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CONTENTS

Editorial

Original Articles

Editorial

Tea and Fitness: Is there a link?

Mohsin Masud Jan
Editor

People are more likely to choose taking a pill or drinking a cup of tea over exercise to stay healthy.

The research by Yale University found one in 14 would not take exercise even if it meant them having an extra five years of life, say scientists.

A survey suggests that only a monthly jab is less appealing than regular physical activity when it comes to combating high blood pressure.

Referred to by doctors as the "silent killer" hypertension affects more than one in four adults in the UK.

It causes around half of all heart attacks and strokes and can be prevented or reduced simply by taking regular exercise.

Brisk walks, jogging or cycling are especially recommended.

In the first survey of its kind heart specialists asked 1,384 men and women about their willingness to adopt any of four 'treatments' to gain an extra month, year or five years of life.

Most were under 45 and had high blood pressure.

Pills came out on top ahead of a daily cup of tea, exercise and monthly or twice yearly injections.

Unsurprisingly, the US participants were more favourable towards each when the benefit was greater.

But some said they would not adopt any - even if it meant living for another five years.

Almost eight in ten (79 per cent) were willing to take a pill for an extra month of life - rising to 90 and 96 per cent for another year and five years, respectively.

The results were almost as high for tea which is sometimes advised because it is rich in antioxidants - 78, 91 and 96 per cent, respectively.

But when it came to exercise there was an overall drop to 63, 84 and 96 per cent, respectively.

A monthly jab was the least preferred option - 51, 74 and 88 per cent, respectively.

However, if it was just one injection every six months this rose to 68, 85 and 93 per cent, respectively.

The study presented at an American Heart Association meeting in Arlington, Virginia, also found at least one in five respondents wanted gains in life expectancy beyond what any of the individual interventions could provide.

we need to tap into this framework when we are talking with patients about options to manage their blood pressure.

We are good about discussing side effects, but rarely do we find out if other inconveniences or burdens may be impacting a person's willingness to take a lifelong medication or to exercise regularly.High blood pressure is a leading risk factor for heart and blood vessel, or cardiovascular, disease. It is dubbed the silent killer because it causes no symptoms.

To prevent high blood pressure, the American Heart Association recommends getting regular physical activity, in addition to other lifestyle changes.

These include eating a healthy diet, limiting alcohol, managing stress, maintaining a healthy weight and quitting smoking.

It is also important to work with a healthcare provider and to properly take blood pressure reducing medications, if prescribed.

Drinking black tea may also help protect against type 2 diabetes, but more study is needed to confirm an association.

When researchers analyzed data from 50 countries, they found that the rate of diabetes was lowest in countries where people drank the most black tea.Type 2 diabetes rates have skyrocketed worldwide in recent decades. It's projected that by 2030 there will be more than 900 million people across the globe with diabetes or with a high risk for developing it.

When researchers used a mathematical model to estimate the impact of drinking black tea on a number of health conditions, they found a link to just one -- diabetes.Of the countries included in the analysis, black tea drinking was highest in Ireland, the U.K., and Turkey. It was lowest in South Korea, Brazil, and China.

Researcher Ariel Beresniak, MD, PhD, of the mathematical research group Data Mining International in Geneva, Switzerland, says the study shows a consistent relationship between black tea drinking and type 2 diabetes risk. But this study does not prove a cause and effect relationship.Black tea may protect against diabetes, but more research is needed to prove this.

Black tea is more highly fermented and, as the name suggests, darker than green or white tea.The fermentation process turns simple flavonoid compounds called catechins in green tea into complex compounds called theaflavins and thearubigins. If black tea is shown in future research to actually lower diabetes risk, the fermentation process may explain why. Dietary and other lifestyle choices known to lower diabetes risk include:

- Limiting foods that contain refined sugar and highly refined white flour.
- Adding fruits, vegetables, whole grains, and low-fat dairy to your diet.

- Getting at least 30 minutes of aerobic exercise, at least three times a week.

Green tea and its extracts have long been studied for health benefits, including cancer prevention.

Now, researchers have new clues about how it may work to help prevent or slow the growth of prostate and breast cancers. Researchers presented the new findings here today at the American Association for Cancer Research meeting on cancer prevention.

Men with prostate cancer who drank green tea had less prostate tissue inflammation, linked to cancer growth, and other changes than those who didn't drink it.

The green tea polyphenols (antioxidants) reached the prostate tissue and they modified inflammation of the prostate. Polyphenols are antioxidants that protect against cell damage. Henning's team assigned 79 men with prostate cancer scheduled to undergo surgery to drink either six cups of brewed green tea or water daily. They did so for three to eight weeks, depending on when their surgery was scheduled. Before and after the study, Henning obtained urine and blood samples. She collected samples of prostate tissue after the surgery.

She reported on the 67 men who finished the study. Levels of prostate-specific antigen, or PSA, were lower after the study in those who drank green teas. Higher levels of PSA, a protein produced by the prostate gland, may reflect prostate cancer. An indicator of inflammation, called nuclear factor-kappaB, was also reduced in those who drank green tea compared to those who didn't, Henning found. Inflammation is linked to cancer growth."We were not able to inhibit tumor growth," she says. But the study length may not have been long enough to show that; a longer-term study is needed, she says.

Prostate cancer is typically a slow-growing cancer, Henning says. That makes it an ideal cancer to try diet interventions to slow it even more."Green tea is high in polyphenols and it's convenient," she says. Other research has found that green tea may slow prostate cancer. An Italian study found that men who had a precursor to prostate cancer and drank green tea were less likely to get prostate cancer, Henning says.

So, as an end note, tea may hold a fraction of the key to longevity, but in the long run, more research is needed to establish any effect. So in the meanwhile, exercise is the only real solution to all our fitness problems..

Original Article

Malaria in Children

Frequency and Type of Malaria in All Febrile Children Up to Five Years of Age

Muhammad Ashfaq, Bader-un-Nisa, Ayesha Altaf and Jamal Raza

ABSTRACT

Objective: To determine the frequency and type of malaria in all febrile children up to five years of age visiting the OPD of NICH.

Study Design: Descriptive / cross-sectional study

Place and Duration of Study: This study was conducted at the Emergency and Outpatient Department of National Institute of Child Health, Karachi from 1st July 2016 till 31st December 2016.

Materials and Methods: All children of 1 month to 5 years of age of either gender having history of fever as primary complain since 24 hours or more were enrolled. Laboratory test was performed and presence of malaria (yes/no) and type of malaria (if malarial positive) was noted.

Results: Out of total 253 children, majority of the patients were presented with ≤2.5 years of age (Mean age 1.48 ±.500 years). The proportion of female children was lower 102 (40.3%) than that of male children 151 (59.7%). Frequency of malaria was found in 17 (6.76%) patients. Frequency of malaria was found in 17 (24.1%) patients. Among these 17 malaria cases, 2 (11.76%) had falciparum while 15 (88.23%) had vivax type of malaria. Educational status of mother (p-value 0.003), father (p-value 0.038) and economic status (p-value <0.001) were significant factors associated with presence of malaria in children.

Conclusion: The frequency of malaria was found to be higher with predominance of vivax type in all febrile children up to five years of age visiting the OPD of NICH.

Key Words: Malaria, Fever, Children, Falciparum, Vivax

Citation of articles: Ashfaq M, Nisa B, Altaf A, Raza J. Frequency and Type of Malaria in All Febrile Children Up to Five Years of Age. Med Forum 2018;29(4):3-6.

INTRODUCTION

Malaria remains a life-threatening issue and creates devastating effects on the health of children especially those who are malnourished and have low immunity status.[1,2]

The increasing epidemic of Malaria could be weighed by the estimates given by World Malaria Report which has revealed approximately 216 million malaria cases from 91 countries in 2016. These statistics are 5 million higher from the estimates reported in 2015.[3]

In spite of this, there are certain countries that has achieved 3 consecutive years of no malaria cases. In particular, World Health Organization (WHO) has certified 7 countries as having eliminated Malaria in recent years that include; United Arab Emirates, Morocco, Turkmenistan, Armenia, Maldives, Sri Lanka and Kyrgyzstan.[4] However, In Pakistan, situation is still not under control. A total estimated malaria cases from 874,000 to 1,933,000 were observed with the estimated deaths in 1100 cases.[5]

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Although studies are available on this topic from different hospitals but the issue is of generalization of results on the population and continues rise in the Malaria cases also urges the need of study that gives the current magnitude of the problem. National Institute of child health is the largest public tertiary care facility in the province of Sindh, which caters patients not only from all over Sindh but also from other part of the country as well. The data collected in this center will represent at least the magnitude of malaria and its type in children up to 5 years of age presenting with fever, of province of Sindh. By virtue of this study, resource allocation, and different strategies could be devised to screen such children thereby further morbidity could be prevented or reduced.

MATERIALS AND METHODS

This descriptive cross-sectional study was conducted at emergency and outpatient department of National Institute of Child Health Karachi from 1st July 2016 till 31st December 2016. Consecutive children of 1 month to 5 years of age of either gender presented with history of fever as primary complain for 24 hours or more were included. Whereas children already on malarial treatment for the last 24 hours or children not presented with high grade fever as primary cause were excluded.

Sample size for the study was calculated with Raosoft calculator, taking prevalence of malaria.[6] as 38.3%,

confidence level 95% and absolute precision 6%. The required sample size came out to be 253.

History taking from the parents and Laboratory test was performed post informed consent from the parents. Venous blood sample (2-3ml) was collected for microscopy. A structured proforma was filled for each patient to record patient's demographics, educational status of mother and father, socioeconomic status, residence, presence of malaria (yes/no) and type of malaria (if malarial positive).

Data were entered and analyzed by SPSS version 21. Mean ±SD was calculated for age. Frequencies and percentages were calculated for gender, educational status of mother and father, economic status, residence, frequency of malaria and type of malaria.

Chi square test was applied to compare the difference of age, gender, educational status of mother and father, economic status and residence on the outcome (frequency and type of malaria). p-value ≤0.05 was taken as significant.

RESULTS

Table No.1: Baseline characteristics of the patients (n=253)

	n	%
Age, years	1.48 ±0.51†	
≤2.5 years	131	51.8
>2.5 years	122	48.2
Gender		
Male	151	59.7
Female	102	40.3
Area of residence		
Rural	198	78.3
Urban	55	21.7
Educational status of the mother		
Illiterate	33	13
Secondary	106	41.9
More than equal to secondary	114	45.1
Educational status of the father		
Illiterate	33	13
Secondary	135	53.4
More than equal to secondary	85	33.6
Economic status		
Lower	81	32
Middle	119	47
Upper middle	53	20.9

†mean ±standard deviation, n: number

Out of total 253 children, majority of the patients presented with ≤2.5 years of age (Mean age 1.48 ±.500 years). The proportion of female children was lower 102 (40.3%) than that of male children 151 (59.7%). Majority of the children, 198 (78.3%) were from rural areas while 55 (21.70%) children were from urban areas. Most of the mothers 114 (45.10%) had intermediate educational qualification while majority of the fathers 135 (53.4%) had primary educational status. (Table 1)

Malaria was diagnosed in 17 (6.71%) patients. Among these 17 malarial cases, 2 (11.76%) had falciparum while 15 (88.23%) had vivax type of malaria. (Figure 1 & 2)

Educational status of mother (p-value 0.003), father (p-value 0.038) and economic status (p-value <0.001) were significant factors associated with presence of malaria in children whereas type of malaria was insignificantly associated with all the variables (p-value >0.05). (Table 2)

Table No.2: Comparison of presence of malaria with respect to baseline characteristics of the patients (n=253).

Variables	Presence of Malaria			
	Yes (n=17)	No (n=236)	Total	p-value
	n (%)	n (%)	n (%)	
Age, in years				
≤2.5	11 (64.7)	120 (50.8)	131 (51.8)	0.269
>2.5	6 (35.3)	116 (49.2)	122 (48.2)	
Gender				
Male	13 (76.5)	138 (58.5)	151 (59.7)	0.144
Female	4 (23.5)	98 (41.5)	102 (40.3)	
Residence				
Urban	2 (11.8)	53 (22.5)	55 (21.7)	0.302
Rural	15 (88.2)	183 (77.5)	198 (78.3)	
Educational status of mother				
Illiterate	8 (36.4)	25 (10.8)	33 (13)	0.003
Literate	14 (63.6)	206 (89.2)	220 (87)	
Educational status of father				
Illiterate	6 (27.3)	27 (11.7)	33 (13)	0.038
Literate	16 (72.7)	204 (88.3)	220 (87)	
Economic status				
Lower	12 (70.6)	69 (29.2)	81 (32)	<0.001
Middle/Upper Middle	5 (29.4)	167 (70.8)	172 (68)	
Chi-square test applied, p-value <0.05 was taken as significant				

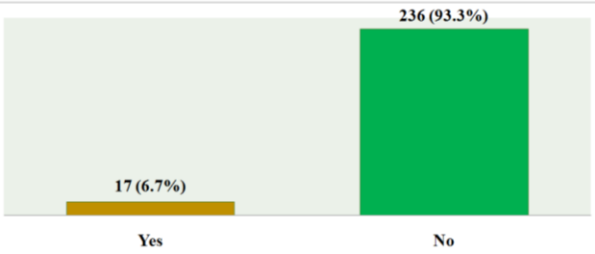

Figure No.1: Presence of malaria

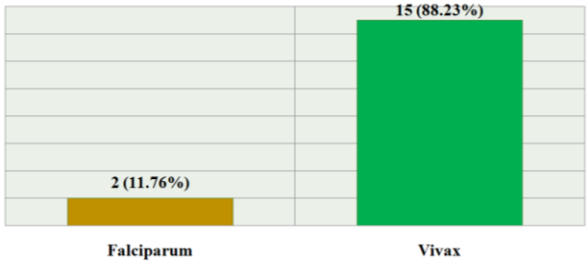

Figure No.2: Type of malaria (n=17)

DISCUSSION

Malaria is a still a leading public health problem in Pakistan. A study in 2013 reported that more than 60% of the Pakistan's population reside in malaria endemic regions.[7] It is reported that five hundred thousand malaria infections and fifty thousand malaria deaths occur each year in Pakistan which shows that the death toll of malaria in Pakistan is on the rise in spite of malaria control programs.[7] In 2010, more than one million malaria cases were reported from the Eastern Mediterranean region, among these 22% were from Pakistan.[8]

In this study, malaria was prevalent in 6.7% of the children under 5 years of age with the preponderance of plasmodium vivax specie. The finding of our study contrast with several studies from Pakistan in which malaria prevalence was found much higher. In a study conducted by Yasinzai MI et al, out of 6119 suspected cases, 38.3% were found to be positive for malarial parasite. However, similar to our study findings, Plasmodium vivax infection was found higher in their study than that of Plasmodium falciparum.[6] Another local study conducted by Fazil M et al has also reported higher frequency of plasmodium vivax.[9] A study from India has reported that out of 120 patients who were positive for malaria parasite, majority of the cases had Plasmodium Vivax followed by Plasmodium Falciparum while small number of individuals had mixed infection.[10]

A preponderance of Plasmodium Falciparum was reported in studies conducted in Quetta, Zhob, East Baluchistan, and Khuzdar.[11-14] The findings of these studies showed that prevalence of Plasmodium Falciparum infection is higher in Baluchistan province than in other regions of Pakistan.

In 2012 reports from WHO also revealed that that the two Plasmodium species prevalent in Pakistan are Plasmodium Vivax and Plasmodium Falciparum.[15] According to the report, these species accounts for more than half and more than one-fourth burden of the reported infections respectively.[15]

Although, Plasmodium Vivax is the most common specie found in majority of the studies. Still, it is hypothesized that the accurate estimate of the prevalence of Plasmodium infection is difficult, mainly because of the diversity in prevalence and species distribution of malaria causing parasites is still mysterious not only in Pakistan but in different parts of the world.[16-18] Further studies are recommended which gives the estimates of malaria and its type from all over the country.

CONCLUSION

The frequency of malaria was found to be higher with predominance of vivax type in all febrile children up to five years of age visiting the OPD of NICH. Educational status and socioeconomic status were the significant factors found to be associated with presence of malaria.

Author's Contribution:

Concept & Design of Study:	Muhammad Ashfaq
Drafting:	Bader-un-Nisa
Data Analysis:	Ayesha Altaf, Jamal Raza
Revisiting Critically:	Bader-un-Nisa, Muhammad Ashfaq
Final Approval of version:	Muhammad Ashfaq

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

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Original Article

Cholecystectomy

A Histopathological Study of Cholecystectomy Specimens in Gujrat – Pakistan

Abdul Rauf[1], Qamar Zaman Choudhary[2] and Muhammad Ali[3]

ABSTRACT

Objective: To study the pattern of histopathological lesions in surgically resected gallbladders.
Study Design: A retrospective / descriptive study.
Place and Duration of Study: The study was conducted at the Department of Pathology, Nawaz Sharif Medical College, University of Gujrat, Pakistan from Jan 1, 2015 to June 30, 2017 (2.5 years).
Materials and Methods: The study consists of 136 gallbladder specimens that were studied histologically by the author. These specimens were received at department of Pathology and in a private hospital in Gujrat. The data of all the cases was retrieved from registers of histopathology. It was compiled and analyzed from various angles including gender, age, cholelithiasis and histopathological lesions. The findings were compared with other studies.
Results: There were 77 females and 31 males in the study with a M:F ratio of 1:3.4. Cholelithiasis was seen in 88.2% (120) of cases. Chronic cholecystitis was present in 77.9% (106) of cases while acute cholecystitis was seen in 19.1% (26). Chlestrolosis was seen in 3.7% (5) and cholesterol polypi in 1.5% (2) of cases. Carcinoma was seen in 5 patients comprising 3.7% of all cases.
Conclusion: The findings in our study are similar to the most studies in literature. Gallstones and chronic cholecystitis were seen in the majority of cases.

