56.2 to 100%. 64% of patients have Dyslipidemia, comparable to the TOPCAT study (61%). Elderly cases with an increase prevalence of obesity with CAD, stroke, diabetes and kidney disease may explain a high incidence of dyslipidemia[21].

52% of cases have Diabetes mellitus and was detected in 23 to 64% of individuals in the various studies. The high incidence of all components of the metabolic syndrome in this study confirms the earlier conclusions of relationship of the metabolic syndrome with HFpEF. In the Metabolic Syndrome- Chronic Heart Failure (MetS-CHF) study, HFpEF was found in 37.7% of cases with the metabolic syndrome[22]. It can result in microbial endothelial dysfunction in the coronary arteries by reducing the availability of protein kinase G and nitric oxide. Eventually, it causes deleterious remodeling of the heart muscle and HFpEF. However, the contributory link between them has not yet been recognized. The study included patients have coronary artery disease (CAD) in 32% and it was comparable with the previous studies which shows 30% and 53%, respectively[23-25]. Breathing difficulties are the main symptom in 98% of patients with HF. The majority of patients (74.10%) were in uncompensated NYHA Class III-IV at the time of reporting. However, they were more compensated than in the Irbesartan Heart Failure Cohort (IPRESERVE) (NYHA IV 73.3% vs. 3%). Crackles at the base of both lungs were the most common symbol, accounting for 96% of the cases found in this study. Primary basal crackles was also found in 95% of patients with HF. 24 cases (80%) have tachypnea, and 19 cases (63.3%) were found with high systolic blood pressure.

CONCLUSION

HFpEF has contributed to nearly a quarter of all hospitalizations for HF in our community. They were younger than the Western HFpEF cohort. They were mainly males with several comorbidities and were presented at the decompensated stage. Though, additional extensive epidemiologic analysis is desirable to better understand the incidence and features of HFpEF patients in Pakistan.

Author's Contribution:

Concept & Design of Study:	Kashif Ali Hashmi
Drafting:	Khawar Abbas, Hafiz Muhammad Rizwan Amjad
Data Analysis:	Muhammad Zohaib Zahoor, Muhammad Amir Shahzad, Raheel Iqbal
Revisiting Critically:	Kashif Ali Hashmi, Khawar Abbas
Final Approval of version:	Kashif Ali Hashmi

Conflict of Interest: The study has no conflict of interest to declare by any author.

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Original Article

Tumor Necrosis Factor (TNF) and Parasite Density in Determining Disease Severity in Falciparum Malaria

Disease Severity in Falciparum Malaria

Shaista Alam[1], Aysha Sarwar[2] and Saman Hussain[3]

ABSTRACT

Objective: This study was designed to investigate the TNF and parasite density in determining disease severity in falciparum malaria by using Giemsa stained slides. Our major aim was to explore the association of TNF levels with anemia, disease severity and mortality ratio.

Study Design: Cross-sectional study

Place and Duration of Study: This study was conducted at the Teaching Hospital of Peshawar Institute of Medical Sciences between February 2019 to November 2019.

Materials and Methods: Total 300 patients were analyzed and 70 infected patients were recruited. For comparison total of 60 healthy individuals were selected. A structured questionnaire was produced for the age, gender and socioeconomic status, educational status, and clinical manifestations of the participants. From each participant, two thin and thick blood with 4% Giemsa stained slides were prepared and observed under the microscope for Giemsa-stained peripheral blood smears and confirmation of Plasmodium presence.

Results: Correlation analysis was performed to understand the relationship of parasite burden with anemia, we observed a negative correlation between HB vs parasitemia, decreased Hb level VS TNF, parasitemia vs red blood count, and parasitemia vs IL-6 level. On the other hand, a positive correlation was formed between HB level vs RBC levels and TNF vs parasitemia.

Conclusion: TNF and IL-6 serves as an early marker of prognosis as TNF was high in patients with even moderate levels of parasitemia and so these patients must be managed indoor and high vigilant care to be given with close monitoring to prevent deterioration.

Key Words: Plasmodium falciparum malaria, Cytokines, parasitemia, Giemsa stained slides

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INTRODUCTION

Malaria is still one of the important global issues in the 21st century. Around three billion people are at risk of malaria every year. In 2015, almost 212 million cases were reported along with 429000 deaths[1]. Pakistan is a region that reports a higher number of deaths with Malarial infection. Plasmodium vivax and plasmodium falciparum are the two most prevalent species of Malaria that cause high morbidity and mortality ratio in Pakistan[2]. In 2013, a WHO report explored that 12% population of Pakistan was affected by plasmodium falciparum[3].

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Annually fifty thousand malarial cases are reported along with the same ratio of death in Pakistan[4]. On the other hand, our neighboring countries Afghanistan and Iran reported a 37% prevalence every year[5]. Northwest areas of Pakistan including Khyber Pakhtunkhwa and especially those areas which share the borders are on the hit list of Malaria[6,7]. Malaria is a seasonal disease that turns into a huge epidemic in areas of Khyber Pakhtunkhwa, Sindh and. Balochistan province. In Khyber Pakhtunkhwa, three districts Banu, Dera Ismael Khan, and Laki Maarwat reported a high prevalence of Malarial infection[8]. The survey reported that August to December is the peak seasons for transmission of plasmodium falciparum in Pakistan[9]. A study conducted on tribal areas of Pakistan reported 13.8% positive cases of plasmodium falciparum using the polymerase chain method[10]. A study conducted in 2020 reported a high prevalence of plasmodium falciparum in Bannu, Hangu, and Thall districts. The prevalence ranges from 16% to 25% in the age group > 14 years[11].

This study was designed to investigate the TNF and parasite density in determining disease severity in falciparum malaria by using Giemsa stained slides. Our major aim was to explore the association of TNF levels with anemia, disease severity and mortality ratio.

MATERIALS AND METHODS

This study protocol was approved by the Ethical committee of Peshawar institute of Medical sciences. The study was conducted between February 2019 to November 2019. This cross-sectional study was conducted in the teaching hospital of Peshawar institute of medical sciences. This hospital is located at Phase V Hayatabad which provides free medical assistance to poor individuals. Malaria-infected patients who were presented to the wards were included in this study. For comparison, we asked healthy individuals who were attending blood banks for donations for voluntary participation. All the adult participants were selected without any biases of ethnicity and socioeconomic status. The objectives of the research were well explained to the participants and written consents were asked before any procedure. The sample size was estimated by raw calculator with a prevalence rate of 28% as described in the previous study of Kwenti et al[17]. Total 300 patients were analyzed and 70 infected patients were recruited. For comparison total of 60 healthy individuals were selected. A structured questionnaire was produced for the age, gender and socioeconomic status, educational status, and clinical manifestations of the participants.

Senior physicians treated patients and identified the severe cases of Malarial infection as described by the WHO guideline until discharge[18]. All the patients >18 years positive for plasmodium parasites with a temperature ≥of 37.5°C were recruited for this research. Patients less than 18 years, pregnant women were excluded. All those patients who were tested positive for dengue virus, typhoid, hepatitis B, and C were also excluded from this research. We performed Malaria diagnosis with rapid diagnostic kits (RDT) and microscopic examination of Giemsa-stained peripheral blood smears. Lactate dehydrogenase of PV in human blood and histidine-rich protein II antigen of Pf were examined by using Ag Pf/Pv rapid diagnostic test kit.

From each participant, two thin and thick blood with 4% Giemsa stained slides were prepared and observed under the microscope for Giemsa-stained peripheral blood smears and confirmation of Plasmodium presence. Parasite densities were measured as parasites/µl of blood (number of parasites counted/number of white blood cells (WBCs) counted × total number of WBCs per µl of blood) or (number of parasites counted/number of RBCs counted × total number of RBCs per µl of blood). For parasitemia, we used the formula as (number of parasites per µl of blood/number of RBCs per µl of blood) × 100[19].

Participants were divided into three major categories; healthy participants, mild cases of malaria, and severe cases of malaria. In the category of healthy individuals those who were tested negative for malarial infection by blood smear and RDT kits.We recruited patients under the SM category with HB level less than 5 g/dl, serum level ≥3 mg/dl, serum bilirubin ≥3 mg/dl, plasma bicarbonate <15 mmol/l), spontaneous bleeding, hypoglycemia (plasma glucose <40 mg/dl), hyperparasitemia (≥10% parasitemia.The intensity of anemia was divided into four categories; non-anemic (Hb ≥11 g/dL), mild anemia (between 8 and 10 g/dL), and severe (5-7 g/dL)[20].

For statistical analysis, we used SPSS 23.0 software. The comparison was performed between cytokine levels and the intensity of anemia. Pearson correlation was used for showing a correlation between continuous variables whereas one-way non parametric Kruskal-Wallis test was performed for multiple comparison. P-value was set as 0.05 for statistical significance.

RESULTS

A total of 70 patients was found to be infected with plasmodium falciparum Malaria type. We observed 32.4 years as the mean age group. During observations, we found that the male population was more prone to malarial infection. Total 45 (64.2%) males were infected with malaria. Among the 70 infected patients, a total of 8 (11.4%) patients were suffered from severe malaria and need hospital admission for treatment (Table 1).

We observed levels of HB, RBC, and plasma levels of cytokines among anemic and nonanemic malarial patients in table 2. We observed a significant increase in the mean percentage of parasitemia ($P \leq 0.0001$). We observed that HB and RBC levels of anemic patients significantly decrease throughout the infection. Whereas the cytokines levels especially TNF and IL-6 increased in the anemic group. However, we did not find any statistical significance between age, gender, and inflammatory cytokines.

Table No. 1: Demographic characteristics of participants

Variables	Plasmodium falciparum n= 70	Healthy Control n= 60
Mean Age group	32.4 (18-65)	29.7 (18-58)
> 45	8 (11.4%)	7 (11.6%)
36-45	24 (34.2%)	24 (40%)
26-35	28 (40%)	24 (40%)
18-25	10 (14.2%)	15 (25%)
Gender		
Female	25 (35.7%)	20 (33.3%)
Male	45 (64.2%)	40 (66.6%)
Mild Malaria	62 (88.5%)	0
Severe Malaria	8 (11.4%)	0

Table No.2: Hematological analysis and cytokines profile of Anemic versus non Anemic patients

Variables	Healthy control - n= 60	Plasmodium falciparum (n= 70)	
		Anemic (n=53)	Non-anemic (n=17)
Hemoglobin (g/dl)	14.1±0.8	7.2±2.3	13.1±1.5
IL-10 (pg/ml	134.1±103.7	549.05±460.5	632.83±414.6
Red blood cells ($\times 10^3/\mu l$)	4.99±0.7	3.71±1.0	4.99±0.7
IL-6 (pg/ml)	87.48±54.3	269.19±188.5	211.11±163.2
Hematocrit	40.88±4.1	27.20±9.6	41.82±6.2
TNF-α (pg/ml)	66.73±29.3	328.87±217.7	212.16±150.0
Mean cell hemoglobin (pg)	26.83±2.9	25.66±2.9	25.95±5.1
Parasitemia	-	0.58±0.7	0.14±0.2
Mean corpuscular volume (fL)	86.59±6.1	82.61±13.7	84.69±9.4
Mean corpuscular hemoglobin concentration (g/dl)	30.76±1.8	29.93±3.6	30.93±3.3

Table No.3: Correlation between Hematological findings and inflammatory cytokine levels

Parameters	Correlation coefficient (r)	p- value
HB VS parasitemia	−0.3426	$P \leq 0.0001$
Parasitemia Vs RBC	−0.2158	0.007
HB VS RBC	0.3854	$P \leq 0.0001$
TNF levesl Vs parasitemia	0.3669	$P \leq 0.0001$
Low HB level VS TNF	−0.4412	$P \leq 0.0001$
Parasitemia Vs IL-6	−0.2892	$P \leq 0.0001$

Table No.4: Inflammatory cytokine levels at different intensity of anemia

Variables	Severe Anemia	Moderate Anemia	Mild Anemia	No Anemia
No. of patients(%)	15 (21.4%)	18 (25.7%)	20 (28.5%)	17 (24.2%)
IL-10 (pg/ml)	155.4 (101.4-183.1)	385.2 (186.4-727)	487.7 (274.2-1047)	585.7 (328-934)
Hb (g/dl)	4.2 (3.5-4.6)	7.2 (6.7-7.7)	10.2 (9.4-10.6)	13 (12.2-13.7)
IL-6 (pg/ml)	445.4 (306.7-516.6)	262.2 (147.6-576.9)	324.1 (198.4-427.1)	181.7 (128.7-324.1)
TNF-α (pg/ml)	678.7 (561.5-882.2)	356.4 (132-591.5)	195.3 (146.4-310.9)	86 (45.9-233)

In table 3, correlation analysis was performed to understand the relationship of parasite burden with anemia, we observed a negative correlation between HB vs parasitemia, decreased Hb level VS TNF, parasitemia vs red blood count, and parasitemia vs IL-6 level. On the other hand, a positive correlation was formed between HB level vs RBC levels and TNF vs parasitemia.

In table 4, patients were classified according to an anemic category, we observed a significant increase in TNF levels, IL-6 levels whereas a decrease was found in the IL-10 levels of all groups. In table 5, observed seven severe anemic patients with severe malarial complications including two cases of jaundice, acute renal function, metabolic acidosis, and hepatic dysfunction. However, one case of hypoglycemia, hyperparasitemia was reported during studies.

Table No.5: Frequency of severe amemia with severe Malarial Complications.

Severe Malarial Complications	Pf (n=7)
Hepatic dysfunction	2 (28.6%)
Acute renal failure	2 (28.6%)
Hyperparasitemia	1 (14.3%)
Jaundice	2 (28.6%)
Hypoglycemia	1 (14.3%)
Metabolic acidosis	2 (28.6%)

DISCUSSION

All around the world, anemia is the major public health problem during Malaria. This not only increases the morbidity duration but also enhances the mortality frequency in many regions[22]. Generally, Plasmodium falciparum malarial cases have more associated with anemia as compared to the other types. But studies by Rahimi et al[23] and Alexandra et al[12] observed found a high association of anemia with plasmodium vivax infection despite the low parasite burden during the PV infection. For this present study, our major goal was to evaluate the effect of PF Malaria on hemoglobin and red blood cells and specify the association of cytokines level with complications of malaria in patients from Peshawar and surrounding areas. We found that Pf malaria is more prevalent in the male gender as compared to females. The affected male patients were mostly laborers who worked in construction buildings which are known to provide ideal breeding and spread of infection[24]. In our study, we observed a significant decrease in the number of red blood cells and hemoglobin levels of the patients whereas the results show a significant increase in parasitemia. On the other hand, we failed to find any significant correlation between increasing parasitemia and decreasing Hb and

RBC levels. Total 8.7% of severe cases were diagnosed during the study period.

Cytokines levels are a huge mediator in the development and severity of Malaria[12]. We further explored the influence of cytokines especially IL-6, IL-10 TNF on the degree of anemia. These cytokines were compared at varying degrees of anemia Usually, TNF-α is released by the macrophages in response to Malaria[13]. Previous studies found a huge contribution of TNF-α to the destruction of RBC levels and suppression of bone marrow when combined with other cytokines[14]. Evidence from a vitro study demonstrates that TNF-α suppressed the proliferation of erythroid progenitor cells in human marrow cultures[15]. We also found a significant positive correlation between parasite density and TNF-α level. These results are in correspondence with the previous study of Lamb et al[25]. On the other hand, a negative correlation was observed between HB and TNF-α levels which depicts that TNF-α level has a huge contribution in anemic severity during malaria[26]. IL-6 also plays a great role in the pathophysiology of severe malarial anemia. TNF-α levels are responsible for the production of IL-6 levels to react together to reduce the parasite burden[27]. In our study, we observed a reciprocal association between IL-6 and parasitemia. During severe malarial anemia, patients reported increased levels of IL-6. This increased level has a strong association with high receptor density and low transferrin synthesis. These results both the Malawian study[28] in which they found a significant correlation between increased IL-6 levels and iron deficiency among children.

CONCLUSION

TNF and IL-6 serves as an early marker of prognosis as TNF was high in patients with even moderate levels of parasitemia and so these patients must be managed indoor and high vigilant care to be given with close monitoring to prevent deterioration.

Author's Contribution:

Concept & Design of Study:	Shaista Alam
Drafting:	Aysha Sarwar
Data Analysis:	Saman Hussain
Revisiting Critically:	Shaista Alam, Aysha Sarwar
Final Approval of version:	Shaista Alam

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Original Article

Knowledge of Mothers Regarding Oral Rehydration Therapy

Muhammad Khalil, Toqeer Ahmed, Ammara Manzoor and Iftikhar Ahmed

ABSTRACT

Objective: To determine the knowledge of mothers regarding the oral rehydration therapy in children with acute watery diarrhea.

Study Design: Cross sectional study

Place and Duration of Study: This study was conducted at the Pediatric Department, Divisional Headquarter teaching Hospital Mirpur AJK over a period of 6 months from Dec, 2020 to May, 2021.

Materials and Methods: 215 mothers along with their children were included though emergency/OPD of pediatric department. Mothers were asked about the knowledge regarding rehydration of their child while having acute watery diarrhea and about oral rehydration solution. A predesigned questionnaire was used to collect the information about knowledge of mothers. Data was analyzed using SPSS v. 22.

Results: The mean age of mothers was 31.20 ± 6.63 years. The mean age of children was 3.86 ± 3.71 years. There were 17 (7.9%) mothers who were post-graduate, 42 (19.5%) were graduate, 49 (22.8%) and education up to matric or intermediate, 72 (33.5%) were middle or primary pass while 35 (16.3%) mothers were illiterate. There were 179 (83.3%) mothers who had good knowledge of oral rehydration solution while 36 (16.7%) had poor knowledge of use of oral rehydration solution.

Conclusion: Thus, it has been observed that there are >80% mothers who are aware of use and benefits of oral rehydration solution.

Key Words: Acute watery diarrhea, oral rehydration therapy, mother, knowledge, children

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INTRODUCTION

Acute diarrhea is described as the occurrence of three or more loose stools (watery consistency) per day in a short period of time. An imbalance in the physiology of the small and large intestine processes involved in the absorption of ions, organic substrates, and therefore water is responsible for the increased water content in the stools.[1] Acute diarrhea mortality is decreasing globally, although it remains high. According to most estimates, diarrhea is the second leading cause of death in children under the age of five, accounting for 18% of the 10.6 million fatalities per year.

Poverty imposes a tremendous extra burden in nations where diarrhea is the most prevalent, and the long-term implications of the vicious cycle of enteric infections, diarrhea, and malnutrition are distressing.[2]

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The Centers for Disease Control and Prevention issued guidelines in 2003 for the treatment of acute pediatric diarrhea in outpatient and inpatient settings, including indications for referral. Oral rehydration, maintenance, and nutritional treatment for children with acute gastroenteritis.[3] Oral rehydration treatment is a sort of fluid replacement that is used to prevent and cure dehydration, particularly diarrheal dehydration. It entails drinking water laced with sugar and salts, particularly sodium and potassium. A nasogastric tube can also be used to administer oral rehydration treatment. Zinc supplements should be taken on a regular basis as part of treatment. The use of oral rehydration solution have reduced the chances of mortality due to diarrhea around 93%.[4]

Vomiting, hypo and hypernatremia, or hypokalemia are all possible side effects. If vomiting occurs, it is suggested that you take a 10-minute break before gradually resuming use.[4, 5] The use of DIY remedies, on the other hand, has not been well researched.[4] Simple home treatment with oral rehydration treatment would have averted it. Mothers role is crucial in its treatment and prevention.[6] Diarrhea is not fatal in and of itself; but, mothers' lack of understanding, poor practice, and negative attitudes, as well as their misguided approach to its care and prevention, result in severe dehydration and, eventually, mortality. [7, 8] In routine, the use of oral rehydration solution is less in local population.

However, mostly people know about the oral rehydration solution. But local evidence was scarce. So we conducted this study to get evidence of local population and implement the results in local setting.

MATERIALS AND METHODS

Study Design: Cross - sectional study
Study Place: Pediatric Department; Divisional Headquarter Teaching Hospital Mirpur AJK, Pakistan.
Study Period: 6 months i.e. from Dec. 2020 to May 2021
Sample Size: Sample size of n = 215 cases was estimated by keeping the 95% confidence level, 6.5% margin of error and percentage of good knowledge i.e. 63.34%[9] among mothers regarding oral rehydration solution
Sampling Technique: Simple random sampling.
Sample selection:
Inclusion Criteria: Mothers of age 17-55 years, presenting with children with acute watery diarrhea were included.
Exclusion Criteria: Mothers who did not want to take part in the study, language barrier was not included.
Data Collection Procedure: After taking approval from hospital ethical committee, 215 mother along with their children were included though emergency of pediatric department, Divisional Headquarter Teaching Hospital Mirpur. Informed consent was taken and demographics (name, age, child age, area of residence, education, occupation) were noted. Then mothers were asked about the knowledge regarding rehydration of their child while having acute watery diarrhea. Then females were asked about knowledge of mothers regarding oral rehydration solution. Source of information was also being noted. A predesigned questionnaire was used to collect the information about knowledge of mothers. All the children with acute watery diarrhea were managed as per standard protocol.
Data Analysis: Data was analyzed using SPSS v. 22. Numerical variables like age of mothers, age of child, were presented as mean and standard deviation. Categorical variables like area of residence, education and occupation of mother, and good knowledge were presented as frequency and percentage. Data was stratified for age of mother, occupation, education, area of residence and source of information. Post-stratification, good knowledge was compared in stratified groups by using chi-square test. The P-value at ≤ 0.05 was kept as significant.

RESULTS

The mean age of mothers was 31.20 ± 6.63 years. The mean age of children was 3.86 ± 3.71 years. There were 94 (43.7%) mothers who came from rural area while 121 (56.3%) mothers belong to urban area. There were 17 (7.9%) mothers who were post-graduate, 42 (19.5%) were graduate, 49 (22.8%) ad education up to matric or intermediate, 72 (33.5%) were middle or primary pass while 35 (16.3%) mothers were illiterate. Out of 215 mothers, 167 (77.7%) were housewives, 10 (4.7%) were labor and 38 (17.7%) were professional. About 98 (45.6%) mothers got information regarding oral rehydration solution from doctors, 76 (35.3%) got information from friends, 5 (2.3%) got information through internet, 12 (5.6%) got information through media, and 24 (11.2%) got information through nurse. The total knowledge score obtained by females was 28.26 ± 2.72. Table 1.

There were 179 (83.3%) mothers who had good knowledge of oral rehydration solution while 36 (16.7%) had poor knowledge of use of oral rehydration solution. Fig 1

Table No.1: Demographics of patients

n	215
Age of mother (years)	31.20 ± 6.63
Age of children (years)	3.86 ± 3.71
Area of residence	
Rural	94 (43.7%)
Urban	121 (56.3%)
Education of mother	
Post-Graduate	17 (7.9%)
Graduate	42 (19.5%)
Matric or Intermediate	49 (22.8%)
Middle or primary	72 (33.5%)
Illiterate	35 (16.3%)
Occupation of mother	
House wife	167 (77.7%)
Labor	10 (4.7%)
Professional	38 (17.7%)
Source of information	
Doctor	98 (45.6%)
Friends	76 (35.3%)
Internet	5 (2.3%)
Media	12 (5.6%)
Nurse	24 (11.2%)
Total score of knowledge scale	28.26 ± 2.72

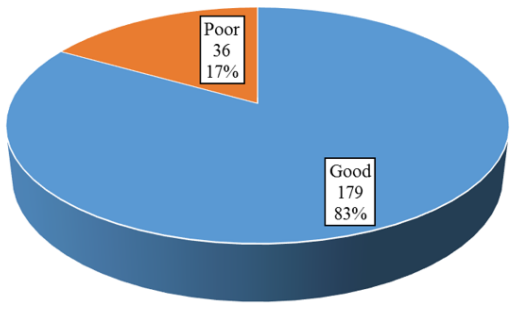

Figure No.1: Knowledge of mothers about oral rehydration solution

It has been observed that in females of any age group, then knowledge was similar (p>0.05). Knowledge of mothers came from rural area had same level of knowledge as mothers came from urban area. But the

knowledge of graduate and post-graduate mothers is significantly better than below matric ($p<0.05$). Table 2.