Key Words: Gallbladder, Gallstones, Cholelithiasis, Cholecystitis

Citation of articles: Rauf A, Choudhary QZ, Ali M. A Histopathological Study of Cholecystectomy Specimens in Gujrat – Pakistan. Med Forum 2018;29(4):7-11.

INTRODUCTION

Surgical removal of gallbladder is a standard treatment for gallstones and other diseases.[1] Most of the patients are females and undergo cholecystectomy in fourth and fifth decades of life.[2] Gallstones are seen in a majority of specimens submitted for histopathology along with a variety of histopathological lesions.[3] Benign lesions are much more common than malignant. There were only about 1% (n=7) malignant cases in a study of 740 cases.[4] Chronic cholecystitis is the most frequently encountered histopathological lesion.[5] Other benign lesions include acute cholecystitis, xanthogranulomatous cholecystitis, eosinophilic cholecystitis, cholestrolosis, polypi, adenomyosis, intestinal metaplasia, pyloric metaplasia and hyperplasias etc.[6] Majority of the malignant neoplasms are carcinomas and adenoacarcinoma in commonest amongst these.[5] Most malignancies of gallbladder are diagnosed late in their course leading to poor prognosis.[7]

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There is variation in incidence of gallbladder cancer in various parts of world. The areas with high incidence include some South American countries and Northern India. Higher incidence is reported from southern part of Pakistan in Karachi.[8]
Generally, all the gallbladder specimens are submitted for histopathology in most centers but some workers have termed it a waste of sources and a burden on histopathologists.[9,10] On the other hand, some studies have opposed the idea of selective histopathology of gallbladders.[11,12] There is no previous study of gallbladder histopathology in Gujrat and adjoining areas. The purpose of this effort is to study the basic pattern of gallbladder disease in this area of country in comparison with other studies within and outside country.

MATERIALS AND METHODS

This is a retrospective study of all the patients whose gallbladders were received by the author for histopathology from Jan 2015 to June 2017 (2.5 years). These were examined grossly and representative sections were taken for processing. Slides were prepared and stained with hematoxylin and eosin. The gross examination of all the specimens and reporting of histopathology slides were done by the author himself as there is no other histopathologist available in the district for consultation or discussion. The grossing and reporting were performed at two places i.e. Pathology department, Nawaz Sharif Medical College in University of Gujrat and at a private hospital in Gujrat

city. The records of all the patients were retrieved and compiled with the help of Microsoft Excel software. These were analyzed from various angles including gender, age, cholelithiasis and various histopathological lesions. The findings were compared with national as well as international studies.

RESULTS

The study consisted of 136 patients. There were 77% (105) females as compared to 23% (31) males with MF ratio of 1:3.4. Age of 133 patients was known. Mean age was 44 years and age ranged from 14-80 years. Most of the patients were in fourth decade i.e. 29% followed closely by 27% in fifth decade. So the age range of 31-50 years i.e. fourth and fifth decades contained 56.4% of patients. Gender wise age distribution is shown in Table 1. Youngest patient was a 14 year old female. Two male patients were the oldest with age of 80 years each.

Table No. 1: Age and gender distribution of cases (n=133).

Age group	Males	Females	Total	%
11-20 years	1	1	2	1.5
21-30 years	4	19	23	17.3
31-40 years	6	33	39	29.3
41-50 years	11	25	36	27.1
51-60 years	4	15	19	14.3
61-70 years	2	10	12	9.0
71-80 years	2	0	2	1.5
Total	**30**	**103**	**133**	**100.0**

Operative procedure was known in 94 patients. It was laparoscopic cholecystectomy in 91% (86) and open cholecystectomy in 9% of patients. Neoplastic lesions were found in 5 (3.7%) gallbladders and were malignant in all these cases. The remaining 131(96.3%) gallbladders were having no neoplastic pathology. Cholelithiasis was the predominant pathology found in 88.2% (120) of cases. Chronic cholecystitis (Fig-1) was seen in 77.9% (106) of cases and acute cholecystitis (Fig-2) was present in 19.1% (26) of cases.

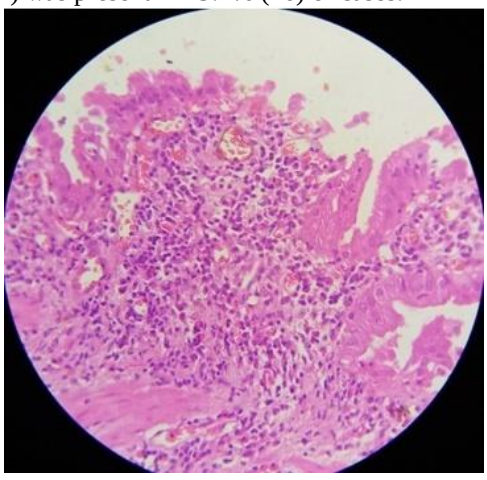

Figure No.1: Chronic Cholecystitis (H&E, X400) showing intense infiltrate of lymphocytes and plasma cells.

Some of the gallbladders contained more than one histopathological finding like one case of acute cholecystitis coexisted with adenocarcinoma. Fourteen cases of acute cholecystitis contained necrotizing/ gangrenous features accounting for 10.3% of all cases.

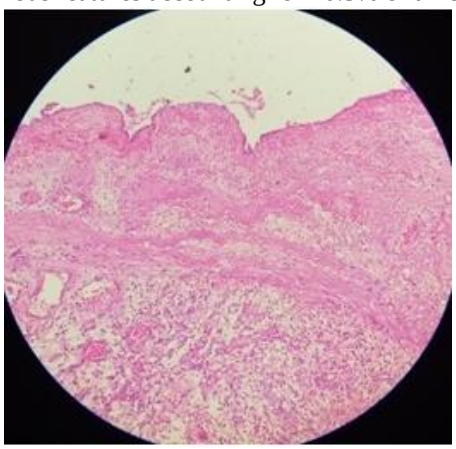

Figure No. 2: Acute Cholecystitis (H&E, X200) showing marked edema of wall and surface ulceration of the lining epithelium.

The frequencies of other lesions are mentioned in Table 2.

Table No.2: Gross and microscopic findings in gallbladders (n=136).

Finding	#	%
Gallstones	120	88.2
Chronic cholecystitis	106	77.9
Acute cholecystitis	26	19.1
Adenocarcinoma	5	3.7
Cholestrolosis	5	3.7
Cholestrol polyps	2	1.5
Empyema	1	0.7
Xanthogranulomatous cholecystitis	1	0.7
Spongiotic hyperplasia	1	0.7

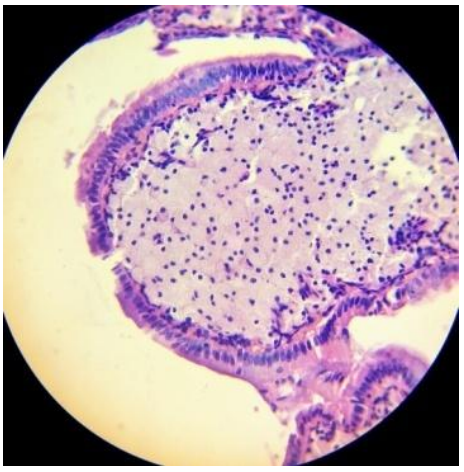

Figure No. 3: Cholestrolosis (H&E, X400), Mucosa containing many foamy macrophages.

All the five cases of malignancy were carcinomas comprising four cases of adenocarcinoma (Fig-4) and one case of an undifferentiated carcinoma.

Table No. 3: Comparison of present study with some recent studies.

	Present Study	Shah H 15	Khan S 16	Memon13	Awasthi14	Thaker & Singh 17
Year (Published)	2017	2016	2013	2011	2015	2017
Total cases	136	400	360	282	732	800
M:F ratio	1:3.4	1:2.4	1:4.7	1:2.9	1:2.6	1:4
Mean Age (years)	44	43	37	45	43.2	42
Age range	14-80	17-75	14-70	15-75	12-81	8-80
4^{th} decade	29.3%	31.2%	30.2%	31.9%	27.2%	27.5%
5^{th} decade	27.1%	32.5%	22.8%	31.9%		
Chronic Cholecystitis	77.9%	82.2%	77.7%	64.8%	97.1%	80.4%
Acute Cholecystitis	19.1%	12.2%	2.7%	31.5%	0.8%	0.25%

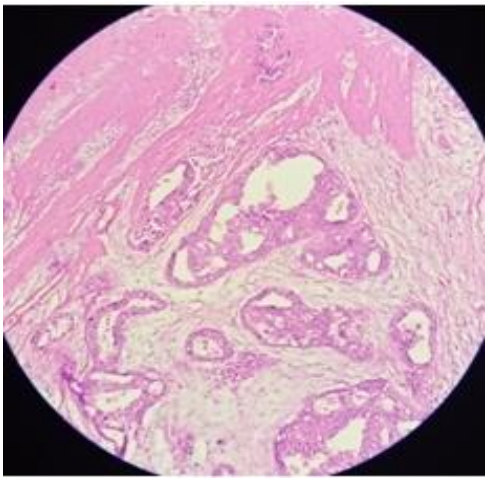

Figure No. 4: Adenocarcinoma (H&E, X200). Neoplastic glands infiltrating the tissue deeper to muscle layer.

All the five patients were females and mean age was 56 years.

Table No.4: Frequency of adenocarcinoma in various studies.

Study	All Malignant cases	Adeno-carcinoma cases	%
Present Study	5	4	80
Shah H et al.15	8	8	100
Khan S et al.16	9	8	88.9
Memon W et al.13	4	4	100
Dowerah & Deori.20	8	6	75
Kumari NS et al.22	1	1	100
Sharma & Choudhury 23	3	3	100
khan F et al.19	2	2	100
Thaker & Singh.17	1	1	100
Total	**41**	**37**	**90.2**

DISCUSSION

Gallbladder is a common surgically removed structure from human body due to pathological lesions. Its lesions are more common in females.[13,14] The M:F ratio in our study is 1:3.4 and this is comparable with several studies as is given in Table 3. Mean age of 44 years and age range of 14-80 years are also comparable with other studies in Table 3.

Most of the patients were found in fourth decade in our study i.e. 29.3%. Other authors have reported most cases in fourth decade like Khan S, Awasthi and Thaker & Singh.[14,16,17] Fourth decade was followed closely by fifth decade with 27.1% of cases in our study. The difference between cases in fourth and fifth decade is not much in our study, a finding similar to Shah H and Memon.[13,15] In the study of Shah H, there are slightly more cases in fifth decade i.e. 32.5% as compared to 31.2% in fourth decade.[15] There is equal frequency of cases in fourth and fifth decades in the study of Memon.[13] Collectively, the majority of gallbladder cases are seen in fourth and fifth decade that comprised 56.4% of cases in the present study. This finding is similar to the studies of Chauhan with 51%, Khan S with 53% and Memon with 63.8% of cases.[3,13,16]

The frequency of neoplastic lesions in our study (3.7%) is similar to a frequency of 5% in the study of Chauhan.[3] Gallstones were seen in a high frequency of 88.2% of our cases. The finding is similar to 89.9% and 91.8% reported by Mazlum and Dattal respectively.[6,18] Other authors have reported even higher frequency of gallstones in their studies like Awasthi: 95.2% and Khan F et al: 98.5%.[14,19] Chronic cholecystitis is the histopathological lesion most frequently encountered in resected gallbladders. Our finding of 77.9% cases of this lesion is in comparison with most others studies as in Table 3.

There were 19.1% cases of acute cholecystitis in our study. Our result is closer to that of Shah H at 12.2%.[15] There is wider variation in frequencies of this lesion as compared to chronic cholecystitis in various studies like

0.25% in the study of Thaker & Singh and 0.8% in the study of Awasthi on lower side and a frequency of 31.5% on higher side by Memon et al.[13,14,17]

Various non neoplastic lesions found in smaller frequencies in gallbladders in present study were cholestrolosis (3.7%), cholestrol polyps (1.5%), empyema (0.7%), xanthogranulomatous cholecystitis (0.7%) and spongiotic hyperplasia (0.7%). The cases of these lesions are mentioned in small frequencies in other studies.[5,6,20]

Gallbladder malignancy is seen in a few cases.There were 3.7% malignant cases in our study, a finding closer to that of Khan S et al at 2.5% and Shah et al at 2%.[15,16] On the other hand Khan UA from Lahore has reported malignancy in 7.2% of cases in his study.[11] Similarly Dowerah & Deori have reported a higher rate of 7.7%.[20]

Gallbladder malignancy in more common in females and is most commonly an adenocarcinoma. Among the five cases of malignancy there were four cases of adenocarcinoma and one case of an undifferentiated carcinoma. All cases were females and mean age was 56 years. The mean age of 56 years is in correspondence with that of 53.4 years reported by Kumar. The higher frequency in females is evident in other studies.[15,16] The high frequency of adenocarcinoma in present study is in accordance with other studies in Table 4.

There was only one case of an undifferentiated carcinoma in present study. Other less common varieties of gallbladder malignancies not found in present study presumably due its small size include adenosquamous carcinoma, squamous cell carcinoma, small cell/ neuroendocrine carcinoma and non-Hodgkin lymphoma.[22-23]

CONCLUSION

The main findings in present study from a small district are in accordance with other studies. Gallstones and chronic cholecystitis are very common. Acute cholecystitis is also seen in a significant number of cases. The frequency of malignant cases appears moderate in this part of country.

Author's Contribution:

Concept & Design of Study:	Abdul Rauf
Drafting:	Qamar Zaman Choudhary, Muhammad Ali
Data Analysis:	Qamar Zaman Choudhary,
Revisiting Critically:	Abdul Rauf, Qamar Zaman Choudhary
Final Approval of version:	Abdul Rauf

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

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Original Article

Thoracolumbar Spine Fractures Treatment

Traumatic Thoracolumbar Spine Fractures: Radiographic Outcome after Transpedicular Screw Fixation

Muhammad Sajjad[1], Mohammad Mushtaq[2], Syed Irfan Raza Arif[3] and Muhammad Usman Anjum[4]

ABSTRACT

Objective: To determine the radiographic outcome of transpedicle screw fixation in patients who had sustained traumatic thoracolumbar spine fractures,

Study Design: Quasi-experimental study,

Place and Duration of study: This study was conducted at the Department of Neurosurgery, Ayub Teaching hospital, Abbottabad from January, 2017 to August, 2017,

Materials and Methods: All patients of both genders who had suffered from traumatic thoracolumbar spine fractures and were between the ages of 20 to 60 years were included in the study. All patients underwent detailed history and clinical examination. Spinal fractures were fixed with transpedicular screw fixation using C-arm guidance and under general anesthesia by an experienced neurosurgeon. Pre- and post-operative spinal radiographs of the affected region were taken in both lateral and anteroposterior views to calculate the height of vertebral body, kyphotic angle and sagittal index.

Results: Out of sixty patients who were included in this study, mean age of study participants was 39.24±7.24 years. There were 46 male patients and 14 female patients with male to female ratio of 3.28:1. The mean vertebral body height, kyphotic angle and sagittal index were 52.42 mm, 9.77 degrees and 21.9 degrees before surgery respectively while they were 9.30 mm, 3.59 degrees and 5.52 degrees after the surgery respectively. Paired t-test showed that the differences were statistically significant (p-value < 0.001).

Conclusion: Transpedicle screw fixation is an effective and reliable way of managing thoracolumbar spine fractures. It not only helps in early restoration of spinal anatomy but also improves functional outcome in these patients. Radiological parameters are helpful in determining the outcome in immediate postoperative period. But, other parameters like clinical and functional must also be taken into account to predict the long term outcome in these patients.

Key Words: Transpedicular, spinal fracture, thoracolumbar, screw

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INTRODUCTION

Spinal trauma is the leading cause of morbidity and mortality even in modern era. The causes of these injuries include road traffic accidents, fall and sports activities.[1-4] Spinal trauma can either affect spine alone or it can also involve spinal cord.[2] Among trauma patients, incidence of spinal fractures is believed to be around 6% whereas in 2.6% of these cases, spinal cord is also involved.[5]

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Injury to spinal cord leads to longstanding debility which has grave consequences based on psychological, physical and socioeconomic reasons.[2] Furthermore, these injuries are associated with an enormous economic burden on a health system. In USA alone, the cost of treating spinal cord injuries is valued to be around $9.7 billion per annum.[6]

After cervical spine, thoracolumbar spine is the second most common spinal area affected by traumatic spine injuries. This region is involved in about 30 to 60% of all cases of spinal trauma. Out of these injuries to thoracolumbar area, 15 to 20% are associated with neurological impairment.[5,7,8] Thoracolumbar injuries follow a bimodal pattern with peaks in those who are less than thirty years of age and in geriatric people.[5] Main aim of treating these fractures surgically is to restore vertebral column stability and to attain spinal cord decompression which in turn leads to early mobilization of the patient.[9] Transpedicular screw fixation of thoracolumbar spinal fractures is a widely

accepted surgical technique for this purpose.[10, 11] We have conducted this study to determine the radiological outcome in patients who had sustained traumatic thoracolumbar fractures and were treated with transpedicular screw fixation technique.