Table No.2: Comparison of knowledge in different groups

	Knowledge		p-value
	Good	Poor	
Age of mother			
<25 years	40	7	0.927
	85.1%	14.9%	
26-40 years	129	27	
	82.7%	17.3%	
41-55 years	10	2	
	83.3%	16.7%	
Area of residence			
Rural	77	17	0.643
	81.9%	18.1%	
Urban	102	19	
	84.3%	15.7%	
Education of mother			
Illiterate	24	11	0.003
	68.6%	31.4%	
Below matric	99	22	
	81.8%	18.2%	
Graduate or post-graduate	56	3	
	94.9%	5.1%	
Occupation of mother			
Housewife	134	33	0.073
	80.2%	19.8%	
Labour	10	0	
	100.0%	0.0%	
Professional	35	3	
	92.1%	7.9%	
Source of information			
Doctor	79	19	0.180
	80.6%	19.4%	
Friends	68	8	
	89.5%	10.5%	
Internet	5	0	
	100.0%	0.0%	
Media	8	4	
	66.7%	33.3%	
Nurse	19	5	
	79.2%	20.8%	

DISCUSSION

Diarrhea is still a major public health problem in children under the age of five in low-resource areas, with rotavirus being the most prevalent cause.[10-12] In our study, there were 179 (83.3%) mothers who had good knowledge of oral rehydration solution while 36 (16.7%) had poor knowledge of use of oral rehydration solution. Sultana et al., discovered that 95.94 percent of the 320 moms had a strong understanding of oral rehydration solution. Only 86.87 percent of moms had proper information about the availability of oral rehydration solution. The majority of moms (37.19%) learned about oral rehydration solution through doctors, followed by the media (25%) and their moms (20 percent).[13] Kadam et al., conducted a study, based on National Diarrheal Disease Control Program and found that 89% of mothers were aware about oral rehydration solution.[14]

Workie et al. conducted a research with 295 volunteers who responded 100% of the time. Around two-thirds of the 295 mothers (65.2%) had good knowledge, but more than half of the mothers (54.9%) had a negative attitude toward home-based care and prevention of diarrhea in children under the age of five. In terms of mothers' attitudes, 58 percent had poor practice when it came to home-based care and prevention of diarrhea in children under the age of five.[6] In another research conducted in Fenoteselam, Ethiopia, 65.9% of mothers had a good understanding of the use of oral rehydration solution in the treatment of diarrhea in children.[15-17] This is mostly owing to the fact that Dire Dawa is a larger, more urbanized city with a plethora of mass media outlets.

During their child's diarrheal sickness, less than half of the participants (42.4%) utilized a homemade remedy. The results differed from those of South Africa's Heidedal community (90 percent), Taung district (83.6 percent), and Swaziland community (97 percent).[18] This might be because the majority of moms in the city sought medical treatment for their children while they were suffering from diarrheal disorders. Around two-thirds of the mothers [184 (62.4 percent)] were aware of the required volume of water for mixing an oral rehydration solution sachet. This is significantly lower than comparable studies conducted in Ethiopia (85.4%), Pakistan (75.5%), Nepal (70%), and India (76.7 percent). This might be rationalized by the fact that, due to a lack of knowledge, these women may not be accustomed with making oral rehydration solutions.[8, 15, 19, 20]

But Gupta et al., conducted a study in India and found that out of 240 mothers, who were interviewed, 86.7% mothers know about the oral rehydration solution and its benefits in diarrhea, while only 20% knew about the appropriate method of preparing the oral rehydration solution and its use in diarrhea. The most common source of information was the health care providers including doctors and nurses. Thus, the understanding on how to utilize and prepare oral rehydration solution for diarrhea management was shown to be insufficient. More steps must be done to increase this understanding and educate women on how to prepare and utilize oral rehydration solution.[21]

Although mothers have a reasonable understanding of diarrhea and oral rehydration solution, the study found that certain issues, such as the use of untreated water for oral rehydration solution preparation, improper

storage of oral rehydration solution, and a lack of understanding regarding the urgency of oral rehydration solution use, are concerning. As a result, educational interventions may be beneficial in changing these erroneous beliefs. [22] Appropriate knowledge regarding the use of oral rehydration therapy during diarrhea helps to prevent the morbidity and mortality in pediatric population due to diarrhea. Knowledge of mothers and their attitudes for the use of oral rehydration solution during diarrhea needs to be improved.[23]

CONCLUSION

Thus, it has been observed that there are >80% mothers who are aware of use and benefits of oral rehydration solution. But still there is a need to spread more information about oral rehydration solution to improve the knowledge and use of oral rehydration solution and prevent complications of acute watery diarrhea and mortality in pediatric population.

Author's Contribution:

Concept & Design of Study:	Muhammad Khalil
Drafting:	Toqeer Ahmed
Data Analysis:	Ammara Manzoor
Revisiting Critically:	Iftikhar Ahmed
Final Approval of version:	Muhammad Khalil

Conflict of Interest: The study has no conflict of interest to declare by any author.

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Original Article

Do Antioxidant Oils Help in Sustaining the Testicular Weight in Phenytoin Induced Toxicity in Rats?

Khalique-ur-Rehman[1], Masood Ali[2], Khalid Shehzad[5], Hina Khan[3], Humaira[4] and Raja Faisal[3]

ABSTRACT

Objective: To evaluate the effective role of anti-oxidant oils in restoring the testicular weight in phenytoin toxicity in rats.

Study Design: Experimental Study

Place and Duration of Study: This study was conducted at the Al-Tibri Medical College and Hospital, Isra University Karachi Campus from October 2019 to March 2020.

Materials and Methods: Total 32 numbers of male albino rats were randomly selected from the animal house of the institute. The animals were divided into three groups Group A induced normal diet, B given intra peritoneal injection of phenytoin, C was given corn oil and D was given virgin coconut oil. The Body weight was evaluated at the initial day and at the final day of the study. At the completion of the study the bilateral testicular weight was evaluated by using a normal digital weight scale, and compare with normal group. The data was represented in the form of Mean and compare the Mean Body weight by applying simple 't' test and the testicular weight was evaluated by applying One-way ANOVA, and the level of significance was considered at P=<0.05.

Results: The study results show no significant difference was found on comparison of initial body weight with the final weight among the different groups. There was a significant different found on comparison of bilateral testicular weight of phenytoin induced toxicity group of animals as compare to other, while in virgin coconut group the animals' testicular weight was well restoring in comparison with corn oil.

Conclusion: The study results show significant reduction of organ weight in experimental group as compare to control group, and the group of virgin coconut oil remarkably maintain the bilateral testicular weight as compare to other. Although the body weight was remains unchanged. Anti-oxidant properties of virgin coconut oil due to its biochemical composition strengthen its role against the free radicals and achieve their desirable effects on male fertility. Virgin coconut oil is easy to use and easily accessible for everyone.

Key Words: Phenytoin, Virgin Coconut Oil, Anti-oxidant

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INTRODUCTION

Prolong usage of antiepileptic drugs among the patients of epilepsy and seizures are commonly found among the population. There are so many drugs listed as an antiepileptic drug, the most common drug found on the large numbers of fertility functions.[1]

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These drugs can faster the metabolic activity of the sex hormones and results in the decrease levels of androgen index. The study proven that the phenytoin alters the level of testosterone hormones by effecting the Leydig cells in the interstitial space, and in turn causes an inhibitory effect on spermatogenesis.[2] These antiepileptic drugs can produces a significant reduction sperm motility, velocity, and profound effects on male fertility and reduce the functional activities of reproductive organs in male.[3] Phenytoin reduces the plasma availability of testosterone hormones, and it may lead to effect the morphological and physiological parameters of the seminiferous tubules. In many of the studies the fertility rate was compromised and can alter the testicular weight and histomorphological changes among the spermatozoa.[4] The corn oil is mainly identifying by its biological name is Zea mays, and it's an essential vegetable oil that is commonly used worldwide. Its anti-oxidant activity can tag it beneficial oil for cooking. Daily usage of oil can reduce the oxidative stress from the body. Linoleic acid is the main composition as a component of poly-unsaturated fatty

acid.[5] Spermatozoa composed of higher numbers of poly un-saturated fatty acids, and oxidative stress can cause massive defragmentation of DNA and leads to infertility.[6] Biological name of virgin coconut oil is well known as Cocoas nucifera**.** Coconut oil also contains myristic acid and palmitic acid, that are an essential anti-oxidant products used worldwide[7]. Myristic acid is mainly found in animal fat, coconut oil, butter fat, palm kernel oil and breast milk. It is also found in spermaceti, that are main component of whale sperm[8]. An average amount of Lauric acid is available in coconut oil, and all these elements having remarkable anti-oxidant impact on male fertility. Virgin coconut oil studies establishing its positive impact on the production of testosterone hormone, and boost up the sperm motility and enhance the physiological function of male reproductive organs.[9]

MATERIALS AND METHODS

After taken an ethical approval from the concerned authority of the institute. The Quasi-experimental study was done at Al-Tibri medical college and Hospital, from October 2019 to March 2020. The animals were taken from the animal house of respected institute, and the male albino rats were randomly taken of weight between 150-200 gms. The rats were kept in different cages with the maintenance of proper light and dark cycle. Total 32 numbers of male albino rats were divided into four groups on the basis of therapeutic study design. Each group having total eight number of rats labeled as:

Group A: Control Group, received an intra-peritoneal injection of 1-unit normal saline solution along with a normal daily diet.

Group B: A dose of Phenytoin 10mg/kg/body wt., intra-peritoneal once everyday

Group C: Received Virgin Coconut Oil (6.7ml) along with Phenytoin 10mg/kg/body wt., intra-peritoneal once everyday

Group D: Received Corn Oil (2.5ml) along with Phenytoin 10mg/kg/body wt., intra-peritoneal once everyday

The study was completed after 6 weeks and body weight of the animals were taken on day 1 and at the end of the study of each group by using a normal digital weight scale. After completion of the study, the animals were anesthetized with ethanol and then the incision was given to abdominal wall in sagittal section from xiphisternum to pubic symphysis then both testes were removed from the scrotum were weighed by using digital measuring scale. For microscopic parameters tissue was removed from the testis and preserved in 10% formalin. The Body weight and testicular weight of right and left site were presented in the form of Mean (standard deviation), and the data was evaluated by means of SPSS version 20.0. The Mean body weight was comparing with simple 't' test and testicular weight were compared by applying One-way ANOVA followed by post hoc Tuckey's test among different therapeutic groups. The level of significance was kept at ≤0.05.

RESULTS

Figure 1: Shows the Comparison of Mean initial and final body weight of animals

Table 1.a: Shows the level of significance on comparison of Mean body weight among the different therapeutic groups

Figure 2: Shows the Mean Right sided testicular weight among different therapeutic groups.

Figure 3: Shows the Mean Left sided testicular weight among different therapeutic groups

Table 1b: Shows the level of significance on comparison of Bilateral Mean testicular weight among the different therapeutic groups.