MATERIALS AND METHODS

This was a quasi-experimental study which was conducted at the Department of Neurosurgery, Ayub Teaching hospital, Abbottabad, from January, 2017 to August, 2017. Sampling approach used was a non-probability consecutive sampling. Study was approved by hospital ethics committee and informed consent was taken. Patients who had suffered traumatic thoracolumbar spine fracture, between the ages of 20 to 60 years and of both genders were included in the study. Whereas patients with spinal fracture secondary to malignancy or pathological spine fractures or multiple spinal injuries or patients with severe spinal cord or neurological injury were excluded from the study. A pre-structured proforma was used to record the demographic data of the study participants. All patients underwent detailed history and clinical examination. Spinal fractures were fixed with transpedicular screw fixation using C-arm guidance and under general anesthesia by an experienced neurosurgeon. Pre- and post-operative spinal radiographs of the affected region were taken in both lateral and antero-posterior views to calculate the height of vertebral body, kyphotic angle and sagittal index, (SI).

SPSS (version 22) was used to manage and analyze data. Data were expressed as percentages, frequencies and mean ± standard deviation as required. Significance between pre- and post-operative variables was determined using paired t-test with p-value < 0.05 was taken as significant.

RESULTS

Table No.1. Pre-operative and post-operative values of radiological parameters, (n=60)

	Preoperative Measurements		Postoperative Measurements		P value
Variable	Mean± SD	Range	Mean± SD	Range	
Vertebral height (mm)	52.42± 4.45	44.75 – 59.90	9.30± 0.58	8.40 – 10.36	.001
Kyphotic angle (degree)	9.77± 1.86	6.88 – 13.25	3.59± 1.37	1.16 – 5.88	.000
Sagittal index (degree)	21.90± 5.23	13.54 – 31.99	5.52± 2.26	2.25 – 9.76	.000

Out of sixty patients who were included in this study, mean age of study participants was 39.24±7.24 years, (range = 28 – 53 years). There were 46 male patients and 14 female patients with male to female ratio of 3.28:1 showing higher predilection for male gender, as shown in Figure 1..

Pre- and post-operative measurements are given in Table 1. The mean vertebral body height, kyphotic angle and sagittal index (SI) were 52.42 mm, 9.77 degrees and 21.9 degrees before surgery respectively while they were 9.30 mm, 3.59 degrees and 5.52 degrees after the surgery respectively.

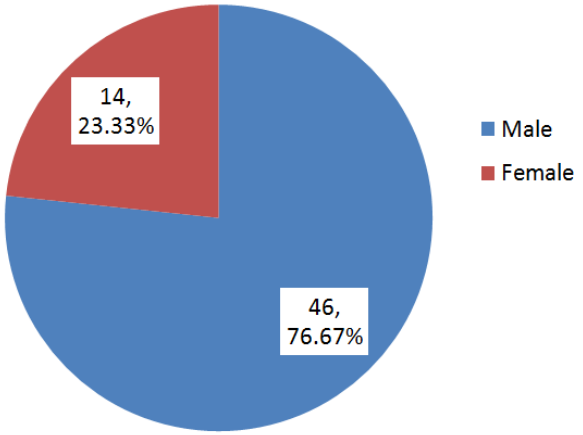

Figure No.1: Gender distribution of study population, (n=60)

DISCUSSION

For many decades, transpedicle screw fixation is used to stabilize thoracolumbar spine and it is one of the robust posterior fixation technique which is used for steadying the thoracolumbar spine, especially in cases of traumatic spinal fractures.[12] It has global acceptance as well as it is found to be more advantageous when compared with other procedures of spinal instrumentation.[13,14] This might be due to the reason that this procedure leads to remarkably higher pedicle screw placement accuracies. A meta-analysis conducted by Tian NF and Xu HZ reported accuracies of up to 89.22% among 7533 transpedicle screws which were placed.[15] Furthermore, it leads to improved mechanical spinal stability as well as neurological functional improvement which in turn leads to early mobilization, timely recovery and reduced inpatient stay.[1, 8]

In this study, average age of study participants was 39 years and there were 76.67% male patients and 23.33% female patients. Davis and Dunn, who had conducted their study in south Africa, found that the mean age of their study patients was 36 years and there were 76.92% male patients and 23.08% female patients[16] Similarly, Butt et al reported, from Srinagar, India, that the mean age of their patients was 33.6 years and 70% of them were males.[1] Likewise, in a Qatari study conducted by

Faramaway et al, mean age of patients was found to be 33.2 years and majority of them, 90%, were males.[2]

There was a significant improvement in radiological parameters in immediate postoperative period in our study, ($p<0.001$). Singh et al have also reported a highly significant improvement in SI in postoperative period from the preoperative values. SI was improved by 10.3° in their study.[17] Likewise, Kim et al have also described significant radiographic improvement in mean kyphotic angle and vertebral height in their Korean patients with thoracolumbar spine fractures.[18] Similarly, according to Butt et al, there was a substantial improvement in the radiological parameters in patients with thoracolumbar spine injuries and who were managed with transpedicle screw fixation using posterior approach.[1] Milenković et al have also described transpedicle screw fixation to be a successful approach to manage thoracolumbar spine fractures in their study. It not only lead to mechanically stable fracture fixation but also marked clinical improvement in their patients postoperatively.[19]

There are complex number of factors which predict the neurological outcome in patients who had sustained thoracolumbar spinal injury and therefore, no single factor can predict the outcome in such patients accurately.[17] Hence, other parameters e.g. clinical and functional must be taken into account along with radiological parameters to accurately gauge the final outcome in such patients.[20]

CONCLUSION

Transpedicle screw fixation is an effective and reliable way of managing thoracolumbar spine fractures. It not only helps in early restoration of spinal anatomy but also improves functional outcome in these patients. Radiological parameters are helpful in determining the outcome in immediate postoperative period. But, other parameters like clinical and functional must also be taken into account to predict the long term outcome in these patients.

Author's Contribution:

Concept & Design of Study:	Muhammad Sajjad
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Data Analysis:	Muhammad Usman Anjum, Muhammad Sajjad
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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

Risk of Factors for Infectious Diseases

Prevalent Risk Factors for Infectious Diseases in Children under 5 Years at a Tertiary Care Hospital in Karachi

Tehseen Iqbal[1], Muhammad Ahsan[1] and Naseem Ahmed[2]

ABSTRACT

Objective: Aim of the study was to determine the risk factors that leads to various infectious diseases (pneumonia, diarrhea, meningitis etc.) in young children at Civil Hospital Karachi. The study identifies the link between the infections and other factors like previous medical history, unhygienic conditions etc. and its impact on the health of under-five children.

Study Design: Cross sectional study.

Place and Duration of Study: This study was conducted at the Pediatrics Unit in Civil Hospital Karachi from March 2014 to August 2014.

Materials and Methods: A sample size of 384 was achieved. Patients of aged 6 months to 5 years with infectious diseases were randomly selected and their mothers were asked questions related to it in a local language. Data was analyzed on SPSS version 16.

Results: Pneumonia 115 (29.9%), Acute gastroenteritis 60 (15.6%) and meningitis/encephalitis 49 (12.7%) were most common diseases. 228 (59.4%) children were born premature, 234 (60.9%) had weight less than or equal to 2.5 kg. Only 74 (19.3%) of children were fully vaccinated. 239 (62.2%) had large family size with 222 (57.8%) claiming to have disease vectors present in their homes.

Conclusion: Prematurity, low birth weight, non-vaccination and poor living conditions around child is linked with occurrence of infectious disease in children under 5 in our scenario.

Key Words: Infectious diseases, pneumonia, meningitis, gastroenteritis

Citation of articles: Iqbal T, Ahsan M, Ahmed N. Prevalent Risk Factors for Infectious Diseases in Children under 5 Years at a Tertiary Care Hospital in Karachi. Med Forum 2018;29(4):16-20.

INTRODUCTION

In 2012, 6.6 million children died before reaching 5 years of their age with pneumonia, diarrhea and malaria being among the leading causes. 99% of these deaths were in low and middle income countries[1] and similar situation was there in 2013, in which Southern Asia constitutes about 25% of the under 5 mortality secondary to pneumonia, diarrhea and malaria[2]. In 2014, UNICEF ranked Pakistan On 26th among the countries with highest under five mortality rate and previously it shared half of total burden of these deaths globally along with few other countries[3,4].

Nearly 4 in every 10 deaths in low income countries are among children under 15 years and death due to infections comprises one third of the total in these countries[1]. Pneumonia solely had a mortality of 1.2 million children globally in 2011[4] 27% of mortality in children under 5 in Pakistan is due to those infectious diseases which can be prevented by immunization and other interventions[5,6]. 19.4 % million of infants worldwide did not have their routine vaccination and Pakistan was among those 10 countries where 60% of these infants live[7].

Weather changes, poor living conditions, presence of pets, inadequate ventilation, overcrowding, malnutrition and lack of vaccination are among major risk factors attributable to respiratory tract infections[8,9]. More than 17% of infectious diseases are vector borne with the most common known disease vectors being mosquitoes and flies[10]. Malnourished children are at more risk of getting infectious diseases and it leads to death in 45% infectious disease (ID) pediatric patients[11]. More than half of emerging infectious diseases are caused by zoonotic pathogens which are spread by poor handling of food and increase interaction between humans and animals[12].

Common practices that are seen in Pakistani rural areas like bottle feeding, early weaning are linked to diarrhea in these children[13]. Preventive measures include vaccination, adequate nutrition, exclusive breastfeeding and proper sanitation and hygiene[11]. Identification of most prevalent risk factors for infections is important and will help and guide to develop strategic measures to reduce its incidence and will help to reduce the mortality and morbidity associated with communicable diseases in Pakistan.

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MATERIALS AND METHODS

This is a cross-sectional study conducted on children admitted to Civil Hospital Karachi to analyze the prevalence of most common infectious diseases in children with the age limit of 5 years but older than 6 month of age. Mothers of (these children who are suffering from infectious diseases are invited to participate in this research work with the assurance of their information to be kept exclusive.

Civil Hospital Karachi have three pediatrics unit. Each pediatric unit was covered for this study. The participants included the mothers of pediatric patients who were admitted in these pediatrics units in Civil Hospital Karachi due to any infectious diseases. A written consent was obtained from mothers of the children.

Inclusion Criteria: This study conducted under following parameters.

a) Pediatric wards of Civil Hospital Karachi would be covered to fill the questioners of this study.

b) Age restriction for children which is greater than 6 month but less than 5 years is mandatory.

c) Only mothers of the child who is a diagnosed case of any infectious disease will be interviewed.

Exclusion Criteria: The following points are avoided while conducting a study.

a) Children diagnosed with non-infectious diseases.

b) Attendant, Other than mother.

With Open EPI version 3.038 keeping prevalence of 50%. The margin error was kept 5% and confidence at 95%. The calculated sample size was 384. Sampling technique was non probability convenient sampling. Pediatric patients with infectious diseases admitted in CHK were randomly selected and their mothers were interviewed. Out of 384 mothers, 26 mothers were unwilling to participate in the research, therefore the cumulative response rate came out to be 93.2% to overcome this. We increased our sample size from 384 to 410.

The data for this research was collected using a survey questionnaire. Since the questionnaire was created using suitable questions modified from related research and individual questions formed by the researcher. 12 trial questionnaires other than sample size of 410 were filled to validate it. The questionnaire consists of 23 questions which were related to risk factors of infectious diseases in children. Mostly questions were in yes or no format. Participants were assured that their information will remain confidential and will only be used for research purposes. As mothers of the pediatric patients were interviewed and the information given was entered in questionnaire carefully by the researchers themselves, therefore no forms were incompletely or inappropriately filled.

RESULTS

Table no. 1 shows the biophysical parameters of pediatric patients. There were nearly equal percent of 188 (49%) male and 196 (51%) female pediatric patients suffered from infectious diseases and were admitted in hospital. Most commonly, 182(47.4 %) children of age group 6 months-12 months suffered from infectious disease and the second most common age group to be affected was 13 months-24 months 83 (21.6%).

Table No.I: Gender and age distribution of the study participants:

Demographic features of patients	Frequency (n:384)	%age
Gender of Patient		
Male	188	49
Female	196	51
Age of Patient:		
6 months- 12 months	182	47.4
13 months -24 months	83	21.6
24 months - 36 months	56	14.6
37 months - 48 months	29	7.6
49 months- 60 months	34	8.9

Table No. 2 showed that among the admitted patients most common diseases seen were pneumonia 115 (29.9 0/6), acute gastroenteritis 60 (15.6%), meningitis/ encephalitis 49 (12.7%)

Table No.2: Most common infectious diseases of the study participants:

Sr. No.	Most Common Diagnosed Cases	Frequency (n:384)	%age
1	Pneumonia	115	29.9
2	Acute Gastroenteritis	60	15.6
3	Meningitis/Encephalitis	49	12.7
4	Dengue/Malaria	47	12.2
5	Gastro enteric fever	23	5.9
6	(Typhoid)	16	4.1
7	Tuberculosis	11	2.8
8	Measles	10	2.6
9	Acute Respiratory tract	07	1.8
10	infection Urinary tract infections Hepatitis	05	1.3

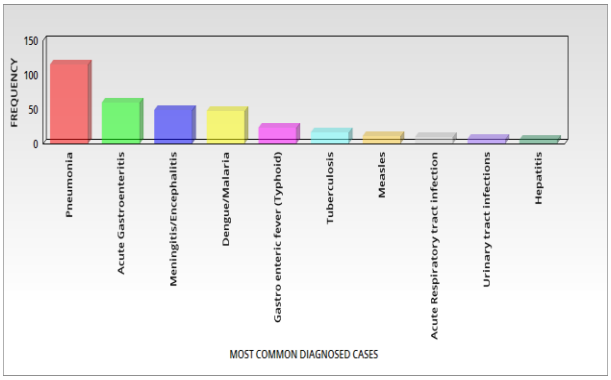

Figure No. 1: Most common infectious diseases of the study participants.

Information regarding past medical history of child is displayed in Table no. 3. 228 (59.4 %) were born premature, 234 (60.9%) were low for birth weight, 250 (65.1 %) were exclusively breastfed up to 6 months, 167 (43.5 %) were partially vaccinated 212 (55.2 %) had their weight appropriate for current age, 150 (39.1%) had chronic illness present along with current infectious disease, 131 (34.1%) had history of recent hospital admission, 116 (30.2 %) had recently travelled to another city 145.2 (37.8%) of mothers reported to had infectious disease history in family in previous 2 months.

Table No.3: Demographic data of past medical history of the children suffering from infectious diseases:

Medical history of patients	Frequency (n:384)	%age
premature at birth	59.4	40.6
Birth weight of less than or equal to 2.5	60.9	39.1
Exclusive breastfeeding for 5 months	34.9	65,1
Current weight of child appropriate for his age	55.2	44.8
Presence of any) associated chronic illness	39.1	60.9
History Of recent hospital admission	34.1	65.9
Recent travel history outside the city	30.2	69.8
History of any infectious disease in family in previous 2 months	37.8	62.2
Current vaccination status Of Child:		
Fully vaccinated		19.3
Partially vaccinated		43.5
Not at all		37.2

Figure No. 2: Was the child exclusively breastfed up to 6 months?

DISCUSSION

In Our study out of most common top 10 diseases, 5 diseases were vaccine preventable with pneumonia being leading cause of hospital admission in pediatric ward, followed by acute gastroenteritis and meningitis/encephalitis (Table 2 & figure 1). Similar finding was reported in annual report of Child health of Pakistan in which most common causes of mortality in age group of more than 1 month to 59 months are pneumonia (29%) and diarrhea (20%)[14.] Incidence of vaccine preventable diseases in our setup is a reflection of poor immunization coverage in Sindh province (29.1%) after Baluchistan (16.4%) as depicted in Pakistan Demographic Household Survey 2012-2013 15)[5]. Pneumococcal vaccination has been proven to be effective in reducing hospitalization

Secondary to community acquired pneumonia in children [(15)]. Majority of research patients were partially vaccinated that have missed vaccinations from their EPI vaccination schedule. (Table 3)

Premature Children are susceptible to acquire severe respiratory infections along with other risks [(16)]. 59.4% of children in Study population were born premature (Table 3). In our study there was a significant association between incidences of infectious diarrhea in under 5 years of children born with low birth weight[17]. Our research participants suffering from infectious disease were mostly had low birth weight that is less than or equal to 2.5 kg (Table nö, 3). Children living in overcrowded house were at risk to suffer from respiratory viral infections[16] and those living with family of greater than 7 members were more prone to experience diarrhea[17]. In Sindh average members per household is 6.13[18]. However 62.2% children in our research lived with more than 7 family members and therefore are at increased chance of getting infections. Large family size leads to overcrowding and this leads to easy transmission of various microbes. Mortality risks are higher in infectious disease patients with coexisting malnutrition. This is for respiratory infections, diarrhea and malaria[19]. In our data, majority were observed to have appropriate weight for their current age (Table 3).

There was reduction in infant infection when exclusive breast feeding continued up to 6 months[20]. Also, inadequate period of breastfeeding is linked to diarrhea and pneumonia[20,21]. In our study, most mothers were found to exclusively breastfed their child for period of less than 6 months. This is either due to lack of education, awareness or due to social stigma regarding breast feeding (Table 3).

Respiratory Tract Infections, Gastrointestinal Tract Infections and Urinary Tract Infections were found to be the most common nosocomial acquired infections in age group > 1 month and < year [(22)]. Most pediatric

patient of this study had a history of recent hospital admission (Table 3).

Being male is identified as a non-modifiable risk factor of acquiring infectious diseases and Infectious disease mortality among infants. This is explained on context that females have a strong immune system when compared to males, but in our study we failed to find any such findings as percentage of males and females pediatric patients were nearly equal (Table 1). In a study, it was found that in infections of different systems, 32% have underlying previous pathology like immunodeficiency that can be either primary or due to chronic illness[23]. However, only less than half of our research study had any previous chronic illness before hospital admission for current infection (Table 3).

Children of average age 4.4 years with recent travel history especially in South Asia were diagnosed with Salmonella typhi, pyogenic abscess and malaria more frequently. Travel history was negative in most of the patients of our study (Table 3).

CONCLUSION

Prematurity and low birth Weight are among the major risk factors for infectious diseases among children less than five years. Exclusive breastfeeding for up to 6 rnonths and recommended immunization have the potential to reduce the frequency of incidence of infectious diseases. The study concludes that improvement in room ventilation and sanitary conditions in and around house are important factors in the elimination of various pathogens culprit of infectious diseases. Knowing these factors that are prevalent in our setup will help in early diagnosis and it's timely management and indirectly will cause a decrement in mortality due to Infectious diseases.

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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

Hyponatremia as a Predicting Factor of Mortality in Chronic Liver Disease

Hyponatremia in Chronic Liver Disease

Muhammad Idrees, Muhammad Awais Joiya and Shehzadi Pulwasha Hameed

ABSTRACT

Objective: To determine the worth of hyponatremia as a predicting factor of poor prognosis and mortality in chronic liver disease.

Study Design: Cross Sectional Study

Place and Duration of Study: This study was conducted at the Department of General Medicine, Primary and Secondary Healthcare DHQ Hospital Narowal from January 2017 to January 2018.

Materials and Methods: A total 192 patients were included in our study. All the patients who were suffering from chronic kidney disease, congestive cardiac failure, already using diuretic drugs and conivaptan/tolvaptan, and on dialysis were excluded from our study. The continuous data including age, MELD score, MELD -Na score, albumin, creatinine, alanine transaminase, aspartate transaminase, gamma glutamyltransferase, total bilirubin level, serum chloride, platelet count, international normalized ratio were analyzed by applying Student T test. All the nominal data including male percentage, etiology of the end stage liver disease and complications of cirrhosis were compared by applying Pearson Chi-square test. SPSS v.23 software used and a P value of <0.05 was considered significant.

Results: Serum levels of alanine and aspartate transaminases (ALT & AST), gamma glutamyltransferase (GGT), total bilirubin and international normalized ratio (INR) was significantly low in the patients with serum sodium levels of ≥139mEq/L (p-value 0.014, <0.001, <0.001, 0.001 and 0.018, respectively) but serum chloride was significantly higher (<0.001) in this group.

Conclusion: This study concludes that the concentration of sodium in the serum < 139 mEq/L combined with MELD- Na score more than 12 can be the extrapolative indicators of poor prognosis and mortality in the patients having chronic liver disease. This can be used to identify the threat of poor outcomes and adequate treatment can be given to improve the serum sodium levels and in turn, improve the prognosis.

Key Words: Hyponatremia, chronic liver disease, poor prognosis.

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INTRODUCTION

Chronic liver disease is a prolonged disease course consisting of various simultaneous processes of progressive liver parenchyma destruction and regeneration[1], which eventually leads to fibrosis and cirrhosis[2]. The minimum time period to tag the liver disease as chronic is six months. There are numerous causes for this pathology which include chronic hepatitis B and hepatitis C virus infection, non-alcoholic fatty liver disease, alcoholic hepatitis, autoimmune hepatitis, cryptogenic hepatitis, hemochromatosis, Wilson's disease, primary biliary cirrhosis, and drug induced hepatitis [3-8]. The factors pre-disposing to the developing chronic liver disease are obesity, poor hygiene, body fluids exchange with the infected persons, sharing of the infected needles and syringes, unprotected sex with infected person or multiple sex partners, toxic work environment, metabolic syndromes and excessive alcohol consumption[9]. Different predisposing factors are related with different etiological type of chronic liver disease.

Chronic liver disease is very long process and takes many years to present its manifestation. The outcome of chronic liver disease is cirrhosis which ultimately results in portal hypertension, hypoalbuminemia, ascites, hypersplenism with or without splenomegaly, esophageal varices, hepatorenal syndrome, hepatic encephalopathy and hepatocellular carcinoma. Liver function tests, ultrasound abdomen and liver biopsy are different modalities used for the definite diagnosis. Hyponatremia often results due to the dysfunction of the water homeostasis of the body. Due to hypoalbuminemia and increased arginine vasopressin, there is excessive water shift into the third space and loss from the kidneys. In turn, kidneys try to replace the lost water via the renin-angiotensin-aldosterone mechanism. The increase in water reabsorption in the collecting tubules of the kidney in response to the over-activation of renin-angiotensin-aldosterone system leads to dilutional hyponatremia.

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In chronic liver disease, there is impaired synthesis of clotting proteins, bilirubin and liver enzymes such as alanine transaminase, aspartate transaminase and γ-glutamyltransferase[10,11]. Altered levels of these components in the serum are somehow related with the risk of morbidity and mortality. The levels of derangements of these components also change according to the serum sodium concentration. Serum electrolyte imbalance is concomitant with poor prognosis. Similarly, when there is altered serum sodium level in the patients having chronic liver disease, there is different pattern of metabolic derangements which can be used to analyze the link of various sodium levels with the level of morbidity and mortality.

Some studies have shown that there is association of hyponatremia with poor prognosis in patients having liver cirrhosis, in Europe and United States of America. There is deficiency of regional data about the clinical significance of serum sodium levels in the chronic liver disease patients and the correlation of serum sodium levels with mortality. This study is directed to evaluate the risk of poor outcomes in patients having low serum sodium levels and the chronic liver disease and the relationship between clinical characteristics and serum sodium concentration.

MATERIALS AND METHODS

Protocol approval for our cross sectional study was obtained from the ethical committee of DHQ Hospital, Narowal. A sample of one hundred and ninety two patients, who had any form of chronic liver disease and were treated from January 2017 to January 2018, was selected consecutively. Sample size was calculated using study by Umemura T et al.[12] as reference. Data was collected by the researcher himself, on a preformed performa, in the general medicine department of the hospital. The study was performed from January 10, 2017 to January 10, 2018.

Written consent was acquired from all the patients who were involved in the study. The patients were diagnosed of chronic liver disease on history, clinical examination and laboratory investigations. Demographic data was noted. Etiology of the chronic liver disease was found by laboratory investigations. Serum levels of sodium, creatinine, albumin, alanine transaminase, aspartate transaminase, gamma glutamyltransferase, total bilirubin level and chloride; and international normalized ratio (INR) along with platelet count were ordered for laboratory testing. Model for End-stage Liver Disease (MELD) score and MELD-Na score were acquired for every patient. All the data was obtained before the start of the treatment, especially diuretics medication. MELD score and MELD-Na score were calculated as using the following formulas:

$$MELD = 11.2\times \log(INR) + 3.78\times \log(\text{Total Bilirubin}) + 9.57\times \log(\text{Creatinine}) + 6.43$$

$$MELD\text{-}Na = MELD + (140 - Na) - 0.025\times MELD\times (140 - Na)$$

Complications of cirrhosis including foot edema, ascites, esophageal varices, spontaneous bacterial peritonitis and hepatic encephalopathy were also included in the clinical information. Ultrasonography and computed tomography were the modalities used to confirm the presence of ascites. Hepatitis B and hepatitis C viral infections were confirmed by the viral markers i.e. hepatitis B viral surface antigen and anti-hepatitis C viral antibody along with polymerase chain reaction (PCR) for hepatitis C RNA (when anti-hepatitis C virus antibody was positive).Serological testing and tissue biopsy of liver for microscopic examination were performed to look for the cases of primary biliary cirrhosis and autoimmune hepatitis. Conventional methods were used to diagnose the cases of non-alcoholic fatty liver disease. All the patients who were suffering from chronic kidney disease, congestive cardiac failure, already using diuretic drugs and conivaptan/tolvaptan, and on dialysis were excluded from our study.

All the continuous data including age, MELD score, MELD-Na score, albumin, creatinine, alanine transaminase, aspartate transaminase, gamma glutamyltransferase, total bilirubin levels, serum chloride, platelet count, international normalized ratio were analyzed by applying Mann-Whitney U-test. All the nominal data including male percentage, etiology of end stage liver disease and complications of the cirrhosis were compared by applying Pearson Chi-square test. SPSS v.23 software used and a value of less than or equal to 0.05 for p was considered significant, statistically.

RESULTS

Total of 192 patients were haphazardly allocated into two groups on the basis of serum sodium levels. Both the groups were compared and were not much different in terms of age and male percentage. In the whole group, MELD score and MELD-Na score was 10 and 12 (Table I), respectively. MELD and MELD-Na score was significantly higher in the patients having serum sodium levels <139mEq/L ($p<0.001$for both). The frequency of different etiologies of cirrhosis such as hepatitis B, primary biliary cirrhosis, non-alcoholic fatty liver disease, autoimmune hepatitis and cryptogenic hepatitis, was similar in both the groups ($p>0.05$), but the prevalence of hepatitis C significantly higher in the patients having serum sodium levels <139mEq/L ($p=0.007$) (Table 2). Symptoms associated with chronic liver disease were seen more frequently in the patients with serum sodium levels <139mEq/L. Leg edema was present in 85.3% and 83.1% ($p=0.679$); esophageal varices in 61.5% and 37.3% ($p=0.001$);

ascites in 56.9% and 30.1% (p<0.001); hepatic encephalopathy in 23.9% and 20.5% (p=0.579); and spontaneous bacterial peritonitis in 28.4% and 12% (p=0.006) of the patients with serum sodium levels <139mEq/L and with serum sodium levels ≥139mEq/L, respectively (Table 3). Serum albumin concentrations, serum creatinine and platelet count was not significantly different in both the groups (p-value 0.410, 0.885 and 0.718, respectively). Serum levels of alanine aminotransferase (ALT), aspartate amino-transferase (AST), γ-Glutamyltransferase (GGT), total bilirubin and international normalized ratio (INR) was significantly low in the patients with serum sodium levels of ≥139mEq/L (p-value 0.014, <0.001, <0.001, 0.001 and 0.018, respectively) but serum chloride was significantly higher (<0.001) in this group. (Table-4)

Table No.1: Baseline Features at Admission Rendering To Serum Sodium Levels

Variable	Whole-Group (n =192)	Na< 139mEq/L (n =109)	Na ≥139mEq/L (n =83)	P - value
Age (years)	63 (59-86)	64 (59-68)	63 (59-68)	0.923
Male	114(59.4)	64 (58.7)	50 (60.2)	0.831
MELD Score	10 (9-12)	11 (9-13)	9 (8-11)	<0.001
MELD-Na Score	12 (9-17)	16 (12.5-19)	8 (7-10)	<0.001

Table No.2: Type of Chronic Liver Disease

Disease Type	Whole-Group (n =192)	Na< 139mEq/L (n =109)	Na ≥139mEq/L (n =83)	P - value
Hepatitis C	90(33.3)	45 (41.3)	19 (22.9)	0.007
Hepatitis B	77(19.8)	20 (18.3)	18 (21.7)	0.565
NAFLD	7(13.5)	15 (13.8)	11 (13.3)	0.919
Primary Biliary Cirrhosis	3(12.5)	12 (11)	12 (14.5)	0.474
Autoimmune Hepatitis	5(12.5)	11 (10.1)	13 (15.7)	0.248
Cryptogenic Hepatitis	10(8.3)	6 (5.5)	10 (12)	0.104

Table No.3: Complications of Cirrhosis

Complication Type	Whole-Group (n =192)	Na<139 mEq/L (n =109)	Na ≥139 mEq/L (n =83)	P - value
Leg Edema	162(84.4)	93 (85.3)	69 (83.1)	0.679
Esophageal Varices	98(51)	67 (61.5)	31 (37.3)	0.001
Ascites	87(45.3)	62 (56.9)	25 (30.1)	<0.001
Hepatic Encepha-lopathy	43(22.4)	26 (23.9)	17 (20.5)	0.579
Spontaneous Bacterial Peritonitis	41(21.4)	31 (28.4)	10 (12)	0.006

After the univariate analysis of the factors predictive of mortality i.e. low serum albumin, low serum sodium and chloride concentrations, low platelet count, high aspartate aminotransferase, alanine aminotransferase, γ-glutamyltransferase, bilirubin, and high MELD and MELD-Na scores, showed a significantly positive predictive worth of these factors (p<0.05).

Table No.4: Hematological Findings

Blood Tests Reports	Whole-Group (n =192)	Na< 139 mEq/L (n =109)	Na ≥139 mEq/L (n =83)	P -value
Albumin (g/dl)	3 .3 (2.7-3.8)	3. 2 (2.6-3.9)	3 .5 (2.8-3.8)	0.410
Creatinine (mg/dl)	0.8 (0.6-1.1)	0.8 (0.6-1)	0.8 (0.6-1.1)	0.885
Alanine Transaminases (IU/L)	48 (35-55)	48 (39-55)	42 (26-55)	0.014
Aspartate Transaminases (IU/L)	56 (45-70)	60 (46-87)	51 (44-63)	<0.001
γ-Glutamyl-transferase (IU/L)	50.5 (39-63)	56 (45-69)	44 (37-57)	<0.001
Total Bilirubin (mg/dl)	1.51 (1.2-2.2)	1.51 (1.3-2.3)	1.50 (1-2.2)	0.001
Chloride (mEq/L)	103 (95-108)	97 (93-105)	105 (97-112)	<0.001
Platelets ($\times 10^3/\mu L$)	10.3 (8-12)	10.3 (8-12)	10.5 (8-12)	0.718
International - Normalized - Ratio	1.23 (1.14-1.40)	1.25 (1.12-1.42)	1.22 (1.14-1.40)	0.018

Data is mentioned as number (percentage) and median (first and third interquartile); MELD= Model for end-stage liver disease; NAFLD=non-alcoholic fatty liver disease.

DISCUSSION

In our study, we observed that there was a significant derangement of the liver enzymes, total bilirubin level and international normalized ratio in the patients having chronic liver who had serum sodium levels below 139mEq/L. The complications of chronic liver disease were also more prevalent in this group. In our cohort, the median value of MELD-Na score was 12. The patients with low sodium levels had MELD-Na score above 12. Lower sodium levels combined with MELD-Na score of more than 12 was associated with the increased possibility of poor outcomes and mortality in the patients with chronic liver disease.

Umemura T. et al.[12] performed a study on Japanese population and found out that MELD-Na score >10.5 and serum Na <139mEq/L was predictive of poor prognosis as well as higher mortality in the patients who has developed liver cirrhosis. Biggins SW et al.[13], after doing research on serum sodium levels in patients with chronic liver disease and incorporated sodium into the Model for End-stage Liver Disease (MELD). They

established MELD-Na model to predict the prognosis in the patients who were on the waiting list for the liver transplant surgery. Kogiso T. et al.[14] witnessed that tolvaptan improved the prognosis and reduced mortality in the in the patient with cirrhosis by improving the serum sodium levels and bringing it within the normal range. In the patients who had developed liver cirrhosis and hyponatremia, normalized serum levels of sodium after one week of treatment with tolvaptan can be a predictive of better outcome and increased survival.

Two studies were conducted, one in England[15] and other in Korea[16]. According to both of them, a combination of Model for End-stage Liver Disease (MELD) score and serum sodium levels can be used to assign the priority to the liver transplant candidates. This can, in turn, result in improved and prolonged survival in patients of chronic liver disease and liver failure. Nishikawa H, et al.[17] directed a study on hepatocellular carcinoma patients and deduced that baseline sodium levels had a predictive significance about the prognosis in hepatocellular carcinoma patients complicated with cirrhosis. Low serum sodium level was related with high Child-Pugh score and advanced stage of hepatocellular carcinoma. In a study conducted by Maruyama H. et al[18] in 2015, it was observed that the serum level of sodium prior to the treatment is a significant predicting factor for good and bad prognosis in the class A and B patients of the Child-Pugh score who had undergone endoscopic sclerotherapy for treatment of esophageal varices.

CONCLUSION

This study concludes that the concentration of sodium in the serum less than 139 mEq/L and MELD-Na score of above 12 can be the predictive indicators of poor prognosis and mortality in the patients having chronic liver disease. This can be used to identify the threat of poor outcomes and adequate treatment can be given to improve the serum sodium levels and in turn, improve the prognosis.

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Original Article

Clinical Profile of Hypophosphatemic Rickets

Frequency and Clinical Profile of Hypophosphatemic Rickets Among Rachitic Children

Taj Muhammad Laghari, Muhammad Ashfaq, Bader-Un-Nisa and Shamsher Ali

ABSTRACT

Objective: To determine frequency and clinical profile of hypophosphatemic rickets among rachitic children at N.I.C.H Karachi, Pakistan.

Study Design: Cross-sectional study

Place and Duration of Study: This study was conducted at the National Institute of Child Health Karachi, Pakistan from 21st January 2015 to 20th January 2016.

Materials and Methods: All consecutive children with age 1 to 14 years of either gender having rickets were enrolled. Hypophosphatemia and its clinical profile like short stature, fractures, family history, bony deformity, joint pain, and dental abnormalities were observed.

Results: Out of total 230 rachitic children, frequency of hypophosphatemic rickets were found in 16(7%) rachitic children. The mean age of the patients was 7.56±4.35 years. Majority Gender distribution showed05(31%) were males and 11(69%) were females. Short stature 11(69%), fracture 02(12.5%), joint pain 04(25%), family history of hypophosphatemic rickets was present in 05(31%). Bony deformity and dental abnormalities were found in 07(44%) and 06(37.5%) patients respectively.

Conclusion: In this study, short stature is the most common clinical profile, followed by bony deformities and dental abnormalities. A diagnosis of hypophosphatemic rickets should be considered in all patients presenting with short stature, bony deformities along with low serum phosphate and normal iPTH and 25 – hydroxy vitamin D.