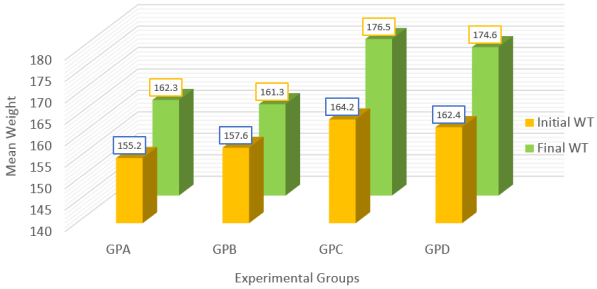

Figure 1: shows the Comparison of Mean initial and final body weight of animals

Table No.1: Shows the level of significance on comparison of Mean body weight among the different therapeutic groups

Groups	Compare the Mean of Initial and Final Body weight(gm)
A	**≤0.001**
B	**≤0.001**
C	**≤0.001**
D	**≤0.001**

P=≤0.05 Simple "t" test was applied

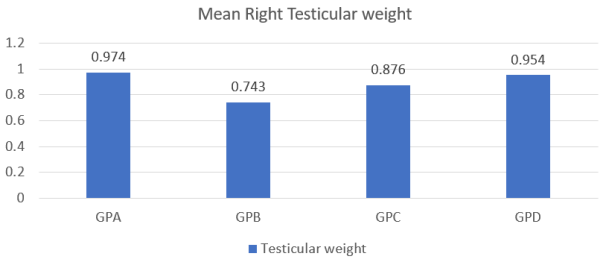

Figure No.2: Shows the Mean Right sided testicular weight among different therapeutic groups

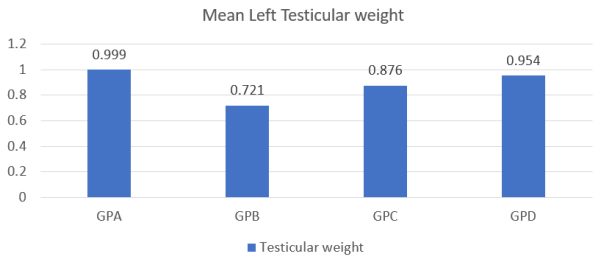

Figure No.3: Shows the Mean Left sided testicular weight among different therapeutic groups

Table No.1b: Shows the level of significance on comparison of Bilateral Mean testicular weight among the different therapeutic groups

Groups	Compare the Mean of Right sided Testicular weight(gm)	Compare the Mean of Left sided Testicular weight(gm)
B vs A	≤0.001	≤0.001
B vs C	≤0.001	≤0.001
B vs D	0.001	0.001
A vs C	≤0.001	≤0.001
A vs D	0.547	0.621
C vs D	0.001	0.001

P= ≤0.05 One-way ANOVA followed by Post hoc Tuckey's test

DISCUSSION

The chronic use of phenytoin effect's male reproductive function. One of the studies was taken in Nigeria regarding effects of chronic usage of phenytoin in male reproductive function in rats which showed that phenytoin reduced fertility in male's rats.[1] In accordance with the results of one of the studies, including the effects of anti-epileptic drugs on the male fertility. The evidence was established the major effects on the male fertility in terms of reduction in testosterone hormones, and markedly interfere in the process of spermatogenesis. They study also revealed the decreased testicular weight as in the present study.[9] One of the randomized studies was done on 28 numbers of male rats with the phenytoin-levetiracetam adjunctive treatment plan. The objective of the study to evaluate their effects on male reproductive function, and the observation established that there were no significant effects on body weight, while the organ weight was reduced with the loss of other cellular function and effects the morphology of the spermatozoa and Sertoli cell. As in the present study, the body weight was not affected with the prolong use of phenytoin, although the toxic group shows significant reduction of bilateral testes weight.[10] The other study showed the combination of different anticonvulsants drugs also has effect not only on cellular function and cell count it is also significantly suppressed the testosterone levels and decreased the weight of testes, seminal vesicle and epididymis. Moreover, these drugs cause the cytoarchitecture of testicular tissue disorganization. Similarly, in the present study, the anticonvulsant drug effects and reduce the cellular function and testicular weight.[11] Over 60 days the administration of oral anti-epileptic drug in rats marked decreased the testicular weight, sperm cell concentration, percentage of live sperms with high motility and cause the elevation of percentage of abnormal spermatozoa. The chronic use of antiepileptic drug also effects the testicular morphology and histopathological changes. As in the present study the anticonvulsant drugs induced toxicity has found almost in every aspect of reproductive system.[12] The study is to evaluate the protective role of corn oil and virgin coconut oil in antiepileptic induced testicular toxicity. The antioxidant oils have tremendous antioxidant effect on male fertility. The coconut oil has antimicrobial agent to kill microorganisms. and corn oil has poly unsaturated fatty acids which is important for normal healthy spermatozoa. The fatty acids are help for fluidity of sperms and promote fertilization. The antioxidant oils protect the reproductive system and enhance the fertilization, as the present study the both antioxidant oils significantly protect the reproductive system and sustain the testicular weight.[13] Another study which has been taken on male albino rats to know the lycopene effect on testicular torsion which cause testicular injury or testicular ischemia. Lycopene is a red pigment (carotenoid) in fruits and vegetables with antioxidant properties. The albino rats were segregates in three groups, and after an induction of ischemia operated animals were treated with lycopene and corn oil by gavage. 5 mins after operation IR (Ischemia reperfusion) decreased sperm motility and count in both sides of testes and elevate abnormal sperm rate bilaterally and in IRL (Ischemia reperfusion with lycopene) there is decreased rate of abnormal sperm count, similarly as in the present study the virgin coconut and corn oil having the same composition of lycopene in their extracts efficiently reduces the abnormal cell count in both testes as well helps in maintaining the organ morphological and functional capabilities. The remarkable effects were shown by virgin coconut oil as compare to other.[14] The study has proven that the anti -oxidative oil reduced oxidative stress. The study executed to know the role of Methanolic extract of Tribulus terrestris fruit (METT) in another anti-epileptic drug induced testicular toxicity. In this randomly male rat were selected. Which are exposed to antiepileptic drug. Orally treated rats with METT have anti oxidative effect and causes

elevation in weight of testes and increase LH, FSH, sperm motility, sperm count and reduced degenerative changes. The present study is also revealing the significant anti-oxidants effects of oils to reduce the oxidation stress or sustain the drug toxication as well. The anti-oxidative therapy is retaining the testicular weight too.[15] In accordance with the study results of consumption of virgin coconut oil in alcohol induced testicular toxicity along with antiretrovirals therapy. The results were shown no significant difference in both testicular weight and body weight. Although in present study the similar oil was help in resurgence of testicular weight along with phenytoin induced therapy, and simultaneously had no harm to body weight.[16] In accordance with the evidences of the study-based results establishing the impact of lycopene (a basic biochemical component of coconut oil) in adriamycin-induced testicular toxicity showed a restoration in sperm count and the physiological function of the different sex hormones. Altogether they contribute to restore the organ weight and enhance the testicular function and their biochemical compositions. Likewise, in the present study the coconut oil boosts up the testicular functions and helps in restore the organ weight.[17].

CONCLUSION

The study results show significant reduction of organ weight in experimental group as compare to control group, and the group of virgin coconut oil remarkably maintain the bilateral testicular weight as compare to other. Although the body weight was remains unchanged. Anti-oxidant properties of virgin coconut oil due to its biochemical composition strengthen its role against the free radicals and achieve their desirable effects on male fertility. Virgin coconut oil is easy to use and easily accessible for everyone.

Author's Contribution:

Concept & Design of Study:	Khalique-ur-Rehman
Drafting:	Masood Ali, Khalid Shehzad
Data Analysis:	Hina Khan, Humaira, Raja Faisal
Revisiting Critically:	Khalique-ur-Rehman, Masood Ali, Khalid Shehzad
Final Approval of version:	Khalique-ur-Rehman

Conflict of Interest: The study has no conflict of interest to declare by any author.

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Original Article

Frequency, Type and Extent of Smoking in COVID-19 Patients and its Association with Disease Severity

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ABSTRACT

Objective: To assess the frequency of smokers in patients who are confirmed to have COVID-19 through PCR testing and to determine the association of cigarette and windpipe smoking with the disease severity

Study Design: Cross-sectional study

Place and Duration of Study: This study was conducted at the Department of Medicines, Shaikh Zayed Hospital, Services Hospital and Ittefaq Hospital Lahore, Pakistan from 13th June 2020 to 15th March 2021.

Materials and Methods: Three hundred and sixty seven patients were taken from different hospitals of Lahore, Pakistan. Only COVID-19 PCR positive patients with age over 25 were selected to be part of the study. The COVID- 19 case was defined as mild moderate and severe based on the severity of symptoms. History of current and former smoking, mode of smoking whether windpipe or cigarette and the no. of pack years smoked was asked from each patient or next of kin in severe disease.

Results: There were 39.5% females and 60.5% males. The smoking population was fairly low to about 12.53% among which 46 were cigarette smokers, 4 used windpipe and the other 4 had used both cigarette and windpipe. The no. of years smoked are divided into three groups and their relation with the severity of disease observed in this study.

Conclusion: There was no significant association found between the disease severity in COVID-19 infection and smoking habit. Also, it was found that the intensity of smoking was unrelated to the severity of symptoms in COVID-19.

Key Words: Frequency, Type, Smoking, COVID-19

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INTRODUCTION

In late 2019, several cases of a novel virus were identified to cause pneumonia in Wuhan, china. This virus named COVID-19 rapidly spread in the whole world and became global pandemic on 11th march 2020.[1] This virus has affected 219 countries worldwide up till now and the number of affected cases is steadily increasing.[2] It is important to identify the possible reasons to why it affects some people more than the others to decrease the spread. To date, many factors are considered to increase the risk of infection as well as development of severe disease such as cardiovascular disease, hypertension, chronic lung disease, diabetes, cancer, chronic kidney disease, obesity i.e. BMI ≥30.[3]

Smoking through windpipe or use of cigarette is known to cause many lung diseases and malignancies but its direct role in increasing the risk of COVID-19 is yet to be determined. Several studies have been done in the world to establish the role of smoking in the development of covid-19 infection and to see connection with the severity of symptoms. As tobacco smoking is known to cause lung diseases primarily like chronic obstructive pulmonary disease and also, acute respiratory distress syndrome (ARDS) which is also a direct complication of COVID-19.[4] So the possibility of smokers having similar risk of acquiring severe COVID cannot be ruled out.

The use of tobacco has a strong impact on respiratory health and it is renowned cause of lung cancer. It is known to cause swelling and rupturing of air sacs in lungs with prolonged usage thereby, decreasing the capacity of lung to transfer gases i.e. oxygen and carbon dioxide.[5] Also, it builds up mucus plugs resulting in coughing and breathing difficulties.

In addition, there is notable increase risk of severe COVID-19 infection in patients who have other chronic illness like cardiovascular disease (CVD) for which smoking is also a risk factor.[6] Moreover, a patient with

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a weak heart condition amid COVID-19 infection is vulnerable to develop severe symptoms.[7]

The largest study population of 1099 patients with COVID-19 was provided by Guan et al. from multiple regions of mainland China. Descriptive results on the smoking status of patients were provided for the 1099 patients, of which some had severe symptoms, and many had non-severe symptoms. Among the patients with severe symptoms, mostly were current smokers and few were former smokers. Thereby, proving there is a link of smoking to the disease severity.[8] In the same way, Zhang et al[9] presented clinical characteristics of 140 patients with COVID-19. The results showed that most were smokers with severe disease giving some association between smoking and COVID infection. Many other researches show contradictory opinion showing no link of smoking and COVID 19 infection.[10] Hence, it is important to gather more evidence to expand our information about the possible relationship of smoking cigarette and windpipe to the severity of symptoms in COVID-19 which can help in designing the management plan. The Prevalence of smoking in Pakistan is 19.1% on average[11], so it is important to determine whether the smokers are at risk of developing complications of this disease. This study was therefore designed to study the frequency of smokers (cigarette and windpipe) in hospitalized patients and to compare the severity of symptoms in smokers and non- smokers.

MATERIALS AND METHODS

This cross-sectional study was conducted at Department of Medicines, Shaikh Zayed Hospital, Services hospital and Ittefaq Hospital Lahore, Pakistan from 13th June 2020 to 15th March 2021. Three hundred and sixty seven patients were taken from different hospitals of Lahore, Pakistan. Only COVID-19 PCR positive patients with age over 25 were selected to be part of the study. The COVID-19 case was defined as mild moderate and severe based on the severity of symptoms. History of current and former smoking, mode of smoking whether windpipe or cigarette and the number of pack years smoked was asked from each patient or next of kin in severe disease. An informed consent was obtained on approaching a patient. Only COVID-19 PCR positive patients were selected for the study. COVID-19 case was defined as ***Mild*** (no or mild pneumonia) Patients with mild respiratory symptoms of low grade fever (<100°F), cough, flu will be considered as mild cases, **M*oderate, p***atients with shortness of breath in addition to above symptoms of fever (>100°F), cough ± sputum, flu will be taken as severe case and **S*evere*** e.g. with respiratory failure, shock, or multiorgan dysfunction. Patients with above symptoms and requiring need of ventilation or have organ damage such as liver or renal dysfunction will fall into category of critical case

A full protocol of donning and doffing was followed to visit the patient by the researcher as per WHO guidelines. An informed consent was taken from patients themselves in mild and moderate case whereas for severe cases it was taken from the first degree relative. The patient details were taken from their medical record in severe case and confirmed from patient themselves in moderate and mild cases. As for severe cases, history was taken from the next of kin. The mild cases were hospitalized due to lack of availability of isolation at home or previously in first wave of COVID, all PCR positive were admitted in Pakistan due to fear of spread of infection. The smokers and non-smokers were identified on basis of history and registered. The mode of smoking whether wind pipe or cigarette was also inquired. They were also categorized into former and current smokers and also, number of pack years for cigarette smoking and no. of years for windpipe or hukka smoking was asked from each patient.