Key Words: Hypophosphatemic rickets, clinical profile, rachitic

Citation of articles: Laghari TM, Ashfaq M, Nisa B, Ali S. Frequency and Clinical Profile of Hypophosphatemic Rickets Among Rachitic Children. Med Forum 2018;29(4):25-28.

INTRODUCTION

Rickets is a worldwide bone disease caused by the problem of mineralization of growing bones in children resulting in bone deformity and growth retardation.[1]Its global prevalence is reported to be approximately 10%.[2] It is stated that calcium deficiency, phosphorous deficiency, or vitamin D deficiency are the most common cause of rickets.[1]In addition, familial history is also reported to be the most important cause of rickets in children.[3]

There are various types of rickets, among these hypophosphatemic rickets have both inherited as well as acquired forms. The "X" linked dominant hypophosphatemic rickets is the most common genetic form caused by mutations in the PHEX gene, which results to increase the level of phosphatonins. This phosphatonins causes renal wasting of phosphate.[4] Some rare hereditary forms of hypophosphatemic rickets are also reported that includes autosomal dominant, autosomal recessive, and hypophosphatemic rickets with hypercalciuria. Moreover, an acquired disorder, oncogenic osteomalacia are usually seen in adults has similar clinical manifestations to the hypophosphatemic rickets.[5]

Patients with hypophosphatemic rickets are resistant to vitamin D therapy and various complications like short stature, bone pain, lower extremity deformity, dental abscesses, enthesopathy, and hearing impairment are reported in these patients.[6]

The rationale of this study is that rickets is common disease in children, an early diagnosis and proper management is required to avoid a lot of morbidity secondary to hypophosphatemic rickets which is an extra economic burden on parents and health facilities of state. Hence thorough investigations and the clinical features of hypophosphatemic rickets, a better understanding and management plan for the disease children could be possible.

MATERIALS AND METHODS

A descriptive cross-sectional study was conducted at Pediatric Outpatient department (OPD) and ward, National Institute of Child Health Karachi, Pakistan from 21st January 2015 to 20th January 2016. All consecutive children with age 1 to 14 years of either

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gender having rickets were enrolled. Whereas children already on treatment of rickets and/or receiving antiepileptic (diphenylhydantoin, phenobarbitone) drugs were excluded.

Sample size was calculated using EPI software 6 on the basis of 23.5% prevalence of dental abnormalities in hypophosphatemic rickets in previous study[7], 95% confidence interval, 6% precision. Sample size was found to be 230.

Detailed history from guardians regarding joint pain, fracture, and family history of rickets were taken. Clinical examination was performed by researcher himself for height and weight, joint pain, bony deformities. Fractures and bony deformities were assessed on x-rays and dental examination regarding delayed eruption, dental abscess, and malocclusion were done by dental surgeon having experience of at least five years.

Rickets was defined as softening and weakening of the bones caused by a lack of vitamin D (Serum vitamin D level less than 16pg/ml), calcium (Serum calcium level less than 8.8mg/dl), or phosphate (Serum Phosphate level less than 3.2mg/dl). Hypophosphatemia was defined as serum Phosphate level (PO_4) less than 3.2mg/dl. Short stature was defined as height that is two standard deviations below the mean height for age and sex. Fractures was defined as displacement of bone, were assessed on X-ray. Family history was defined as history of rickets from parents. Bony deformity was defined as presence of genu varum (bowed legs inward in the standing position will be assess clinically and will be confirm on X-ray showing outward bowing of the lower leg of an archers bow), genu valgum (Knee angle in and touch one another when legs are straightened assess clinically and will be confirmed on X-ray showing distal position of the knee joint which bends outward and thus the proximal portion seems to be bent inwards) and coxavara; any of them were labeled as bony deformity.

Joint pain was defined was assessed clinically and presence of Visual analogue score of ≤ 3 was labeled as joint pain. Dental abnormalities were defined as delayed eruption (6 months delay of teeth eruption from its normal period), dental abscess (collection of pus that's from teeth and spread to the surrounding tissues were assessed on periapical X-ray) and malocclusion of teeth; any of them was labeled as dental abnormality.

Statistical package for social sciences (SPSS) version 22 was used for the purpose of statistical analysis. Mean and standard deviation was calculated for age. Frequency and percentage were calculated for gender, hypophosphatemic rickets, short stature, bony deformity, joint pain, fractures, dental abnormalities and family history of rickets. Stratification with respect to age and gender were done. Post stratification chi-square test was applied. P-value ≤ 0.05 was taken as significant.

RESULTS

A total of 230 rachitic children were included. The mean age of the children was 7.56 ±4.35 years.

Majority of children were males (n=124, 53.9%) while 106 (46.08%) children were females.

Table 1: Comparison of Clinical profile of hypophosphatemic rachitic children with age and gender of the patients (n=230).

Variables	Age, years			Gender		
	≤7	>7	p-value	Male	Female	p-value
Short Stature						
Yes	5 (45.5)	6 (54.5)	0.838	4 (36.4)	7 (63.6)	0.513
No	2 (40)	3 (60)		1 (20)	4 (80)	
Fracture						
Yes	0 (0)	2 (100)	0.182	2 (100)	0 (0)	0.024
No	7 (50)	7 (50)		3 (21.4)	11 (78.6)	
Family history of Rickets						
Yes	3 (60)	2 (40)	0.377	1 (20)	4 (80)	0.512
No	4 (36.4)	7 (63.6)		4 (36.4)	7 (63.6)	
Bone Deformity						
Yes	1 (14.3)	6 (85.7)	0.036	2 (28.6)	5 (71.4)	0.838
No	6 (66.7)	3 (33.3)		3 (33.3)	6 (66.7)	
Joint Pain						
Yes	0 (0)	7 (100)	0.002	2 (28.6)	5 (71.4)	0.838
No	7 (77.8)	2 (22.2)		3 (33.3)	6 (66.7)	
Dental abnormalities						
Yes	2 (22.2)	7 (77.8)	0.049	2 (22.2)	7 (77.8)	0.377
No	5 (71.4)	2 (28.6)		3 (42.9)	4 (57.1)	

All data presented as number (%)

Chi-square test applied, p-value <0.05 was taken as significant

Frequency of hypophosphatemic rickets was found in 16 (7%) patients. (Figure 1) A significant difference of hypophosphatemic rickets was observed with respect to age (<0.001) and gender (p-value 0.035). (Figure 2&3)
Clinical profile of hypophosphatemic rachitic children showed that short stature was found 11 (69%) children, fracture in 02 (12.5%), positive family history of rickets in 5 (31%), bony deformity in 07 (44%), joint pain in 6 (37.5%) while dental abnormalities was observed in 7 (44%) children.
Comparison of clinical profile of hypophosphatemic rachitic children with age and gender of the patients showed significant difference in between bony deformity and age (p-value 0.036), joint pain and age (p-value 0.002), dental abnormality and age (p-value 0.049), while gender was only significantly associated with fracture (p-value 0.024). (Table 1).

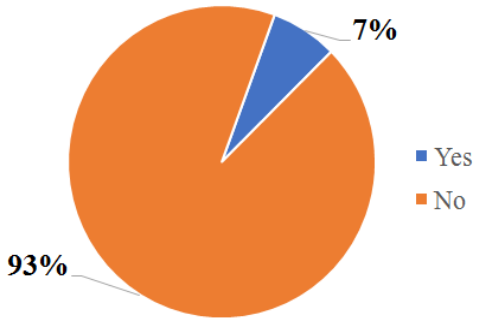

Figure No.1: Frequency of hypophosphatemic rickets

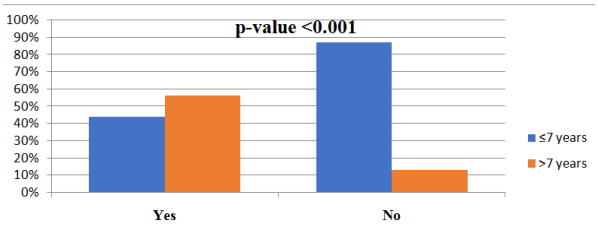

Figure No.2: Comparison of hypophosphatemic rickets with respect to age

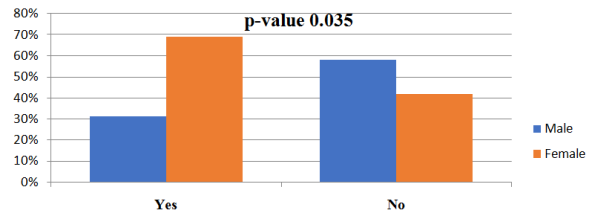

Figure No.3: Comparison of hypophosphatemic rickets with respect to gender

DISCUSSION

Hypophosphatemic rickets is a form of rickets that is characterized by low serum phosphate levels and resistance to treatment with ultraviolet radiation or vitamin D ingestion.[8-10] The findings of our study have showed hypophosphatemic rickets in 7% of the children with rickets. In our study, the presenting age of hypophosphatemic rachitic patients was 7.5 years, which was similar to studies done by Saggese Get al[11] (7 years) and Vaisbich MH et al[12] (6 years).
In our series of patients, hypophosphatemic racket was found higher females (69%),this was similarly reported by Bhadada SK et al (70.5%).[7]This may be due to reason that hypophosphatemic rickets are mostly X linked dominant conditions, which are more common in females.[3]
An outstanding feature of familial hypophosphatemic rickets is short stature, which was reported 69% in our patients and this was found 58.8% by Bhadada SK et al.[7] The short stature associated with this condition is disproportionate, resulting from deformity and growth retardation of the lower extremities. At the time of weight bearing leg deformities (e.g., bowing) are seen. Lower limb involvement is more common.[5]
Fracture 12.5%, joint pain 38% and bony deformities were observed in 44% of our series, while these features were higher in study of Bhadada SK et al which were 29.4%, 52.94% and 58.8% respectively.[7]
In our study family history of rickets was positive in 31% of the children, which was nearly same 35.3% in study conducted by Bhadada SK et al.[7]Dental abnormalities were 44% in our patients and 23.5% were observed in Chandigarh by Bhadada SK et al.[7]
A significant relationship with respect to age and gender in our study revealed that rachitic children were usually diagnosed after 7 years of age,with a greater lag time at diagnosis from the onset of the symptoms. This can be attributed to the lack of awareness to the approach of this entity among the internists and frequent neglect of health-related matters by the ailing individuals. Other than that, most of these patients were treated with cholecalciferol and calcium supplementation for variable period of time without much clinical response. Moreover, it is stated that hereditary hypophosphatemia is rare renal phosphate wasting disorders and its diagnosis is based on clinical, radiological and biochemical features. Furthermore, it may require genetic testing to be confirmed.[13-17]
Fracture was also found significant in our study. However, this feature was only observed in males and not in our female patients. Regarding short stature, bony deformities, dental abnormalities and joint pain, there were no significant difference between male and female children. Bony deformities, dental abnormalities, and joint pain were significantly observed in older age group children, while short stature and fracture have not significantly associated between two age groups.

CONCLUSION

It is to be concluded that short stature is most common clinical profile followed by bony deformity and dental abnormalities in rachitic children. A diagnosis of hypophosphatemic rickets should be considered in all patients presenting with short stature, bony deformities

or musculoskeletal pains along with low serum phosphate level with normal level of iPTH and 25 – hydroxy vitamin D.

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Original Article

Comparison of the Effects of Different Light Sources on Reading and Optical Performance

Farhan Ali, Hafiza Hina Rasheed, Muhammad Bilal Khan and Zain Mukhtar

ABSTRACT

Objective: To compare the effects of different light sources on reading and optical performance.
Study Design: Prospective observational study.
Place and Duration of Study: This study was conducted at the Mayo Hospital, Lahore from June 15, 2017 to December 15, 2017.
Materials and Methods: Eighty four participants (42 males and 42 females) were presented passages to read under four lighting conditions, followed by contrast assessment. Color vision was assessed with 17 Ishihara pseudo-isochromatic slides. Fifteen minutes were given for adaptation under all four lights. All the data was put in SPSS v.23 software. Data was analyzed with one way ANOVA and Friedman test. P value < 0.05 was considered statistically significant.
Results: The difference of reading rate was statistically significant ($p<0.001$) under various light sources in both male and female subjects. In males, reading rate was fastest under compact fluorescence light while in females, reading rate was fastest under light emitting diode light. One way analysis of variance with Friedman's test showed a significant relevance between visual performance and various illumination sources in males ($P <0.001$) and females ($P <0.001$)
Conclusion: We concluded that there was a significant association between reading performance and the type of illumination. Most male suggested the use of compact fluorescent light and most females suggested the use of light emitting diodes as a source of light. Tungsten bulbs were the least recommended source of light for study purpose. Fluorescent and light emitting diode lights are the suitable sources of light to perform study tasks.
Key Words: Optical performance, illumination, light sources, reading rate.

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INTRODUCTION

Various light sources have been recognized and studied as a standard for reading[1-3]. But there are some concerns and issues in the general population about the suitable light to be used for different specific tasks [4, 5]. Same light is produced by the light emitting diodes (LED) as by other bulbs, but there is less consumption of power. Light emitting diodes (LED) are both cost and energy efficient. There has been very slight concern about their influence on ocular health and visual ease. Some studies have shown that pupil size is decreased and visual acuity is improved by the scotopic rich fluorescence light source illumination. But these effects were only assessable with low-contrast stimuli which were presented briefly[6]. Some researchers further found that mood, visual performance and the participant's feeling of easy reading and visual activity was enhanced under the artificial light emitting diode lighting [7].

Nagy et al. [8] observed that visual tasks such as color and contrast perception were affected by the differences in the spectral dispersal of ambience lighting. Color chromaticity also variates with light emitting diode lighting. Mott et al.[9] performed a quasi-study to compare natural and artificial light and showed that student's reading performance was improved with the improvement of lighting conditions. Lin CC [10] found out that reading performance was much better under white light as compared to under yellow light. Light color also significantly affected visual performance. Eo IS et al.[11] used light emitting diode lamps of many colors and studied their effect on student psychology. Different colors changed the mood of art and music rooms and students' creative skills improved by this lighting modification. Light emitting diodes had a positive effect over creative skills as compared with the fluorescent light. Legge GE et al. [12] studied the reading ability of different print sizes and revealed that size of the print is of critical importance for reading clearly. Succar TA et al. [13] revealed that reading performance was significantly affected by different levels of illumination in the patients of low visual acuity.

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Fluorescent light contain low pressure mercury-vapors which use fluorescence for production of visible light. Mercury vapors are excited by the passage of electric current and short wave ultraviolet light is produced. This makes the phosphor coating on the inner surface of bulb to glow. Same mechanism enclosed in small sized tubes of the size of incandescent bulbs makes compact fluorescent light. Tungsten lamp is the one in which tungsten filaments are heated up to incandescence by the passage of electric current. Low pressure inert gas, usually argon, is filled in the glass bulb which encloses the tungsten filament. Addition of small amounts of halogen such as iodine is added to increase the intensity of light and the lamp is called tungsten-halogen lamp.

The effect of different light sources on individual reading performance and visual activity has not been studied adequately. Moreover, there is lack of regional data on different light sources. Current study is targeted at examining the influence of commonly used light source on visual activity and reading capability of individuals.

MATERIALS AND METHODS

The study was performed in Nishtar Mayo Hospital, Lahore after acquiring ethical approval from the departmental ethical committee. The duration of our study was 6 month from June 15, 2017 to December 15, 2017. Eighty four participants, half males and half females were selected using the non-consecutive random sampling technique. All the subjects were eighteen to twenty three years old and were medical students at the same hospital. Sample size was calculated using the study by Ram MS [1] as reference. Written and informed consent was taken from all the subjects. The students who has 6/6 visual acuity for far vision at a distance of six meters and N6 for near vision, no color blindness and good health were included in the study while those not meeting the inclusion criteria, recent history of ocular pathology, had refractive errors, and vitamin A deficient were excluded from our study.

This study was completed in two stages, initial examination and the investigational stage. We used a digital photometer (model- HS1010, Taiwan Tai Shi TES Company, China) to measure the intensity of light. The light sources used were (i) Compact fluorescence light (CFL), 3400-kelvin color temperature, 12 watt; (ii) Light emitting diode, 3100-kelvin color temperature, 8 watt; (iii) Fluorescent tube light, 3000-kelvin color temperature, 20 watt; (iv) Tungsten light, 3000-kelvin color temperature, 100 watt. All lights are of warm white color except tungsten light, which is a warm orange color light. The intensity of light was kept at 400 lux over all the light sources, the specific intensity picked based on many photometric values by lighting institutions, and it was checked by the digital photometer. Psychophysical analog of radiance which is known as luminance was provided by following the standards of the International Lighting Commission of Industrial Engineering (CIE) [14]. Reading time was recorded with a digital stopwatch. Reading pad was adjusted to grasp the reading material. Color vision was assessed by the use of Ishihara color vision slides and contrast was assessed by the use of Baily Lovie 10% Contrast sensitivity chart. All the participants were seated in a silent and well lighted room. The reading material for the assessment of near vision was placed at 40 cm distance from the eyes of the participants. An overhead lighting source was also arranged at 1 meter directly above the reading material. Reading passages were created which were of same readability score, in accordance with standardized psycholinguistic text readability consensus calculator software tool [15]. Text which was to be used for assessment of near vision was validated using a software. The text was presented to the participants in fifteen lines, Times New Roman, 12-points, black colored font, printed on the non-lustrous sheet of white paper. The content of the passages presented to all the participants was different but of equal readability score. The passages were presented randomly to all the participants. All the participants were asked to read the passages out loud in a closed room and were tested by the researcher himself for accuracy.

The investigational processes were executed under all lighting sources. All the participants were presented passages to read under four lighting conditions, followed by contrast assessment, after which color vision was assessed by with 17 Ishihara pseudo-isochromatic slides. Fifteen minutes were given for adaptation under all four lights. We used a closed ended questionnaire for visual performance, satisfaction level and visual ease of all the participants under all for light sources.

Table No.I: Questionnaire form

No.	Question	Yes	No
1.	Feeling of too much tearing or a desire to rub the eyes?		
2.	Experience of glare?		
3.	Experience of a burning sensation?		
4.	Double vision?		
5.	Pain in the eyes?		
6.	Confusion of color perception?		
7.	Experience of headache?		
8.	Gritty feeling in the eyes?		
9.	Tiredness of eyes?		

All the data was put in SPSS v.23 software. Reading rate, contrast sensitivity and number of color vision slides recognized were compared by applying one way ANOVA test; and visual performance was analyzed by Friedman analysis of variance. $P > 0.05$ was considered statistically insignificant.

RESULTS

In male subjects, the reading rate was 127.6±9.04 under compact fluorescence light, 118.5±11.22 under light emitting diode light, 122.1±7.44 under fluorescence light and 105.2±8.68 under tungsten light. In female subjects, , the reading rate was 125.9±8.28 under compact fluorescence light, 129.9±7.99 under light emitting diode light, 124.7±5.68under fluorescence light and 108.7±8.05 under tungsten light. The difference of reading rate was statistically significant (p<0.001) under various light sources in both male and female subjects. In males, reading rate was fastest under compact fluorescence light while in females, reading rate was fastest under light emitting diode light. Number of color vision slides which were recognized under various light sources were not statistically different in male subjects (p=0.661) and female subjects (p=0.378). In both the groups, contrast sensitivity was also comparable (p>0.05). On the other hand, one- way analysis of variance with Friedman's test showed a significant relevance between visual performance and various illumination sources in males (P <0.001) and females (P <0.001). (Table-II and III)

When all the subjects were requested to give suggestions about appropriate illumination source according to their experience of reading and visual ease, 80% of the males suggested compact fluorescence light and 75% of the females suggested light emitting diode light.

Table No.1: Comparison of Variables under Different Illumination Sources Among Male Subjects (N=42)

Variable	Compact Fluorescence Light	Light Emitting Diode Light	Fluorescence Light	Tungsten Light	p-value
Reading Rate (correct words per minute)*	127.6 ±9.04	118.5± 11.22	122.1± 7.44	105.2 ±8.68	<0. 001
Contrast sensitivity (log units)*	1±0.0	1±0.0	1±0.0	1±0.0	>0. 05
Color vision (No. of slides recognized)*	14.9± 0.76	15.1±0. 82	15.0±0. 88	15.2± 0.79	0.6 61
Visual performance**	3.7±2. 10	6.5±2.6 1	4.7±2.6 7	12.7± 3.71	<0. 001

Data is mentioned as mean ± S.D. *One way ANOVA test was applied; **Friedman test was applied.

Table No.2: Comparison of Variables under Different Illumination Sources Among Female Subjects (N=42)

Variable	Compact Fluorescence Light	Light Emitting Diode Light	Fluorescence Light	Tungsten Light	p-value
Reading Rate (correct words per minute)*	125.9± 8.28	129.9± 7.99	124.7±5. 68	108.7± 8.05	<0.0 01
Contrast sensitivity (log units)*	1±0.0	1±0.0	1±0.0	1±0.0	>0.0 5
Color vision (No. of slides recognized)*	14.9±0. 79	15.3±0. 70	15.1±0.9 4	15.1±0. 85	0.37 8
Visual performance**	3.8±2.2 8	6.9±2.3 5	5.1±2.39	12.7±2. 61	<0.0 01

Data is mentioned as mean ± S.D. *One way ANOVA test was applied; **Friedman test was applied.

DISCUSSION

We observed in our study that there was significant association between reading rate and type of illumination. In males reading rate was in following order: Compact fluorescence light>fluorescent light>light emitting diode light>tungsten light. In females, reading rate was in following order: light emitting diode light>Compact fluorescence light>fluorescent light> tungsten light. In the study by Ram MS et al. [1], similar sequence of speed of reading was observed n males, but rate was highest under fluorescent light in females and there was no significant relationship between reading rate and the type of illumination source. The results of current study in the female group are in accordance with the results of the study conducted by Yamagishi M. et al. [8]. According to them, mood, visual performance and the participant's feeling of easy reading and visual activity was enhanced under the artificial light emitting diode lighting.

In our study, we observed high visual discomfort and slow reading rate under tungsten light. But majority of the male students (80%) was satisfied with compact fluorescent lights and suggested its use whereas the majority of female students (75%) was satisfied with light emitting diode luminance and suggested its use in schools. Similarly in 2014, Eo IS et al. [11] used light emitting diode lamps of many colors and studied their effect on student psychology. Different colors changed the mood of art and music rooms and students' creative

skills improved by this lighting modification. Light emitting diodes had a positive effect over creative skills as compared with the fluorescent light. We observed that reading performance was improved under white compact fluorescence light. These results were consistent with the results of the quasi-study by Mott et al. [9] which was performed a to compare natural and artificial light and showed that student's reading performance was improved with the improvement of lighting conditions with artificial sources. Color and intensity of light affect the performance of visual tasks[17]. Best performance is under normal illumination[16]. Both low and high intensity of light affect the visual performance negatively [16, 18].

CONCLUSION

We concluded that there was a significant association between reading performance and the type of illumination. Most male suggested the use of compact fluorescent light and most females suggested the use of light emitting diodes as a source of light. Tungsten bulbs were the least recommended source of light for study purpose. Fluorescent and light emitting diode lights are the suitable sources of light to perform study tasks.

Author's Contribution:

Concept & Design of Study:	Farhan Ali
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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

Evaluation of Efficacy and Safety of Misoprostol in Medical Termination of Pregnancy Using International Federation of Gynaecology and Obstetrics (FIGO) Protocol

Fatima Nazim, Zartaj Hayat and Arifa Bari

ABSTRACT

Objective: To evaluate the efficacy and safety of misoprostol administration in medical termination of pregnancy using FIGO protocol

Study Design: Prospective descriptive study

Place and Duration of study: The study was conducted at the Department of Obstet & Gynae, Fauji Foundation Hospital, Rawalpindi from Jan.2016 to June.2017.

Materials and Methods: 73 patients were recruited in the study using non probability consecutive sampling technique. Patients with incomplete miscarriages, missed miscarriages up to 24 weeks and induced miscarriages due to fetal anomaly, anhydramnios, chorioamnionitis, intrauterine fetal demise and medical problems were included in the study. Patients fulfilling the selection criteria were admitted in the hospital. After detailed history and examination, baseline investigations and clotting profile were sent. Written informed consent was taken. Misoprostol administration was done according to the FIGO protocol. The efficacy was determined by successful expulsion of products of conception without surgical intervention. Safety profile was determined by occurrence of severe haemorrhage requiring blood transfusion, infection, retained placenta, uterine rupture.

Results: The mean age of study population was 38years +. 5years. 38% of the patients were between 36 to 40 years of age.73%of the patients were multiparous. 17.8% of the patients were with history of prior caesarean section. First trimester missed miscarriage was the most common indication of termination of pregnancy. . The overall success rate was found to be 97.59% with no adverse side effects.

Conclusion: FIGO protocol for Misoprostol administration is an effective and safe option for medical termination of pregnancy.

Key Words: Misoprostol, FIGO protocol, Medical Termination, Miscarriage.

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INTRODUCTION

Early pregnancy loss is the commonest complication encountered by women in their reproductive life.[1] It accounts for 10-20% of the clinically recognized pregnancies.[2] In Pakistan, the annual rate of miscarriage is 2.9% in the second and fourth decade of woman's life, responsible for 10-12% of maternal mortalities.[3] Approximately 56 million cases of miscarriages are occurring worldwide annually, thus making it a global health issue demanding safety and efficacy of its management options.[4]

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The available options for termination of pregnancy include expectant, medical and surgical management.[5] Surgical termination of pregnancy carries a considerable risk to woman's life[6] so the use of Misoprostol ,PGE_1 analogue, has largely replaced other methods.[7]Although its primary indication was treatment and prevention of gastric ulcer, however, due to its strong uterotonic effect it is a viable option for medical termination of pregnancy, cervical priming before surgical procedures, labour induction, treatment and prophylaxsis of postpartum haemorrhage.[8] It can be administered orally, sublingually, vaginally and through rectal and buccal route.[9]

The side effects include nausea, vomiting, diarrhoea, fever and chills. Another concern with use of misoprostol is its association with uterine rupture especially in patients with previous uterine scar. However literature review revealed that it is rare in first trimester and the risk increases with increasing gestational age, the highest being in third trimester when it is used for induction of labour.[10] Cost effectiveness, easy availability and stability at room

temperature makes Misoprostol a useful option especially in low resource setting.[11] However the dosage protocol used for termination of pregnancy at different gestational ages vary according to the hospital settings.

This study aims at using Misoprostol administration protocol devised by International Federation Of Gynaecology and Obstetrics (FIGO) and World Health Organization (WHO) which is also endorsed by Society of Obstetrics and Gynaecology, Pakistan (SOGP) for medical termination of pregnancy in different types of miscarriages at various gestational ages and determining its efficacy and safety so that a uniform dosage protocol can be implemented.

MATERIALS AND METHODS

After approval from hospital ethical committee , this prospective descriptive study was conducted in the department of Obstet and Gynae, Unit 2, Fauji Foundation Hospital, Rawalpindi from Jan. 2016 to June 2017.A total number of 73 patients were recruited in the study using non probability consecutive sampling technique. Patients presenting with incomplete miscarriages, missed miscarriages upto 24 weeks and induced miscarriages due to fetal anomaly, anhydramnios, chorioamnionitis, intrauterine fetal demise and medical problems were included in the study. Patients with septic abortion, acute asthama, glaucoma and allergy to the prostaglandins were excluded from the study. Patients fulfilling the inclusion and exclusion criteria were admitted in the hospital. After detailed history and examination, baseline investigations and clotting profile were sent. A written informed consent was taken. Misoprostol administration was done according to the FIGO protocol as shown in table 1.

The dose of misoprostol was reduced to half in patients with prior caesarean section presenting in second trimester. The efficacy of misoprostol was determined by successful expulsion of products of conception without requiring surgical intervention. Safety profile was determined by occurrence of severe haemorrhage requiring blood transfusion, postabortal infection, retained placenta, uterine rupture. Results were recorded in proforma and analysed by SPSS 20 version.

RESULTS

A total number of 73 patients were included in the study. The mean age of study population was 38years +_ 5years. Majority (38%) of the patients were between 36 to 40 years of age (table 2).

Seventy three per cent of the patients were multiparous (figure 1).

First trimester missed miscarriage was the most common indication of termination of pregnancy (table 2).

Out of total 73 patients, six were lost to follow up. The efficacy of Misoprstol was determined in 67 patients. The overall success rate was found to be 97.59% (table 3). Surgical evacuation due to failed medical TOP was done in two patients, both with missed miscarriage at 20-22weeks of gestation having history of previous two cesarean sections.

No cases of severe haemorrhage, post abortion infection, retained placenta or uterine rupture was reported.

Table No.I: Dosage protocol of misoprostol administration

Indications	Dose of Misoprostol
First Trimester	
Induced abortion	800mcg sublingually or vaginally 3hrly max. 3 doses within 12 hrs
Missed miscarriage	800mcg vaginally 3hrly max 2doses
Incomplete miscarriage	400mcg sublingual ly single dose
Second trimester	
Induced abortion	400mcg vaginally 3hrly max. 5 doses
Intrauterine fetal death	13-17weeks: 200mcg vaginally 6hrlymax .4 doses
	18-26weeks:100mcg vaginally6hrly max 4 doses

Table No.2: Age distribution of study population (n=73)

Age groups (Years)	No. of patients	Percentage
20-25	11	15.06%
26-30	17	23.28%
31-35	13	17.8%
36-40	28	38.35%
>40	04	5.4%

Table No.3: Indications for termination of pregnancy (n=73)

Indications	No. of patients	Percentage
First Trimester		
Incomplete miscarriage	11	15.06%
Missed miscarriage	27	36.98%
Induced miscarriage	01	1.36%
Second Trimester		
Missed miscarriage		
13-17weeks	14	19.17%
18-24weeks	06	8.21%
Induced miscarriage		
Fetal anomaly	05	6.84%
PPROM+Chorioamnionitis	03	4.10%
Choronic kidney disease	01	1.36%
IUD(26-30wks)	05	6.84%

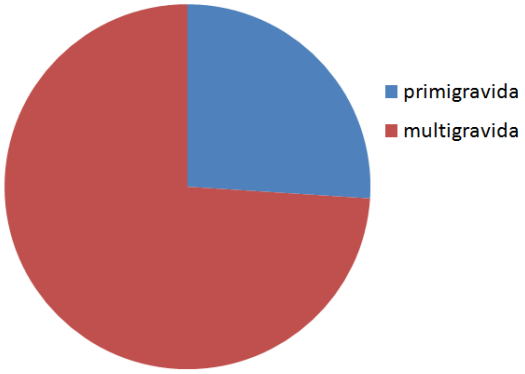

Figure No.1: Parity of study population (n=73)

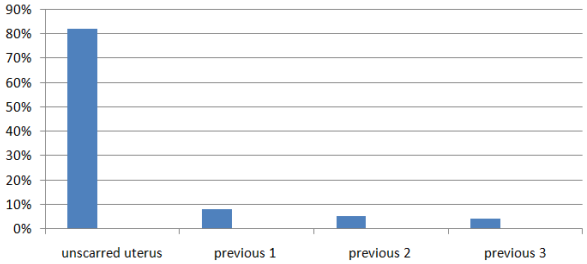

Figure No. 2: Percentage of Patients with Prior Caesarean Section (n=73)

Table No.4: Efficacy of misoprostol in medical termination of pregnancy (n=67)

	No. of patients	%age
Complete expulsion within one cycle	40	59.70%
Patients requiring repeat cycle of misoprostol after 24hrs rest	15	22.38%
Patients with spontaneous expulsion after 1 week rest	07	10.44%
Patients requiring repeat cycle of Misoprostol after 1week rest	3	4.4%
Patients requiring surgical evacuation after failed TOP	2	3.17%

DISCUSSION

Management options available for termination of pregnancy include expectant, medical and surgical treatments. Using Misoprostol for medical termination of pregnancy has been in clinical practice but the dosage protocol remained controversial. Different randomised controlled trials have been conducted in the past to determine which treatment option is better. Miscarriage treatment trial(MIST)[12] was conducted in 2006 by J Trinder et al comparing medical and expectant managements with surgical management of first trimester miscarriages and concluded that the incidence of gynaecological infection after surgical, medical and expectant management was low(2.3%) and did not depend upon the type of the method used. The optimum regimen for Misoprostol administration needs to be determined and future research in this regard is lacking. Dosage protocol of Misoprostol administration devised by FIGO and WHO, endorsed by Society of Gynaecology and Obstetrics Pakistan in 2003 was used in this study with an aim to determine its efficacy and safety.

The mean age of the study population was 38 ± 5 years. 38% of the patients were between 36-40 years of age. A study conducted by Anee Marie et al tried to find out the association between maternal age and risk of spontaneous miscarriage and concluded that the incidence of miscarriage increases with maternal age, highest being in late 30 years or more.[13]About 36.9% of medical terminations were done due to first trimester missed miscarriage and was the most common indication.53.4% of the patients had gestational age less than 13 weeks. Ammon Avalos L and colleagues studied the expected rates of miscarriage by gestational age and found out a cumulative risk of 11-22% for 5 to 20 weeks of gestation.[14] Our study results show a slightly raised percentage of patients presenting in first trimester.

The overall success rate of medical termination of pregnancy in our study was found to be 97.59%. Only 2 patients required surgical evacuation. Both patients had history of previous 2 cesarean sections and late second trimester miscarriages. The ultrasound showed formed foetuses having parameters of 14 to 16 weeks. On vaginal examination the cervix was anteriorly placed with retroverted uterus. During surgical evacuation the foetuses were removed piecemeal. Liaquat FN et al conducted a study on 54 patients to evaluate the efficacy of 50mcg of misoprostol repeated at 4hrs interval for termination of second trimester fetal demise and the success rate was found to be 96.3% within 48 hours comparable to our study.[15] Prachasilpchai and colleagues had reported a success rate of 89.5% within 48hrs in 94 patients admitted for second trimester termination of pregnancy using 400mcg vaginally every 12 hrs.[16] Nielsen S et al conducted a randomised controlled trial to compare the efficacy of mifepristone (antiprogesterone) in combination with misoprostol and expectant management. He concluded that 82% of the patients had complete expulsion of products of conception within five days in medically treated group as compared to 76% of the patients who had received expectant management.[17] In our study 39 patients received medical termination due to first trimester missed, incomplete and induced miscarriages. Six patients were lost to follow up. Out of 33 patients, 63% had expulsion within 24 hours and 30.3% had complete

expulsion within seven days, making an overall success rate of 93.3% which is comparable to the study results mentioned. However mifepristone was not used due its non-availability in Pakistan.

Different routes of administration of misoprostol have been compared in various studies including oral, vaginal and sublingual routes. Shah N and colleagues compared the effectiveness of vaginal and sublingual misoprostol for termination of missed miscarriage with gestational age less than 20wks. They found no statistically significant difference in the rates of expulsion between the two routes.[18] Another randomised controlled trial was conducted by Hemleta and colleagues to compare oral versus vaginal route of misoprostol administration for termination of pregnancy between 12-26 weeks of gestation. The success rate for oral route was 94% as compared to 86.8% with vaginal route.[19] However, oral route was associated with unpleasant taste. We only used vaginal route of administration in all our patients to avoid gastrointestinal side effects.