The patients with age above 25, Covid PCR positive and symptomatic COVID case as per case definition were included in the study. The patients diagnosed case of Diabetes for more than 10 years[12], having asthma or active tuberculosis; bronchiectasis and cerebrovascular accident[13] based on history alone were excluded. A full record was maintained for each patient along with their demographic details. The patient's details were recorded by researcher to minimize spread of infection. Later, patients were thanked for their participation and mobile phone was disinfected on leaving the isolation.

Data analyzed using SPSS version 23. Categorical data summarized as counts and percentages and other data presented as means and standard deviation if normally distributed or as medians and interquartile ranges if data is Skewed. P value of ≤ 0.05 is considered statistically significant.

RESULTS

The mean age of participants is 51.06±15.73 of which 60.5% were males and 39.5% were females. The results show that men are more affected by COVID-19 than the women. The highest frequency of COVID PCR positivity is between age group of 58-67 which may be because of low immunity in people of advanced age. Only 46 individuals were found to have smoking history of which 34 were currently smoking at the time of admission. Of the total smokers, 38 were cigarette smoker, 4 smoked only windpipe and 4 smoked both windpipe and cigarette. Most of the smokers had used for over a decade. Most of them were retired 21.52 while 19.61% were employed when they were infected (Table 1).

The individuals were grouped in smokers and non-smokers category where it was seen that smokers were slightly more affected for severe disease from non-smokers. In contrast, most non-smokers had only mild

disease. For moderate symptoms i.e. slight respiratory involvement there was no significant difference in both groups. The details of individual categories are more precisely explained in Table 2

Table No.1: Distribution of patients by COVID-19 severity, smoking status of study participants and their smoking habits

Variable	No.	%
COVID-19 cases		
Mild	93	25.3
Moderate	191	52.0
Severe	83	22.6
Smoking status		
Non-smoker	321	88.0
Smoker	46	12.0
Type of smoker		
Current smoker	34	9.3
Former smoker	12	33.0
Mode of smoking		
Cigarette	38	10.4
Windpipe	4	1.09
Both	4	1.09
Years of smoking (years)		
≤10	15	4.1
11-20	8	2.2
>20	19	5.2
Gender		
Male	222	60.5
Female	145	39.5
Profession		
Students	56	15.25
Business	66	17.98
Employed	72	19.61
Housewife	45	12.26
Professional	49	13.35
Retired	79	21.52
Age (years)		
25 – 38	156	
39 – 67	190	
68 – 97	20	

Based on the smoking history; former smokers had more severe disease in comparison to former smokers by only a minor difference of 1%. 8.3% and 11% had only mild symptoms of COVID 19 infection for former and current smokers respectively. There was no significant difference found for severity of disease in respect to smoking now or in past. Of the total of 46 smokers majority (38) smoked cigarette; 11 had severe disease, 22 had moderate symptoms 5 had mild cough or fever. Among the 4 windpipe smokers; 2 had moderate infection and 2 had severe infection and same was seen for people who smoked both cigarette and windpipe. For extent of smoking, number of years smoked; there was no significant correlation found with the severity of symptoms. The pack year of smoking was grouped into <10, 10-20 and more than 20 as group 1, 2 and 3 respectively. Group 1 and 3 had same number of individual showing no difference between the extents of smoking to the disease severity. For group 2, mostly had moderate infection and few had mild or severe disease (Table 3).

Table No.2: Association between COVID-19 cases and smoking

Smoking status	COVID -19 cases			χ^2 value	P value
	Mild	Moderate	Severe		
Non-smoker	88 (94.6%)	165 (86.4%)	68 (81.9%)	6.87	0.032
Smoker	5 (5.4%)	26 (13.6%)	15 (18.1%)		

Table No.3: Association between COVID-19 cases and years of smoking

Pack years of smoking	COVID -19 cases			χ^2 value	P value
	Mild	Moderate	Severe		
<10	3 (60%)	10 (38.5%)	6 (40%)	1.35	0.852
10-20	1 (20%)	5 (19.2%)	2 (13.3%)		
>20	1 (20%)	11 (42.3%)	7 (46.7%)		

DISCUSSION

There is contradictory evidence of direct relation of smoking to COVID 19 infection. It seems important as we have faced the worst pandemic in history unexpectedly in this new era to identify the factors which are responsible for predisposing a person to this possibly fatal infection. If we are able to identify modifiable risk factors such as smoking to add on the spread of the infection, we can possibly take measures to stopping this ongoing nightmare. It is therefore, self-explanatory that this information is vital to our survival. This study shows that more males than females were affected by this infection. The cause may be that men are more exposed to the risk of disease as they go outside more often or are mostly breadwinner of the family. Only small proportioned of the study population; who belonged to different ethnic and social groups, was smoker. Cigarette smoking was more common than wind pipe or hukka as mode of smoking. Former and Current smokers were relatively equally affected with the disease severity. The years smoked had no significant influence on the intensity of disease symptoms of COVID infection.

Most of the prior work shows association of smoking to the severity of disease and they also prove significant correlation of smoking habit and worsening of symptoms.[14,15] However, some researchers successfully provided evidence that tobacco neither directly increase the susceptibility to COVID -19 infection[16] or other respiratory comorbidities[9,17] nor has effect on its progression. Lippi and Henry[10] reported that the results of this preliminary meta-analysis based on Chinese patients suggest that active smoking does not

apparently seem to be significantly associated with enhanced risk of progressing towards severe disease in COVID-19.

This research was conducted due to this controversy arising about whether smoking habit is directly related to adverse outcome in COVID 19 patients. Due to high prevalence of smoking in Pakistan[11], we were of the opinion to get a random cross sectional survey which will provide necessary information to support this ideation. The possible mechanisms involved include up regulation of ACE-2 gene expression in the epithelium of major airways in COPD patients and active smokers which could lead to adverse symptoms in this infection.[18] Also, places where virus is found commonly like paper or plastic can be easily contaminated through smoke from the affected individuals indirectly contributing to the spread of infection.[19]

This study had some limitations, firstly patients who were being mechanically ventilated; smoking history was taken from next of kin who might not know about the patient's habit or former history. Secondly, several patients might have felt judged by researcher or other admitted patients and might have hidden the correct details. Thirdly, patients who have recently quit, just before to admission insist on being classified as non-smokers and do not tell about their former smoking habit. Fourth, most patients being females and as our country has low prevalence of smoking in females, this might have caused additional bias. Finally, due to small study sample the results can vary and cause false impact of the studied correlation.

CONCLUSION

Both current and former smoking is not associated with increased presentation or morbidity in patients who are in hospital with COVID-19. As a result of possible misclassification of smokers as non-smokers, the analysis may underestimate the likelihood of severity in such patients. As the global pandemic continues to escalate due to genetic mutations of corona virus, the policy makers and healthcare workers should prioritize managing the undeniable risk factors contributing to the crisis. To add on, the healthcare workers are working to their full capacity to address this pandemic, other relevant researches in similar population can aid in determining the true course of illness in relevance to the smoking habit.

Author's Contribution:

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Original Article

Comparison of Burnout Syndrome Among Public and Private Sector Physiotherapists

Muhammad Asrar Yousaf[1], Samrood Akram[1], Rahat Afzal, Anam Abbas, Naveed Anwar and Asad Ahmad[1]

ABSTRACT

Objective: To compare the level of burnout syndrome among public and private sector physiotherapists.
Study Design: cross-sectional study
Place and Duration of Study: This study was conducted at the UHS, Lahore, Nur International University, Lahore and Riphah International University, Lahore from July 2019 to December 2019.
Materials and Methods: Data were collected through convenient sampling technique. Physiotherapists of age range 25-40 years were participated in the study. Outcome measure was valid and reliable Maslach Burnout Inventory Scale. SPSS version 20 was used for analysis of data. Chi square and Mann Whitney U test was used in analyzing the data.
Results: Mean & standard deviation of age for public and private sector Physiotherapists (PTs) were found to be 27.90±6.28 and 28.94±4.04 years, respectively. Out of total 387 physiotherapy practitioners, there were 105 working in Public Sector and 282 working in Private sector. Majority (43.8%) had symptoms of burnout syndrome at borderline in public and only 2.9% had developed while 53.2% PTs from private sector had developed burnout syndrome and 10.6% were with severe burnout level. P value of <0.001 showed strong positive association of burnout syndrome with sector system where private sector PTs were highly affected with burnout than of public sector PTs.
Conclusion: Physiotherapists significantly demonstrate burnout syndrome presence of which private sector has predominantly more burnout syndrome levels among their physical therapy employees as compared to public sector. Gender differences are also evidently present where male PTs are majorly impacted by this syndrome in both sectors than female PTs.

Key Words: Burnout Syndrome, Health Care Professional, Occupational Anxiety, Physical Therapy, Work Related Stress

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INTRODUCTION

Webster's Medical Dictionary defines burnout as "physical or mental exhaustion due to long-term stress" The basic need for mental health promotion is to identify and limit the sources of stress in the workplace.[1, 2] Burnout is a negative psychological experience including sentiments, states of mind and desires, which regularly brings about negativity, loss of individual achievement and depersonalization.[3,4]

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Maslach and Jackson proposed that burnout is characterized by three components; emotional exhaustion: An inability to cope at a psychological level. [5]

This is the key aspect of burnout, Depersonalization: The development of negative and attitudes towards clients, causing them to seem less than human and lack of personal accomplishment: The capability to have negative views about the achievements with clients.[6]The indications of burnout are: mental and emotional exhaustion, depersonalization and lack of personal accomplishment.[7,8] Freudenberg gave the concept of 'burnout' to describe physical and emotional exhaustion. Poor self-concept, negative attitude towards job and lack of attention and concern for clients are the manifestations of the burnout syndrome. [9]Burnout develops in an individual due to long term exposure to stresses and anxiety, which goes beyond the level of tolerance and exceeds the coping abilities. [10]This syndrome frequently occurs in individuals working in health care department due to ongoing stress and emotional instability they are facing at their work. [11]It has been suggested that emotional exhaustion and

depersonalization, the two components of burnout are more predominant in recently qualified physiotherapists.

Most of the time burnout is related with lessened self-esteem, work repulsion and loss of consideration. It is a significant issue bringing about dislike for job and a reduction in quality of care, which influences customers as well as the general population related inside the workplace.[12,13] It has been shown that individuals working in close contact with clients show higher level of burnout that's why physiotherapists are more prone to develop burnout because they get deeply involved with their clients throughout their career. Burnout is a gradual process. The signs and symptoms are vague at the beginning, but with the passage of time they get worse. Features of burnout are emotional exhaustion, fatigue and depression, mental and physical symptoms are more predominant than physical, work-related symptoms are present, burnout may occur in individuals without any history of psychopathology and negative attitudes lead to the decreased effectiveness and decreased work performance.[14] Sources of stress include work overload and its effects, poor management, dealing with ill patients and managerial responsibilities. [15]

Burnout syndrome is becoming very common among different health care practitioners due to increasing stress. Hence, the study is conducted to find out the level of burnout syndrome among physiotherapists and to evaluate the related factors. The significance of study was to determine different intervention strategies and methodologies to anticipate burnout syndrome in physiotherapists. This study may help to know how different emotional, physical and mental factors influence the mind state of therapists. This study can help physical therapists have glance on various factors which are compromised in their practice in different organizations. This can lead to define pathway to minimize burnout thus increasing performance. The minimization can be done with policy making and supporting physical therapists found with symptoms of burnout.

MATERIALS AND METHODS

It was a cross sectional survey which conducted within six months. The data were collected from 387 physical therapists working in Government and Private sector hospitals / Clinical and academic setups in Lahore. The respondents were informed about the aims and objective of research and it was assured that their privacy and confidentiality will be secret including name of organization in which they were working. Respondents had right to withdraw and furthermore respondents uncomfortable with emotional, physical or social questions during survey were also free to stop and were excluded. Calculated sample size was based on the epitool sample size calculator by using "n = (Z2 x P x (1 - P))/e2" formula. Where;

Z = (Z=1.96 for 95% CI)

CI = 95%

P = expected true proportion = 0.52 [16]

e = desired precision = 0.05

It was calculated as 384 and by keeping the dropout in mind, questionnaires were distributed to 400 physiotherapists through email and other web based social media. Total 387 questionnaires were received after completion and thus, sample size was considered 387 instead of 384. Non-probability convenient sampling technique was followed to collect the data from all the physiotherapists who signed the consent form, physiotherapists of both genders, aged between 25-40 years, working clinically or academically in public and private sectors. Physiotherapists who were graduated or post graduated but were not working anywhere or working as interns were excluded from the study.

Ethical Review Committee of Kana Physiotherapy and Spine Clinic reviewed the study proposal and approved with the reference number (PT/2019/REC/IRB/012). The data were collected by questionnaire comprised of demographic variables and Burnout as per measured by The Maslach Burnout Inventory (MBI-Human Services Survey). This questionnaire is validated and showed reliability of 0.95 in addition with internal consistency of 0.922. [17]

Data Analysis: SPSS 20.0 version was used to analyze data. Mean±SD was calculated for continuous variables. Frequency (Percentage) was calculated for all categorical variables. To compare the impact of burnout and association of variables, chi square statistics was used. Data were checked for normality by applying Kolmogorov Smirnov and Shapiro Wilk tests. Both tests showed insignificant results because of that, non-parametric test of independent sample t test; the Mann Whitney U test was applied to evaluate if there were significant differences of burnout syndrome between PTs from public and private sectors. P value <0.05 was considered significant.

RESULTS

Results showed that mean &standard deviation of age for public and private sector Physiotherapists (PTs) were found to be 27.90±6.28 and 28.94±4.04 years, respectively. Burnout syndrome elements were analyzed for all physiotherapists from both sectors. Total score of burnout scale was also calculated which was 154.16±52.67 for public and 174.33±46.89 for private sector PTs. Median and standard error were also taken for total burnout score because standard deviation for both; public and private sector was very high (Table-1).

Out of total 387 physiotherapy practitioners, there were 105 working in Public Sector and 282 working in Private sector. In all physiotherapy practitioners, there were 35 males and 70 females in Public Sector whereas 127 males and 155 females in Private Sector. There were 36 married practitioners in Public Sector while 131 married PTs in Private Sector. There were 66 temporaries and 39 registered practitioners in Public Sector whereas 77 temporaries and 205 registered practitioners in Private Sector. About 97 PTs were working in morning and 8 in afternoon shift in Public Sector while 151 PTs in morning, 108 in afternoon shift and 23 PTs were doing night shifts in Private Sector. Among all PTs, majority was of graduate PTs in both Public Sector and Private Sector (Table-2).

Majority (43.8%) had symptoms of burnout syndrome at borderline in public and only 2.9% had developed while 53.2% PTs from private sector had developed burnout syndrome and 10.6% were with severe burnout level (Table-3).

Table No.1: Descriptive Statistics (n=387)

	Public Sector		Private Sector		
	Mean	SD	Mean	SD	P value
Age	27.90	6.28	28.94	4.04	<0.001
Total prediction score	21.61	6.25	24.12	6.66	<0.001
Total Score of Emotional Exhaustion	30.97	12.88	32.61	11.28	<0.001
Total score of personal accomplishment	28.91	12.28	33.55	8.33	<0.001
Total score of Depersonalizations	12.72	7.55	17.11	8.39	<0.001
Total Score of Burnout Scale	154.16	52.67	174.33	46.89	<0.001
Median for total burnout score	157.00		181.00		
Standard Error for total burnout score	5.14		2.79		

Table No.2: Other demographic variables (n=387)

Variables	Public Sector		Private Sector			P-value
Sector	105 (27.1%)		282 (72.9%)			
Gender	Male	Female	Male	Female		
	35 (33.3%)	70 (66.7%)	127 (45%)	155 (55%)		0.038
Marital Status	Married	Unmarried	Married	Unmarried		
	36 (34.3%)	69 (65.7%)	131 (46.5%)	151 (53.5%)		0.032
Work Status	Temporary	Registered	Temporary	Registered		<0.001
	66 (62.9%)	39 (37.2%)	77 (27.3%)	205 (72.7%)		
Work Shift	Morning	Afternoon	Morning	Afternoon	Night	<0.001
	97 (92.4%)	8 (7.6%)	151 (53.5%)	108 (38.3%)	23 (8.2%)	
Education	Graduate	Master	Graduate	Master		0.001
	76 (72.4%)	29 (27.6%)	158 (56%)	124 (43.97%)		
Perform any Sports	Yes	No	Yes	No		0.064
	47 (44.8%)	58 (55.2%)	156 (55.3%)	126 (44.7%)		

Table No.3: Level of Burnout Syndrome in Public and Private Sector (n=387)

Sector	**Burnout Syndrome Levels**	**Frequency**	**Percentage**	**P-Value**
Public	No Burnout Syndrome	23	21.9%	
	Borderline Burnout Syndrome	46	43.8%	
	Burnout Syndrome	33	31.4%	<0.001
	Severe Burnout Syndrome	3	2.9%	
Private	No Burnout Syndrome	40	14.2%	
	Borderline Burnout Syndrome	62	22%	
	Burnout Syndrome	150	53.2%	<0.001
	Severe Burnout Syndrome	30	10.6%	

Chi square association was analyzed between burnout syndrome and public, private sectors of practicing PTs. P value of <0.001 showed strong positive association of burnout syndrome with sector system where Private sector PTs were highly affected with burnout than of public sector PTs (Table-4).

Mann Whitney U test showed statistically significant differences ($p<0.001$) in burnout syndrome between public and private sectors while Private sector's PTs

were predominantly affected with burnout syndrome than those in public sectors. Mean rank values of private sector PT burnout were higher than of public sector PTs. Although there were higher number of females participated in this study, males were majorly affected with burnout syndrome than females in both public and private sectors and p<0.001 showed statistically significant differences on basis of gender as well(Table-5).

Table 4: Chi Square Association between Burnout Syndrome level and Sector of Practice (n=387)

		Sector		Total	P-Value
		Public	Private		
Burnout Syndrome Level	No Burnout	23	40	63	<0.001
	Borderline Burnout	46	62	108	
	Burnout Syndrome	33	150	183	
	Severe Burnout Syndrome	3	30	33	
Total		105	282	387	

Table 5: Mann Whitney U Test

	Sector		Mean Rank	P-Value
Burnout Syndrome Level	Public		151.74	<0.001
	Private		209.73	
Burnout Syndrome Level	Public Sector	Males	68.79	<0.001
		Females	45.11	
	Private Sector	Males	148.33	
		Females	135.91	

DISCUSSION

In the study 387 physiotherapists from public and private sector have participated. The mean age in public sector group is 27.90 ±6.28. Mean age in private sector group is 28.94 ±4.04. Borderline burnout syndrome is found in majority of the participants in public sector group while burnout syndrome is found in participants of private sector group in the study. Males are more affected than females in current study. To the author's best knowledge there is a lot of work done to find out the prevalence of burnout syndrome in different professions like physiotherapy, nursing etc. But no work is found in which burnout syndrome is compared in physiotherapists working in public or private sector.

According to a study by Bruno Corrado et. al 45% of the physiotherapists are at high risk of developing burnout out syndrome. While 16% of the physiotherapists had burnout out syndrome in the study[18] which is much less than the burnout out syndrome observed in Pakistani physiotherapists working in public and private sectors of Lahore. Both of the studies states that emotional exhaustion, depersonalization and personal accomplishment are the factors that brings out burnout syndrome in physiotherapists.

In contrast to the above studies a study conducted by De Araujo STL et. al found that stress or other socioeconomic factors are not bringing burnout syndrome among Brazilian physiotherapists. But the study found that 49% of the physiotherapists were at risk of developing burnout syndrome because of psychic wear and indolence.[19] Similar to the current study another study by Agnieszka Bejer et. al found that males were more prone to the burnout syndrome than females. The reason may be that males also have to bear the financial burden. The results of the burnout syndrome in private sector in the current study are in accordance with the results of the above study which found that personal accomplishment is the factor that is mostly found in the physiotherapists.[20]But in contrast to physiotherapists working in public sector in the current study emotional exhaustion was mostly found.

Burnout syndrome in physiotherapists whether working in public sector or private sector is concerning. Physiotherapists are the part of our healthcare system and if they are stressed out that will cause a negative impact on the health care of the patients. All the factors that are causing burnout syndrome in physiotherapists working in different sectors should be rule out first and steps should be taken to eradicate them. Workplace conditions should be improved. The hospitals should provide better working environment to the healthcare staff including physiotherapists. There should be enough physiotherapists working in a hospital to lessen the workload.

CONCLUSION

Physiotherapists significantly demonstrate burnout syndrome presence of which private sector has predominantly more burnout syndrome levels among their physical therapy employees as compared to public sector. Gender differences are also evidently present where male PTs are majorly impacted by this syndrome in both sectors than female PTs.

Recommendations & Limitations: It is recommended that the working environment of physiotherapists should be comfortable so that they do not feel exhausted. Working atmosphere should be calm and there should be proper time management for work. This research had some limitations also. Study was generalized in Physiotherapists from both academic and clinical practices where it should be assessed that which area has more burnout rates. Risk factors evaluation and coping strategies were not assessed which should be considered in future researches to lower the burnout syndrome in Physiotherapy professionals as this is affecting their physical, mental health and working efficiency.

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Original Article

Frequency of ABO Incompatibility in Neonates Presenting with Unconjugated Hyperbilirubinemia

Saqib Munir[1], Samia Ijaz[1], Mimpal Singh[1], Ayesha Abdul Kareem[2] and Kashif Mehmood[1]

ABSTRACT

Objective: To find the frequency of ABO incompatibility in newborns presenting with neonatal jaundice.
Study Design: Cross sectional study
Place and Duration of Study: This study was conducted at the Medicine Unit II, Pediatric Department, Mayo Hospital, Lahore from November, 2017 to May, 2018.
Materials and Methods: 100 neonates who fulfill the inclusion criteria were included in the study. Then blood sample was obtained by using pricker from foot and three drops will be obtained. Antigens A & B was applied and blood group of neonate was noted. Blood group of mother was also assessed. If blood group of neonate was A, B or AB and blood group of mother was O, then ABO incompatibility was labeled. All data was entered in specially designed Performa. The data was analyzed through SPSS version 21.
Results: The neonates mean age was 16.53±9.99 hours. There were 59 (59%) male and 41 (41%) female neonates. The mean gestational age of neonates at birth was 37.67±1.71 weeks. The mean birth weight of neonates was 2354.58±379.16 grams. The mean unconjugated bilirubin level was 7.55±1.45 mg/dl. There were 28 (28%) had ABO incompatibility.
Conclusion: Thus the frequency of ABO incompatibility was high in neonates with hyperbilirubinemia. So ABO incompatibility can be a risk factor for neonatal hyperbilirubinemia.

Key Words: ABO incompatibility, neonates, neonatal jaundice, hyperbilirubinemia

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INTRODUCTION

Hyperbilirubinemia, or jaundice, is a life threatening disorder in newborns. It is a multifactorial disorder with many symptoms. The most frequent type of jaundice is physiological jaundice, however pathological jaundice is also widespread in some areas.[1] It is one of the most prevalent clinical conditions in neonates.[2] The incidence of jaundice is in 50% of term infants and 75% of preterm infants.[3]

Neonatal hyperbilirubinemia is a common clinical problem encountered during the neonatal period, especially in the first week of life.[4] The most common cause of hemolytic illness in newborns is ABO incompatibility, It occurs when the mother's and infant's ABO blood groups are incompatible.[5]

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Newborn children with maternal-fetal ABO incompatibility are more likely to have serious hyperbilirubinemia, and thus, prediction of possible risk factors, like the degree of hemolysis, gains importance.[5, 6] One study showed that the frequency of ABO incompatibility was 22.5% among neonates with neonatal jaundice.[7] In another study ABO incompatibility was found in 30.0% neonates.[8]

Literature has shown that the frequency of ABO incompatibility among neonates with jaundice or hyperbilirubinemia is not negligible. But very few work has been done in this regard. So through this study, we want to get the evidence so that we may be able to implement the results of this study in future and will be able to recommend to screen the neonates for ABO incompatibility and manage neonate accordingly.