The role of misoprostol in patients with prior uterine scar was a much debatable issue in the past. However literature review has shown that misoprostol can be administered safely in these patient in first and second trimesters. Since it is rare in first trimester, so in FIGO protocol the dose of misoprostol is same for scarred and unscarred uterus. However in second trimester the dose is reduced to half in patients with prior caesarean sections. In our study, out of 73 patients, there were 13 patients with scarred uterus and no case of uterine rupture was reported. J E Dickinson studied 720 patients who underwent termination of pregnancy due to fetal anomaly having previous one or more caesarean sections with misoprostol 400mcg repeated at 6hourly interval and no case of uterine rupture was reported.[20] Daskalakis and colleagues evaluated the safety of misoprostol in 108 patients between 17-24 weeks of gestation with history of previous caesarean delivery. They found it safe and efficacious drug and no case of uterine rupture was reported.[21] Mazouni C et al studied the role of misoprostol in medical termination of pregnancy in 250 patients, out of which 50 patients were with scarred uterus and reported only one case of uterine rupture presenting in late second trimester.[22] The use of misoprostol in third trimester requires maternal surveillance due to increased risk of uterine rupture in scarred uterus.

The limitation of this study is its small sample size. For generalization of our results more studies with larger sample size should be conducted in future. The FIGO has revised the recommended regimens for misoprostol only in 2017 for medical termination of pregnancy. The future recommendations include implementation of this revised protocol in our hospital setting and soon we will come up with the results.

CONCLUSION

Misoprostol is a safe and effective drug for medical termination in first and second trimesters. The success rate is quite high using FIGO protocol for misoprostol administration and should be implemented.

Author's Contribution:

Concept & Design of Study:	Fatima Nazim
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Revisiting Critically:	Fatim a Nazim, Zartaj Hayat
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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

Role of Ultrasound in the Diagnosis of Acute Appendicitis and its Correlation with Neutrophil Count

Muhammad Ashraf Kasi

ABSTRACT

Objective: The objective of this study was to assess the role of ultrasound in the diagnosis of acute appendicitis and its correlation with neutrophil count.
Study Design: Descriptive study.
Place and Duration of study: This study was conducted at the Department of Radiology, Bolan Medical Complex Hospital, Quetta from September 2016 to June 2017.
Materials and Methods: A total 70 patients were selected from emergency and outdoor departments of Bolan Medical complex Hospital Quetta. The patients were presented with pain and tenderness in right lower quadrant. Ultrasound findings were correlated with neutrophil count.
Results: Total of 70 patients in which 35 (50%) were males and 33 (47%) were females. 56(80%) patients presented with acute appendicitis, 4(6%) with appendicular abscess, 7(10%) with appendicular lump and 3(4%) patients with appendicular rupture. The most common age presentation was 11-20 years 31 (44%), the least common age presentation was 41 years and above 2 (3%), 21-30 year range was 18(26%), 0-10 years range was 16 (23%) and from 31-40 years was 3 (4%). Patients with increased neutrophil (Neutophilia) count were seen in 63 (90%) and with normal neutrophil count were 7 (10%).
Conclusion: Ultrasound is safe, easily available and effective tool in the diagnosis of acute appendicitis.
Key Words: pain, tenderness, right iliac fossa, Doppler ultrasonography, acute appendicitis, Neutrophil count.

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INTRODUCTION

The appendix is a blind ended tubular structure connected to the cecum approximately 2cm below the ileocecal junction in right iliac fossa.[1]

The length of appendix is variable and usually on average 9cm long and width between 7 and 9mm. The blood supply arises from appendicular artery a branch of ileocolic artery and venous drainage from appendicular vein. Lymphatic drainage of appendix drains into the upper and lower ileocolic lymph nodes, which surrounds the ileocolic artery. The presence of lymphoid tissue suggests that the appendix may role in the immune system in addition to the digestive system. It is worm like structure attached to the base of first part of large intestine in the right iliac fossa. The appendix is suspended by a small triangular fold of peritoneum, called the mesoappendix. It has no known function thought to be vestigial remnant. The appendix is not vital organ and medical researchers still debate its function in human body.

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The blockage leads to increased pressures in the appendix, decreased blood flow to the tissues of the appendix, and bacterial growth inside the appendix causing inflammation.[2] If the blockage is not treated, the appendix may rupture and the infection may leads to peritonitis. It is possible the pain could localize to the left lower quadrant in people with situs inversus totalis.

The positions of the appendix is variable but the most common positions are retrocecal and subcecal. McBurney's point is the name given to the point over the right side of the abdomen that is one third of the distance from the anterior superior iliac spine to the umbilicus. The point roughly corresponds to the most common location of the base of the appendix where it is attached to the cecum. Congenital anomalies of vermiform appendix are rare but occasionally seen as duplication, triplication or agenesis.

The acute appendix is assessed by doppler ultrasonography machine using convex and high resolution linear probes. These findings were correlated with neutrophil count. The classic presentation was abdominal pain. The pain was periumbilical initially and then migrates to the right lower quadrant.[3] In Asian and African counties the incidence of acute appendicitis is lower because of dietary habits. They take high fiber diet and less carbohydrate. With the right diagnostic tests and antibiotics, most cases are identified and treated without complications.

MATERIALS AND METHODS

Total of 70 patients were included in the study irrespective of age group and gender. The study was conducted in the department of radiology Bolan medical complex hospital Quetta. The referral of the patients was from the Emergency department and outpatient departments of the hospital. The patients mostly presented with abdominal pain and tenderness, followed by nausea and or vomiting and fever. The other pathologies were excluded from the study.

The diagnosis of acute appendicitis is difficult to diagnose on the basis clinical examination alone. This should be supplemented by radiologist operated doppler ultrasonography and laboratory investigations. The study was conducted using convex and linear probes and correlated with neutrophil count. Doppler ultrasonography is non-invasive, easily available and cost effective tool. Ultrasonography is operator dependent and needs expertise in the proper diagnosis. Visualization of blind ended non compressible blind ended appendix measures greater than 6 mm diameter with or without other findings like appendicoliths, echogenic periappendicular fat, and abscess and pericecal fluid collection was the diagnostic of appendicitis.

There is mild male predominance. The incidence of appendicitis gradually rises from birth, peak in late teen age and gradually declines in old age. Appendicitis is rare in infants. Young patients have incidence of perforations. The clinicians must maintain a high suspicion in all age groups. The other conditions should be kept in differential diagnosis may include stump appendicitis, epiploic appendagitis, right psoas abscess, inflammatory bowel disease, Meckel's diverticulitis and typhlitis.

RESULTS

Total of 70 patients in which 35 (50%) were males and 33 (47%) were females (Table 1). 56(80%) patients presented with acute appendicitis, 4(6%) with appendicular abscess, 7(10%) with appendicular lump and 3(4%) patients with appendicular rupture. The most common age presentation was 11-20 years 31 (44%), the least common age presentation was 41 years and above 2 (3%), 21-30 year range was 18(26%), 0-10 years range was 16 (23%) and from 31-40 years was 3 (4%). Patients with increased neutrophil (Neutophilia) count were seen in 63 (90%) and with normal neutrophil count were 7 (10%). (Table 2)

Table No. I: Gender distribution

Male	Female
35 (50%)	33(47%)

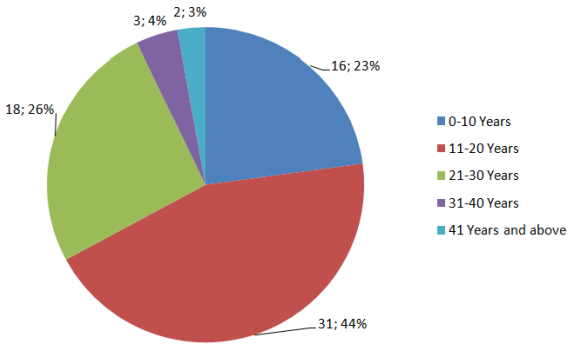

Figure No.1: Age Distribution.

Table No. 2: Leukocyte count in Appendicitis

Leukocyte count	Appendicitis
Increased	63 (90%)
Normal	7 (10%)
Total	70

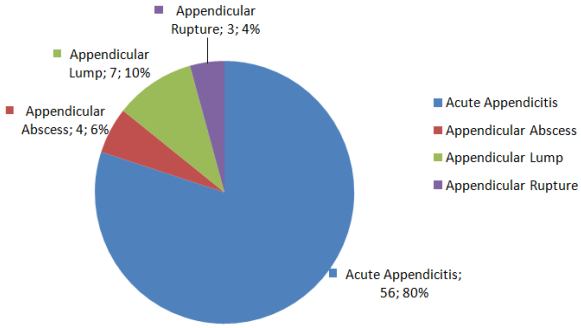

Figure No. 2: Ultrasound Findings

DISCUSSION

It is important to know that the position of appendix is variable.

Appendicitis can happen at any time, but it occurs most often between the ten and twenty years. It is more common in males than in females. Dull Pain usually started from periumbilical region shifting to the right lower quadrant at McBurney's point. Followed by nausea and or vomiting, rebound tenderness and low grade fever. The location of the base of the appendix is much variable, especially as the length of the appendix has an extensive range 2-20cm[4]. Appendicitis is more common in developed nations. The reason for this discrepancy is unknown; causes may include family history, low fiber diet, infection and high sugar level. Acute appendicitis is an acute surgical emergency needs urgent attention to perform appendectomy. Acute appendicitis can presents in typical or atypical manner. Timely diagnosis of atypical appendicitis remains clinically challenging and is one of the missed problems in the emergency department. Furthermore the consequence of missing appendicitis, leading to

perforation significantly increases the morbidity and prolongs hospitalization.[5] Appendicitis is caused by direct luminal obstruction usually secondary to fecoliths, lymphoid hyperplasia, impacted stool or rarely appendiceal/ cecal tumors. The neutrophil count is increased in ninety percent patients while in ten percent of patients it was normal or decreased. The diagnosis of appendicitis is delayed in elderly patients. Even with inflamed appendix there is no pain or fever.

Research focusing on various aspects of ultrasound imaging in the diagnosis of acute appendicitis has gained major importance over recent years as radiation protection, broad availability and cost-effectiveness became increasingly important aspects of modern imaging techniques in the diagnosis of acute appendicitis.[6] CT is not easily available and is not cost-effective. Additionally CT has radiation effects on the human body. Computerized tomography (CT) can only be done for inconclusive studies to avoid complications like appendicular perforation. Appendicular lumps are treated conservatively followed by surgery. Appendicular rupture was managed by emergency laparotomy. Appendicitis is one of the main reasons for abdominal surgeries in young patients. A recently described dynamic ultrasound technique using a sequential 3 step patient positioning protocol has been shown to increase the visualization rate of the appendix.[7]In the study patients were initially examined in conventional supine position followed by left posterior oblique and again supine position. Urine analysis may be sometime useful in the diagnosis of acute appendicitis. Ultrasonography also excludes other pathologies like ureteric calculi and ovarian torsion/hemorrhagic cysts. In women with reproductive age ectopic pregnancy should also be excluded. Usually normal appendix is not visualized on ultrasonography. When becomes inflamed the diameter of appendix will be increased and non-compressible. Neutophilia is usually seen in patients with acute appendicitis. In infant and elderly patients WBC count is unpredictable because these patients may not normal response to infection. Appendicitis is considered a preventable disease due to the effect such as diet on its development.[8] Epidemiologic and demographic studies report the appendicitis to vary according to age, gender, race, socioeconomic status, food culture and seasonal changes[9]. In the first year of life, the appendix is funnel shape, perhaps making it less likely to become obstructed. Lymphoid follicles are interspersed in the colonic epithelium that lines the appendix and may obstruct it. These follicles reach their maximum size during the adolescence.[10] The most common non obstetric emergency needing surgery in pregnancy is appendicitis.[11]Pregnant women are less likely to have a classic presentation of appendicitis than non pregnant women, especially in late pregnancy.[12] A recent large scale case control study has suggested a reduction in the incidence of appendicitis during the pregnancy; particularly during the third trimester.[13] Pregnant women are less likely to have classic presentation of appendicitis than non pregnant women, especially in late pregnancy. The most common symptom of appendicitis, ie, right lower quadrant pain, occurs close to McBurney's point in the majority of pregnant women, regardless of the stage of pregnancy, [14] hewever, the location of appendix migrates a few centimeters cephald with the enlarging uterus, so in the third trimester, pain may localize to the mid or even the upper right side of the abdomen.[15] The presence of pus cells in the urine does not exclude the acute appendicitis. Irritation of ureter by inflamed appendix can cause pyuria and hematuria. Despite large number of tests available, the diagnosis of appendicitis is challenging.

CONCLUSION

Doppler ultrasonography is non invasive, easily available and cost effective imaging tool, used in the diagnosis of acute appendicitis. And it also helps to exclude the other pathologies. Increased neutrophil count further strengthening the diagnosis of acute appendicitis**.**

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Original Article

Diabetic Care Provision

Diabetic Care Provision and Glycemic Control in a Pediatrics Diabetic Clinic: An Audit

Sabahat Amir, Jan Muhammad, Arshia Munir and Fazlur Rahim

ABSTRACT

Objective: To study the glycemic control and factors associated with glycemic control of children with type 1 diabetes mellitus attending the diabetic clinic of pediatric department of Khyber teaching hospital.
Study Design: Retrospective / observational study.
Place and Duration of Study: This study was conducted at the Diabetic Clinic of Pediatric Department, Khyber Teaching Hospital, Peshawar from January 2015 till December 2017.
Materials and Methods: An audit of all the diagnosed diabeticpatients attending the diabetic clinic for at least one year of pediatric department of Khyber teaching hospital. Every scheduled follow up visit was recorded by a resident doctor on a Performa. The self-monitored blood glucose record, insulin dose, injection site, technique and site rotation were checked. Dietary compliance was checked and 24 hour dietary record taken. Any change in dose needed was planned and a follow-up date was given. All these follow up Performa were studied and data was extracted from them.
Results: The number of patients that completed the study were 54(27 males and 27 females). The mean age of patients in this study was 8.5 years. Mean duration of diabetes was 1.89 SD 0.6. The mean HbA1c at the beginning of the study was 10% and at the end of study was 8.5%. The number of patients with good glycemic control were18 and with intermediate were 14 and poor were 22.
Conclusion: Good glycemic control was significantly associated with parent being literate, frequent home blood glucose monitoring, regular follow up visits and good dietary compliance.
Key Words: Diabetes mellitus, Children, Glycosylated hemoglobin

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INTRODUCTION

Diabetes mellitus is a common, chronic, metabolic syndrome characterized by hyperglycemia as a cardinal biochemical feature[1]. Type 1 diabetes is caused by deficiency of insulin secretion by damage to the beta cells of pancreas[1].

American Diabetic Association target values for HbA1c in relation to age are as follows: 7. 5% to 8.5% at age <6 years, <8.0% at age 6 to 12 years, <7.5% at age 13 to 18 years and<7.0%at 19 years and above. Individuals who met the ADA target were classified as good control; those with HbA1c > 9.5% regardless of age were classified as poor control. The value between poor and good are classified as intermediate control.[2]

The glycemic control is monitored by glycosylated hemoglobin (HbA1c), which provides a retrospective insight of blood glucose over the past 2 to 3 months[1], weighed toward the most recent 4 weeks. However the most recent week glycation is reversible and not included.[3]

Better quality of life and reduced or delayed development of macro and micro vascular complications in the long term is dependent on better glycemic control in diabetic children and adolescents[4,5]. The long term complications are monitored by micro albumin in urine and retinal examination of children. Improved glycemic control is also essential for reducing potentially serious acute complications such as ketoacidosis and hypoglycemic episodes[5,6].

The management of type 1 diabetes involve a complex interaction between life style modification, dietary compliance, insulin, management of comorbidities and input of care takers(parents, guardians) and healthcare professionals in an attempt to lower the blood glucose level to normal values[7,8]. The provision of a motivated multidisciplinary team of diabetic specialist is thought to be vital in attaining optimal glycemic control. Majority of studies continue to report HbA1c level above the targets desirable for reduction of complications[9,10,11]. The various factors (demographic factors of patient, disease related factors, care takers and health provider) associated with glycemic control are studied[12,13]and need to be studied further[14].

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The goals of this audit were to find the mean glycemic control of patients provided with separate care than with general outpatient department patients and to study the demographic and disease related factors associated with glycemic control.

MATERIALS AND METHODS

This retrospective study was carried out at the pediatric diabetic clinic of Khyber Teaching Hospital Peshawar. Patients were classified into good, intermediate and poor glycemic control according to ADA target level of HbA1c for each specific age group.

All the diagnosed children with type1 diabetes on insulin, attending the diabetic clinic, under 18 years of age and at least one year since diagnosis were included. At enrollment demographic data (age, gender, date of birth, weight, height, address, education of care taker, contact number) and disease related factors (date of diagnosis of diabetes, age of onset of disease, type and dose of insulin, injection technique, site, site rotation, diabetic knowledge, follow up visits regularity) were noted. Investigations (HbA1c, urine for micro albumin, blood count, thyroid function test and coeliac screen) were ordered. The follow-up visit of each patient is recorded and conducted by the same team of medical officer and consultant. A structured follow up visit proforma was completed noting date, height, weight, insulin dose, checking technique, site rotation and injection site, self-monitored blood glucose value, dietary compliance and further plan. HbA1c, eye examination and urine micro albumin value is checked every three months.