MATERIALS AND METHODS

The cross sectional study was conducted from 04-11-2017 to 04-05-2018 in the Medicine department of Mayo Hospital, Lahore. It was after obtaining permission from the Institutional Board of the hospital. Informed written consent was obtained from patients. 100 sample size was calculated with 5% level of significance, 8.5% margin of error & taking expecting percentage of ABO incompatibility i.e. 22.5% in neonates with neonatal jaundice.

All neonates with after birth either gender presenting with unconjugated serum bilirubin level of >5 mg/dl were included from the study. Direct bilirubin level >2 mg/dl r >20% of total serum bilirubin levels were excluded from the study.

Demographic variables (name, age at presentation, gestational age at birth, gender and birth weight) was also obtained. Then blood sample was obtained by using pricker from foot and three drops will be obtained. Antigens A & B was applied and blood group of neonate was noted. At the same time serum sample was obtained for serum bilirubin levels. Blood group of mother was also assessed. If blood group of neonate was A, B or AB and blood group of mother was O, then ABO incompatibility was labeled (as per operational definition). All data was entered in specially designed Performa (attached).

All Data was entered in SPSS version 21. Quantitative data like age (hours), birth weight, unconjugated bilirubin & gestational age at birth were presented by Mean and SD. Qualitative variables like gender, blood group of mother and neonate and ABO incompatibility was presented as frequency & percentage. Data was stratified for gestational age at birth (on dating scan), gender and birth weight. Post-stratification, chi-square test was applied with P-value ≤0.05 was taken as significant.

RESULTS

In our study, total 100 neonates were included. The mean age of neonates was 16.53±9.99 hours. There were 59 (59%) male and 41 (41%) female neonates. The mean gestational age, birth weight, unconjugated bilirubin level of neonates was 37.67±1.71 weeks, 2354.58±379.16 grams and 7.55±1.45 mg/dl respectively. Table: 1.

There were 33 (33%) neonates with blood group A, 21 (21%) neonate had blood group B, 22 (22%) neonates had blood group AB while 24 (24%) had blood group O. There were 22 (22%) mothers with blood group A, 25 (25%) neonate had blood group B, 17 (17%) mothers had blood group AB while 36 (36%) had blood group O. Table: 2 There were 28 (28%) had ABO incompatibility while 72 (72%) did not had ABO incompatibility. Table: 3

Data was stratified for age of neonates. In neonates aged 1-12 hours, ABO incompatibility was present in 10 (25%) neonates. In neonates aged 13-24 hours, ABO incompatibility was present in 10 (25.6%) neonates. In neonates aged 25-36 hours, ABO incompatibility was present in 8 (38.1%) neonates. P value was insignificant (p>0.05). Table: 4

Data was stratified for age of neonates. In neonates aged 1-12 hours, ABO incompatibility was present in 10 (25%) neonates. In neonates aged 13-24 hours, ABO incompatibility was present in 10 (25.6%) neonates. In neonates aged 25-36 hours, ABO incompatibility was present in 8 (38.1%) neonates. P value was insignificant (p>0.05). Table: 4

Table No.1: Descriptive statistics of Age, Gender, Gestational Age, Birth Weight

		Frequency (%)
Age	Mean± SD	16.53± 9.99
Gender	Male	59(59%)
	Female	41(41%)
Gestational Age(weeks)	Mean± SD	37.67± 1.71
Birth Weight(grams)	Mean± SD	2354.58± 379.16
Unconjugated bilirubin(mg/dl)	Mean± SD	7.55± 1.45

Table No.2: Frequency of Neonatal and Maternal Blood Group

	Frequency(%)			
	A	B	AB	O
Neonatal Blood Group	33(33%)	21(21%)	22(22%)	24(24%)
Maternal Blood Group	22(22%)	25(25%)	17(17%)	36(36%)

Table No.3: Distribution of ABO incompatibility

	Frequency(%)
Yes	28(28%)
No	72(72%)

Table: 4 Comparison of ABO incompatibility with Age, Gender, Gestational age, birth weight & unconjugated bilirubin

		ABO Incompatibility		**P value**
		Yes	**No**	
Age in hours	1-12	10(25.6%)	30(75%)	0.510
	13-24	10(25.6%)	29(74.4%)	
	25-36	8(38.1%)	13(61.9%)	
Gender	Male	11(18.6%)	48(81.4%)	0.012
	Female	17(41.5%)	24(58.5%)	
Gestational Age	Preterm	13(32.5%)	27(67.5%)	0.413
	Term	15(25%)	45(75%)	
Birth Weight (gm)	1500-2000	8(42.1%)	22(57.9%)	0.314
	2001-2500	11(25%)	33(75%)	
	2501-3000	9(24.3%)	28(75.7%)	
Unconjugated bilirubin	5.1-7.5	15(30%)	35(70%)	0.656
	7.6-10.0	13(26%)	37(74%)	

Data was stratified for gestational age of neonates. In preterm neonates, ABO incompatibility was present in 13 (32.5%) neonates. In term neonates, ABO incompatibility was present in 15 (25.0%) neonates. The difference was insignificant (p>0.05). In neonates weighted 1500-2000 grams, ABO incompatibility was present in 8 (42.1%) neonates. In neonates weighted

2001-2500, ABO incompatibility was present in 11 (25%) neonates. In neonates weighted 2501-3000 grams, ABO incompatibility was present in 9 (24.3%) neonates. There was insignificant difference between these variables. (p>0.05). Table 4

Data was stratified for unconjugated bilirubin. In neonates with unconjugated bilirubin 5.1-7.5 mg/dl, ABO incompatibility was present in 15 (30%) neonates. In neonates with unconjugated bilirubin 7.6-10.0 mg/dl, ABO incompatibility was present in 13 (26%) neonates. P value was insignificant (p>0.05). Table 4.

DISCUSSION

Neonatal jaundice is the most common phenomena worldwide, and is the leading cause of admission in the 1st week of life.[9] The epidemiology of newborn jaundice has been documented to vary widely around the world. In the first three days of life, almost 60% of full-term neonates and 80% of pre-term babies present with jaundice. [10] In Bangladesh, ABO & Rh incompatibility were found to be the cause of jaundice in 13.29% or 3.31 percent of neonates, respectively.,[11] while these factors had rates of 27.39% & 9.01% in Iran study.[12]

One of the most common disorders in newborns is hyperbilirubinemia, which affects 60.0-70.0 percent of term & 80.0 percent of preterm infants. It's known to be related with significant disease like neonatal bilirubin encephalopathy & even death. [13]

There were 33 (33%) neonates with blood group A, 21 (21%) neonate had B blood group, 22 (22%) neonates had AB blood group while 24 (24%) had blood group O. There were 22 (22%) mothers with blood group A, 25 (25%) neonate had B blood group, 17 (17%) mothers had blood group AB while 36 (36%) had O blood group. There were 28 (28%) had ABO incompatibility while 72 (72%) did not had ABO incompatibility.

One study showed that the frequency of ABO incompatibility was 22.5% among neonates with neonatal jaundice.[7] In another study ABO incompatibility was found in 30.0% neonates.[8] One study 2016, ABO incompatibility was seen in 5.2% in neonates.[14]

Kalakheti et al., found that A total of 37(18.49%) babies had acquired hyperbilirubinemia, with 14(38%) from the group of babies with the ''O'' positive blood group & 23.0(62.0%) from the group of babies with blood groups other than the 'O' +ve blood group. There was 2.60 times greater chance of having hyperbilirubinemia in babies with ABO incompatibility than ''O'' Positive babies after other important variables.

Among different variables associated significantly, ABO incompatibility was found to be a main risk factor for neonatal hyperbilirubinemia. Hyperbilirubinemia was shown to be two times more often in neonates with ABO incompatibility than in newborns with the O '+ve' blood group.[15]

In a local study, HDN was diagnosed in 20.5% associated with ABO incompatibility.[16] The most common hemolytic outcome of maternofetal blood group incompatibility is ABO hemolytic disease of the newborn, which affects predominantly non-group-O newborns born to group O mothers with immune anti-A or B antibodies.[17]

In babies with ABO incompatibility, only blood group-O can be used for exchange transfusions. The best option would be group O (Rh compatible) packed cells that are suspended in O group / AB plasma total blood (Rh compatible with baby).[1]

Considering that ABO incompatibility between the mother and the baby can result in severe newborn jaundice required an exchange transfusion & even kernicterus, the importance of predicting possible risk factors for hyperbilirubinemia, including the degree of hemolysis.[18]

CONCLUSION

Thus the frequency of Abo incompatibility was high in neonates with hyperbilirubinemia. So ABO incompatibility among neonates with jaundice or hyperbilirubinemia is not negligible. ABO incompatibility can be a risk factor for neonatal hyperbilirubinemia. Now in future, we will recommend to screen the neonates for ABO incompatibility and manage neonate accordingly.

Author's Contribution:

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Original Article

Safe Practice of Bipolar Current for Hemostasis in Pediatric Circumcision with Plastibell at a THQ Hospital Lahore: A Single Surgeon Experience

Sidra Dil Muhammad[1], Muhammad Saad Faisal[2], and Muhammad Rizwan Saeed[4]

ABSTRACT

Objective: To determine the outcome of use of bipolar current for hemostasis in pediatric circumcision with Plastibell performed by a single surgeon at a THQ hospital in order to recognize safe use of bipolar current was the objective of this study.

Study Design: Retrospective Study

Place and Duration of Study: This study was conducted at the Government THQ Hospital Sabzazar, Lahore form June, 2018 to December, 2020.

Materials and Methods: 541 uncircumcised infants, aged 1-9 months. Infants with Congenital Cardiac & respiratory disorders, Jaundice, Bleeding disorders, Urinary tract infection, Balantitis, Paraphimosis, buried penis and for Revision circumcision, were excluded. All circumcisions were performed with the use of Plastibell device by the single consultant surgeon under local anesthesia. Bipolar current with short burst was utilized at frenulum to secure hemostasis. Infants' demographics and postoperative outcome were recorded.

Results: The mean age of infants was 3.07±1.94 months (Range: 1-9 months). Only one infant (0.18%) had congenital abnormality i.e. albinism. Mean clotting time and Mean Bleeding time were 10.04±1.29 min. and 3.51 ±0.98 min, respectively. Mean duration of surgery and Mean hospital stay were 5.97±4.01 min. and 20.54±10.96 min., respectively. There was penile swelling in 4.25% infants, Hemorrhage in 0.0%, Glans injury in 0.0%, Meatus injury in 0.0%, Urine retention in 0.0%, Penile/ glans necrosis in 0.0% and Wound infection in 0.0% infants. Removal of Plastibell for hemostasis was not required in any case (0.0%) in our study.

Conclusion: Bipolar current for hemostasis in pediatric circumcision is safe in experienced hands.

Key Words: Bipolar Current; Hemostasis; Pediatric Circumcision; Plastibell

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INTRODUCTION

Circumcision is the primogenital surgical procedure.[1] Being the oldest procedure, many medical and non-medical personals are trained to perform this procedure. Worldwide, people are ready to go for this procedure for ritual & non-ritual purposes.[2] According to WHO, approximately 30% males are circumcised, globally.[3,4] However, in Muslim countries, this operation is mandatory for every male child.[5]

Technique of circumcision has suffered several modifications in every era. [5,6] Though none of these is gold standard procedure but all practices focus on safe and simple circumcision.[7] Circumcision is not free of complications and overall complication rate is 0.2% to 2%.[8,9] Bleeding being the number one complication, hemostasis in circumcision has given the priority in all techniques. Incidence of post circumcision hemorrhage ranges from 0.1% to 35%. [10,11]

Surgeons rely on electric current for hemostasis. Electro surgery has gained a renowned position in this regard. However, use of bipolar current in controlling bleeding during circumcision is always remain controversial.[12] In a retrospective study by Harty NJ[13] et al, post-operative hemorrhage after using bipolar current was reported in 0.6% for the single surgeon. However, in a study by Rasool N, none of the child was observed with postoperative bleeding after bipolar cauterization of frenular band.[14] The purpose of this study was to determine the outcome of use of bipolar current for hemostasis in pediatric circumcision with Plastibell

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performed by a single surgeon at a THQ hospital Lahore in order to recognize safe use of bipolar current.

MATERIALS AND METHODS

This retrospective study was conducted at the Government THQ Hospital Sabzazar, Lahore form June 01, 2018 to December 31, 2020. This study included 541 uncircumcised infants between 1 to 9 months of age. Infants with Congenital Cardiac & respiratory disorders, Jaundice, Bleeding disorders, Urinary tract infection, Balantitis, Paraphimosis, buried penis and for Revision circumcision, were excluded from the study. The study was approved from Ethical Review committee as per institutional guidelines. All circumcision was performed with the use of Plastibell device by the single consultant surgeon under local anesthesia (plain lignocaine 2%) as penile block. Bipolar current (9 watt) with short burst was utilized at frenulum on small amount of tissue (1-2 mm) at one time to secure hemostasis. Infants demographics and Perioperative data including operating room time, length of stay, Post-operative Hemorrhage, swelling, wound infection, urine retention, Glans or meatus injury, penile necrosis after procedure & on follow up visits (2 weeks post-circumcision) were recorded. All the collected data was entered into SPSS version 22 and analyzed. Outcome was presented as frequency and percentage.

RESULTS

Characteristics of infants are shown in Table I. The mean age of infants was 3.07±1.94 months. Only one infant (0.18%) had congenital abnormality i.e. albinism. Perioperative outcome of pediatric circumcision is shown in table 2.

Table No.1: Characteristics of infants (n=541)

Variables		No. of patients (%)
Age (months)	Mean±SD	3.07±1.94
Congenital abnormality		1 (0.18%)
Clotting time	Mean±SD	10.04±1.29 min.
Bleeding time	Mean±SD	3.51 ±0.98 min.

Table No.2: Perioperative outcome of pediatric circumcision (n=541)

Operative outcomes	No. of patients (%)
Mean duration of surgery (Mean±SD)	5.97±4.01 min.
Hemorrhage	0 (0.0%)
Penile Swelling	23 (4.25%)
Urine retention	0 (0.0%)
Glans injury	0 (0.0%)
Meatus injury	0 (0.0%)
Penile/ glans necrosis	0 (0.0%)
Wound infection	0 (0.0%)
Removal of Plastibell for hemostasis	0 (0.0%)
Mean hospital stay	20.54±10.96 min.

DISCUSSION

Bleeding is a renowned post circumcision complication that doesn't need any introduction. Medical and non-medical personnel all are very much aware of it. Several practices are established to minimize this complication. One of these is electrosurgery which is well practiced these days for hemostasis. But the frequent use of electrosurgery doesn't eliminate the risk of electrosurgical burn. Safe use of electrosurgical current is decidedly endorsed in circumcision as electrosurgical burn can lead to penile necrosis, which is stressed as malpractice and a medicolegal case.[15] Bipolar modes of electrosurgery is well respected in open and laparoscopic surgery because of its safe use. Present study shared the outcome of use of bipolar current for hemostasis in pediatric circumcision with Plastibell to recognize safe use of bipolar current by consultant surgeon.

We included infants only in present study with a mean age of 3.07±1.94 months (Range: 1-9 months). Similar to our study, 96.5% was infants (range: 8 days -13 months) in a study by Okeke LI[7] et al. Conversely, in a study by Rasool N [14], 78.23% children were neonates, 19.68% infants, 2.07% children were between 1-2 years of age. A higher age group (Mean±SD; 3.7 ± 4.9 years) was studied by Harty NJ [13] et al. However, Mujawar P[16] et al, included all age groups (1-60 years) in his study and majority i.e.52.0% was <5 years of age. In our study, Mean duration of surgery was short i.e. 5.97±4.01 min. as compared to a study by Mujawar P[16] et al, who reported a longer mean operative time i.e. 21 min.

Out of 541 infants who underwent circumcision in present study, penile swelling was observed in 4.25% infants which was managed conservatively. A higher number of post circumcision swelling (6.0%) was reported by Mujawar P[16] et al. However, post circumcision complications i.e. Plastibell impaction on glans and post-operative phimosis were observed in 1.03% cases (0.51% each) in a study by Rasool N [14]. Okeke LI[7] et al, reported post circumcision complications in 20.2% of cases i.e. redundant prepuce (53.8%), excessive loss of prepuce (24.6%), skin bridges (16.9%), amputated glans (3.1%) and buried penis (1.5%).

Similar to a study by Rasool N [14], incidence of hemorrhage after circumcision was not reported in any infant (0.0%) in present study. However, Harty NJ [13] et al, reported incidence of bleeding in 0.6% cases and all cases managed conservatively. Mujawar P[16] et al, reported hematoma formation in 6.0% cases in his prospective study. Similar to a study by Mujawar P[16] et al, no inury to glans (0.0%) and urthera (0.0%) or infection (0.0%) was observed in any infant in present study.

Complication rate is very low (4.25%) and of minor intensity i.e. penile swelling in present study that was managed conservatively. None of the infant (0.0%) was required removal of Plastibell in order to deal with post circumcision mishap. Use of bipolar current with short burst and small amount of tissue coagulated at one time are the possible explanations of low complication rate in our study. Other reason is that all circumcision was performed by consultant surgeon however in a study by Okeke LI[7] et al, only 35.1% circumcision was performed by doctors. Furthermore, the tight knot application around Plastibell device after adequate removal of foreskin up to corona of glans aids in inhibiting blood oozing from cut skin margins and proximal migration of Plastibell device. All circumcision in present study was performed for ritual purpose like Okeke LI[7] et al, conversely Mujawar P[16] et al, who executed circumcision with medical indications i.e. balanoposthitis, also, however there was no stated surgical site infection in either of these studies.

This is one of the largest study in literature. Further studies in different setups are needed to evaluate the outcome.

CONCLUSION

It is concluded that the bipolar current for hemostasis in pediatric circumcision is safe in experienced hands. So, the extracted formula of safe and swift circumcision from present study is the circumcision by open technique (with Plastibell device), utilizing bipolar current for hemostasis by proficient surgeon.

Author's Contribution:

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Original Article

To Evaluate the Neurotropic Effects of Methylcobalamin on Atrophied Cerebellar Granular Cell Layer in Albino Rats

Tazeen Kohari[1], Faryal Azhar[2], Meshaal Azhar[2] and Usama Faruqui[3]

ABSTRACT

Objective: As there is scanty research literature on the neurotropic effects of Methylcobalamin on the Cerebellar Granular cell layer of cerebellum, our present study was carried out to evaluate the neurogenetic effects of methylcobalamin on Cerebellar granular cell layer.

Study Design: Observational, Experimental study

Place and Duration of Study: This study was conducted at the Animal House of Basic Medical Sciences Institute (BMSI) JPMC, Karachi from 30 June and ended at 30 July 2013.

Materials and Methods: We selected 18 albino rats weighing 140-185 animals and each group contained six animals. In Group A there were six, animals which were fed Lab diet and water, Group B contained six albinos which were given Lithium carbonate at a dose of 20 mg/g OD for four weeks and Group C received Lithium carbonate at a dose of 20 mg/kg OD in flour pellets along with Injection 500 microgram of Methylcobalamin.

Results: The results showed regeneration and improved thickness of Granular layer due to vitamin b12.

Conclusion: The strength of this study proved that the use of vitamin b12 is resulted in restoring the cerebellar Granular cell layer of cerebellar gray matter.

Key Words: Cerebellar Granular layer, Degeneration, Regeneration

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INTRODUCTION

Cerebellum a part of hindbrain is present posterior to the brainstem and fourth ventricle,[1] it consists of two cerebellar hemispheres[2] which comprises of Gray and White matter.

The cerebellar cortex consists of three layers, the outer is the low cell or Molecular layer, the interface or middle is the Purkinje cell layer and the innermost Cells rich layer is called the Granular cells layer[3]. The innermost layer is easy target for deleterious Opoid agents such as Morphine[4], metals like Zinc[5] and Lithium.[6]

Lithium carbonate is frequently prescribed in Pakistan in Bipolar affective disorders.[7]

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Lithium ingestion causes neurological signs in patients[8] these neurological deficits[9]were found to be reversed by use of Methylcobalamin as documented by Kaji, et al 2019[10].

We found that there is insufficient data on the Neuroprotective role of Methylcoba- lamin on cerebellar cortex including Granular Cerebellar layer ,therefore this study was carried out to collect further observed data on the beneficial effects of Vitamin B 12 on Granular layer in Albino rats.

MATERIALS AND METHODS

The Animal House of Basic Medical Sciences Institute, JPMC, Karachi affiliated with the Anatomy department of Basic Medical sciences Institute is the place where our research was conducted, for four weeks. For this study eighteen adult albino rats weighing almost 140 to 185 grams were selected. The animals were divided in three groups, each group comprised of six rodents. Six in Control Group A were given Lab diet and Six Group B rodents ingested Lithium Caronate at a dose of 60 mg /kg OD[11] in flour pellets for four weeks and Group C albinos who were six in number were given Methylcobalamin 500mcg for four weeks along with Lithium carbonate 60 mg /kg OD for above time period in flour pellets.

At completion of four weeks the animals were sacrificed, brain was removed; the cerebellum was separated from the rest of the brain and fixed in Formaldehyde[12] for 24 hours.

The cerebellar tissue was dehydrated by passing through ascending grades of alcohol cleared by xylene and infiltrated by paraffin. The fixed tissue blocks were sectioned and obtained on glass slides four micron thick sections were collected for staining with Haematoxylin and Eosin.[13]

The changes of the thickness of Granular layer were observed under light microscope in all groups. Observations were recorded at the end of four weeks. Measurement of thickness of Granular layer was recorded under 40 x objectives in selected fields of the tissue. The data was subjected to statistical analysis by using software SPSS (Statistical Program for Social Sciences) 2007 version-16.

A statistical difference between means and experimental data was carried out by student 'T' test.

Statistical Analysis: Statistical analysis of the thickness of Granular cell layer was documented in major group-A (Lab diet group) shows a highly significant increased thickness of inner layer at 4 weeks' time interval as compared to the major group-B (Lithium treated) but a highly significantly increased thickness of Granular cell layer was visualized and recorded in Group C (Methylcobalamin) compared to Group B animals.

RESULTS

Group-A (lab diet) which was 178 ±0.89 microns at 4 weeks was observed and showed normal histology and thickness of Granular layer Table: 1

Observations showed a highly increased thickness of Granular layer P value <.001 Table 2 in Group Animals

Group- B (Lithium treated Group at 4 weeks)

A highly significantly (P<0.001) decreased in the mean values of thickness or of Granular layer was observed in group B (90.1±0.34 µm)

Group-C shows highly significant P value <(.001) increase in thickness of molecular cell l ayer172.5±1.96 microns.

Results proved that Methylcobalamin restored thickness of molecular layer.

Table No.1: Measurement of granular cell layer in microns at 4 weeks in Group A, B and C

Groups	No. of Subjects	4th Week	
		Mean	SEM
A Normal Diet	6	178.6µm	0.89
B Normal Diet + Lithium Carbonate	6	90.1µm	0.34
C Normal Diet + Lithium Carbonate+ Inj. Methylcobalamin	6	172.5µm	1.96

Table No.2:P Value in group A, B and C

Groups	Weeks	P value
A	4th Week	P<0.001
B	4th Week	P<0.001
C	4th Week	P<0.001

DISCUSSION

Methylcobalamin the vitamin B12 play a vital role in neuronal DNA synthesis[14] in degenerated neuronal tissue and leads to proliferation of neurons as seen by Idiris and Belge[15]. The same results of Neuroregeneration by Methylcobalamin were found in our study and we documented that Methylcobalamin treatment in group C animals alleviated the damage of alkali metal on Cerebellar granular cell layer. Methylcobalamin restored the thickness of granular cell layer. This may be due to the fact that Methylcobalamin causes Antioxidative effects and decreases neuronal Apoptosis.

The same results of regenerated Granular cell neurons and Granular layer were observed by Okada, et al 2010[16] their Research documented that Methylcobalamin ameliorated the damage to the Granular layer and increased the thickness of Granule cells layer. This may be due to the fact that methylcobalamin enhances the methylation cycle in neurons and increases the neuronal protein kinases and DNA methylation. Our research is in accordance with their results.

CONCLUSION

Our population suffering from neuronal damage should be prescribed Methylcobalamin.

Author's Contribution:

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Data Analysis:	Faryal Azhar, Usama Faruqui
Revisiting Critically:	Tazeen Kohari
Final Approval of version:	Tazeen Kohari

Conflict of Interest: The study has no conflict of interest to declare by any author.

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When appropriate, may be included.

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