Statistical Analysis: The data was recorded and analyzed using spss version 20. The continuous variables were presented as mean and standard deviation and categorical variables as percentages. Pearson Chi-square test was used to study the relation of variables with glycemic control. Predictors of good glycemic control were compared with poor glycemic control using multinomial logistic regression. For all the analysis p value of <.05 was considered as significant.

RESULTS

The patients included in the study were 54;27 were male and 27 females; 1:1 ratio. The mean age was 8.29(SD 4), HbA1c at enrollment 10.1(SD 2.6), HbA1c at the end of study 8.7(SD 2.4). Out of the 54 patients 18(33.3%) had good glycemic control, 4(25.9%) had intermediate and 22(40.7%) had poor glycemic control. Demographic characteristics of these patients are shown in table number 1.

Table No.1. Demographic data of the patients.

Number of patients	54
Gender	27 males, 27 females
Mean age	8.2
Parents education	33 literate (61.1%) 21 illiterate (38.9%)

There were equal number of males and females. There were 16 (29.6%) patients with age range of 0-5years, 29(53.7%) in 6-12years and 9(13.7%) in 13-18years age range. Their glycemic control is shown in table 2.

Amongst the demographic factor parental education was associated with good glycemic control as compared to poor. The rest of the factors were not significant. Disease related factors along with their number and percentages are shown in table 3.

The comparison of glycemic control of disease related factors which has a p value of <.05 is shown in table 4.

Table No.2: Distribution of glycemic control of diabetic patients by demographic characters.

Variables	Glycemic control			Total (n=54)	*P*
	Good (n=18)(%)	Intermediate (n=14)(%)	Poor (n=22)(%)		
Age range 0-5 % within glycemic control	5(31.2), 27.8%	5(31.2) 35.7%	6(37.5) 27.3%	16(29.6%)	0.98
6-12% within glycemic control	10(34.5) 55.6%	7(24.1) 50%	12(41.4) 54.5%	29(53.7%)	
13-18% within glycemic control	3(33.3) 16.7%	2(22.2) 14.3%	4(44.4) 18.2%	9(16.7%)	
Gender					0.24
Male % within glycemic control	7(25.9) (38.9)	6(22.2) (42.9)	14(51.9) (63.6)	27(50%)	
Female %within glycemic control	11(40.7) (61.1)	8(29.6) (57.1)	8(29.6) (36.4)	27(50%)	
Parents/education					0.047
Literate % within glycemic control	15(45.5) 83.3%	8(24.2) 57.1%	10(30.3) 45.5%	33	
Illiterate % within glycemic control	3(14.3) 16.7	6(28.6) 42.9	12(57.1) 54.5	21	

Table No.3: disease associated factors in patients with diabetes

Variables		N	%
glycemic control	Good	18	33.3%
	Intermediate	14	25.9%
	Poor	22	40.7%
time since diagnosis	<1 year	14	25.9%
	1-5 years	32	59.3%
	6-10years	8	14.8%
insulin regimen	Premix	42	77.8%
	MDI	12	22.2%
injection technique	Good	40	74.1%
	Poor	14	25.9%
injection given by	Parent	31	57.4%
	under supervision	3	5.6%
	Self	19	35.2%
	Sibling	1	1.9%
dietary compliance	Poor	21	38.9%
	Fair	13	24.1%
	Good	20	37.0%
follow-up visits	Regular	18	34%
	Irregular	36	66%
diabetic knowledge	Poor	18	33.3%
	Fair	21	38.9%
	Good	13	24.1%
	Excellent	2	3.7%
Total		54	100.0%

Frequent blood glucose monitoring, good dietary compliance and regular follow up visits were associated with good glycemic control as compared to poor. There was no significant difference in glycemic control of patients on premix insulin and multidose injection of insulin using intermediate acting and three short acting insulin. Similarly other factors like injection site, technique, rotation of injection site and disease duration were found to be insignificant.

DISCUSSION

In this study, the mean HbA1c at the beginning was 9.7 and at the end of the study was 8.5 better than the studies conducted in Egypt and Saudi Arabia and is comparable to a study by Deborah A buttler.[9,15,16]

In this study amongst the demographic factors parent education was found to be a significant factor for glycemic control.In the disease related factors frequent home blood glucose monitoring, dietary compliance and regular follow up was associated with a better glycemic control.

Children who had literate parents had a better good glycemic control.Similar results are found in a number of studies.[17,18]In one of these studies significant difference was found in HbA1c of children with educated parents especially if father is educated with professional degree[17]. Good glycemic control was found in another study with educated mothers taking care of diabetic children[18].The reason of a better glycemic control of childrenwith educated parents may because of good record keeping and diabetic knowledge.

Table No.4: Distribution of glycemic control of diabetic patients by significant diseaseassociated factors.

Variables	Glycemic control		Total (n=54)		*P*
	Good (n=18) (%)	Inter-mediate (n=14) (%)	Poor (n=22) (%)		
Blood glucose monitoring frequent % within glycemic control	 12(44.4) 66.7%	 6(22.2) 42.9%	 9(33.3) 42.9%	 27(100) 50.9%	.04
Infrequent % within glycemic control	5(33.3) 27.8%	2(13.3) 14.3%	8(53.3) 38.1%	15(100) 28.3%	
None % within glycemic control	1(9.1) 5.6%	6(54.5) 42.9%	4(36.4) 19.1%	11(100) 20.8%	
Dietary compliance. Good					0.02
% within glycemic control	11(55) 61.1	3(15) 21.4	6(30) 27.3	20 37%	
Fair - %within glycemic control Poor - %within glycemic control	2(15.4) 11.1% 5(23.8) 27.8%	3(23.1) 31.4% 8(38.1) 57.1%	8(61.5) 36.4% 8(38.1) 36.4%	13 24.1% 21 38.9%	
Follow up visit					0.047
Regular %within glycemic control	10(52.6) 55.6%	4(21.1) 28.6%	5(26.3) 22.7%	19 35.2%	
Irregular % within glycemic control	8(22.9) 44.4%	10(28.6) 71.4%	17(48.6) 77.3%	35 64.8%	

At present the safest recommendation for improving glycemic control generally in all children is to achieve the lowest HbA1c that can sustain without disabling or severe hypoglycemia while avoiding prolonged periods of hyperglycemia and episodes of DKA. Frequent glucose monitoring is necessary for these goals to be achieved.[19]The children who had frequent and daily self-monitoring of blood glucose had a lower HbA1c levels similar results were observed in a study reporting that parents monitoring blood glucose frequently and regularly in children had good glycemic control[20].

The nutritional care of patient with diabetes is complex. Diabetes management requires an understanding of the relationship between treatment regimens and changing physiological requirements, including growth, varying nutritional requirement and physical activity. Evidence suggest that it is possible to improve diabetes outcomes through attention to nutritional management and an individualized approach in education[21].Adherence to dietary compliance was associated with lower HbA1c level in this study and by other studies.[21, 22, 23]

The American Diabetes Association proposed guidelines recommending regular visits with a health care provider and glycosylated hemoglobin (HbA1c) testing for good glycemic control and that close monitoring improves management and reduces complications[2]. Consistent with prior studies this study also support that regular follow-up visits were associated with good glycemic control[24,25]. Other studies showed that irregular visits were associated with poor glycemic control[26,27,28].. It is likely that patients with less frequent visits may miss opportunities to receive knowledge and skills needed to perform diabetes self-care, manage crises and to make lifestyle changes to successfully manage the disease[29].

CONCLUSION

This study concluded that parent's education level, regular follow up, dietary compliance, and self-monitoring of blood glucose is associated with better glycemic control in patients with diabetes. Pediatrician need to be aware of factors associated with better glycemic control in children with type 1 diabetes, so that more effective measures can be taken to achieve and maintain control.

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Original Article

Obstructive Sleep Apnea

Mallampatti Score as a Predictor for Risk of Obstructive Sleep Apnea

Tariq Bashir, Saima Javaid Joyia and Iqra Batool

ABSTRACT

Objective: To observe the association of high Mallampatti score with obstructive sleep apnea and to see its predictive value for high risk individuals.

Study Design: A Prospective Cross Sectional Study.

Place and Duration of Study: This study was conducted at the Department of Anaesthesia Bahawal Victoria Hospital Bahawalpur, from July, 2017 to January, 2018.

Materials and Methods: Body mass index was calculated from weight and height. Mallampatti score was evaluated besides Berlin questionnaire, snoring, Epworth sleeping scale. Patients were divided into four groups on the basis of Mallampatti score. Mallampatti score was cross tabulated against snoring grades, Berlin score risk, Epworth score classes and body mass index categories and was compared by applying Chi-square test. SPSS v.23 was used, considering $p \leq 0.05$ statistically significant.

Results: In group III and IV of Mallampatti score, there was significantly more snoring of grade III and grade IV (p=0.043). Mallampatti score difference was not statistically significant among normal, overweight and obese persons (p=0.962). On the basis of Berlin Score risk, the difference was not found to be of any statistical significance (p=0.366). There was a statistically significant increase in Mallampatti score when we moves from class I to class IV of Epworth Sleep Score (p=0.031).

Conclusion: We concluded that high Mallampatti score is greatly interrelated with snoring and high Epworth sleep score. This shows a strong relationship between high Mallampatti score and obstructive sleep apnea. Therefore, Mallampatti score can be used to predict the risk of obstructive sleep apnea.

Key Words: Obstructive Sleep Apnea, Mallampatti Score, Epworth Sleep Score, Berlin Score

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INTRODUCTION

Episodic fractional or complete obstruction of the respiratory tract during sleep characterize a condition called obstructive sleep apnea (OSA). During inspiration, when negative airway pressure exceeds the muscular expanding pressure, airway collapses and obstructive sleep apnea occurs[1,2]. The level of obstruction can be at uvula, above or below it or all the way through upper respiratory tract. There is a positive correlation of obstructive sleep apnea with age and obesity. Obesity is inversely related to the pharyngeal area. The smaller the size of pharynx and upper airway is, the greater the negative pressure develops, considering the equivalent inspiratory stream. There might be some neurogenic base for this disorder [3]. There may be inadequate neuronal drive to the airway dilator muscles or its incoordination with the neuronal drive to the muscles of diaphragm.

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Although obstructive sleep apnea can occur in any stage of sleep, but it happens more during the rapid eye movement sleep. The situation can be improved by applying the nasal continuous airway pressure, as it increases the upper respiratory tract pressure and maintains the airway patency [4].

If there is loss of tone of pharyngeal musculature and fractional collapse of pharynx but it is still able to let the inspired air to move around the epiglottis, tongue or uvula, it will result in the occurrence of hypopnea and snoring. During sleep, the occurrence of hypopnea and apnea is known as sleep-disordered breathing (SDB). Patient awakes from sleep due to increase in the inspiratory exertion and arterial hypercapnia and hypoxemia, as it is necessary to survive the apneic spell. This stimulates the sympathetic nervous system, resulting in pulmonary hypertension and myocardial ischemia, cardiac arrhythmias and sudden death [5]. There may be reflux from the high pressure stomach to the low pressure esophagus. The symptoms of obstructive sleep apnea depend on the individual experience, which includes sleep cycles, airway obstruction, awakening, re-establishment of breathing and again going to sleep. This all leads to the low quality of sleep and increase in sleepiness during the day and early morning headaches, poor work

performance, and increased tendency to work-related and domestic mishaps [6].

Obesity and old age are increasing now a days due to which obstructive sleep apnea incidence is on the rise [10]. In USA, there has been observed a rise in obesity and high body mass index, even in children[7]. Anesthesiologists are especially concerned about this issue because it can lead to excessive perioperative morbidity and mortality [8]. In almost eighty percent of the patients, obstructive sleep apnea is not diagnosed and there is need to be aware of the clinical presentation and symptomatology of obstructive sleep apnea [9]. It can be present in young and apparently healthy persons. Obstructive sleep apnea can be diagnosed clinically in up to sixty percent of the patients but the conformation requires laboratory testing. The pattern of snoring, too much daytime somnolence, observation of sleep apnea and body mass index >35 are very much suggestive of obstructive sleep apnea. The gold standard test to diagnose obstructive sleep apnea is polysomnography. For the identification of high risk patients, likely to develop obstructive sleep apnea, Epworth and Berlin questionnaires have been developed. During general physical examination, high Mallampatti Score was seen in patients presenting with obstructive sleep apnea [10].

Some studies suggested that Mallampatti score could be used independently to assess the risk of obstructive sleep apnea, while some suggested otherwise. Polysomnography is an expensive test and requires overnight stay at the hospital. There is lack of data on the association of Mallampatti score and obstructive sleep apnea. We aim to look for a cost effective way for the diagnosis of obstructive sleep apnea in a developing country like Pakistan.

MATERIALS AND METHODS

It is a prospective questionnaire based study conducted in Department of Anaesthesia Bahawal Victoria Hospital Bahawalpur, from July, 2017 to January, 2018, after taking permission from the Department ethical committee. Sample size was calculated by using the study by Naqvi SU et al[14] as reference. A total of one hundred and thirty four individuals was selected randomly. Medical students, medical staff and old patients of both the genders were part of our study.

Informed consent was obtained from all the participants. Mallampatti score was evaluated besides Berlin questionnaire, snoring, Epworth sleeping scale. Height and weight of every participant was noted to calculate body mass index. Every participant was asked to sit, open the mouth and protrude the tongue, to the maximum extent. The structures visible were noted. No tongue depressor was used. The score was assessed using the modified Mallampatti score. (Table-I)

The patients who had past history of oro-dental surgery and tonsillectomy, acromegaly, facial fractures, epilepsy, cleft lip, cleft palate, dental prosthesis, and children as well as pregnant women were excluded from our study.

Age, gender, weight and height were measured. Body mass index was calculated from weight and height. Patients were divided into four groups on the basis of Mallampatti score. Descriptive data was compared among the groups by ANOVA test. Mallampatti score was cross tabulated against snoring grades, Berlin score risk, Epworth score classes and body mass index categories and was compared by applying Chi-square test. SPSS v.23 was used, considering $p \leq 0.05$ statistically significant.

RESULTS

One hundred and thirty four candidates were recruited in our study. All the candidates were divided into four group on the basis of Mallampatti Score. All four groups were comparable in terms of mean age (p=0.859) and male to female ratio (p=0.323). Mean body mass index was significantly more in Group IV in comparison with other groups (p=0.016). (Table-2)

In group III and IV of Mallampatti score, there was significantly more snoring of grade III and grade IV (p=0.043). Mallampatti score difference was not statistically significant among normal, overweight and obese persons (p=0.962). On the basis of Berlin Score risk, the comparison was done between low risk and high risk candidates and the difference was not found to be of any statistical significance (p=0.366). There was a statistically significant increase in Mallampatti score when we moves from class I to class IV of Epworth Sleep Score (p=0.031). (Table-3).

Table No.1: Modified Mallampatti Score

Class	Structures Visible
I	Hard Palate, Soft Palate, Uvula, Fauces, Pillars
II	Hard Palate, Soft Palate, Uvula, Fauces
III	Hard Palate, Soft Palate, Base of Uvula
IV	Only Hard Palate

Table No.2: Baseline Characteristics of Four Mallampatti Score Groups

Variable	I (n=37)	II (n=42)	III (n=30)	IV (n=25)	p-value
Age (years)	41.05 ±8.85	39.71±8.87	39.40±8.31	40.12±7.33	0.859
Male	15 (40.54)	25 (59.62)	13 (43.33)	11 (44)	0.323
BMI (kg/m^2)	23.24 ±2.91	23.71±2.72	24.57±3.63	26.12±5.49	0.016

Variables are **mentioned** as Mean ± S.D or Number (Percentage); BMI=Body Mass Index; Chi-Square test and ANOVA test applied.

Table No.3: Comparison of Mallampatti Score and other General Characteristics of the Candidates

	Mallampatti Score				
Snoring	**I(n=37)**	**II(n=42)**	**III(n=30)**	**IV(n=25)**	**p-value**
I	12 (32.4)	12 (28.6)	8 (26.7)	6 (24)	0.043
II	13 (35.1)	15 (35.7)	4 (13.3)	3 (12)	
III	6 (16.2)	11 (26.2)	14 (46.7)	8 (32)	
IV	6 (16.2)	4 (9.5)	4 (13.3)	8 (32)	
BMI, Kg/m^2					
Normal	15 (40.5)	13 (30.9)	10 (33.3)	7 (28)	0.962
Over weight	11 (29.7)	13 (30.9)	9 (30)	8 (32)	
Obese	11 (29.7)	16 (38.1)	11 (36.7)	10 (40)	
Berlin Score Risk					
High Risk	10 (27)	12 (28.6)	7 (23.3)	11 (44)	0.366
Low Risk	27 (73)	30 (71.4)	23 (76.7)	14 (56)	
Epworth Sleep Score					
I	20 (54)	15 (35.7)	8 (26.7)	3 (12)	0.031
II	7 (18.9)	14 (33.3)	7 (23.3)	5 (20)	
III	5 (13.5)	6 (14.3)	8 (26.7)	9 (36)	
IV	5 (13.5)	7 (16.6)	7 (23.3)	8 (32)	

Variables are mentioned as Number (Percentage); BMI=Body Mass Index; Chi-Square test was applied.

DISCUSSION

Out of one hundred and thirty four individuals, forty five were of normal body mass index, forty one were overweight and forty eight were obese. The difference in the Mallampatti score was not any different in all these groups. However, there was significant snoring in the patients who had high mallampatti score. Snoring is caused by partial upper airway obstruction, this shows that the obstructive sleep apnea is more likely to develop in people with high Mallampatti score. Sleep apnea score was also significantly high in high Mallampatti score class, as observed by Epworth Sleep Scale. This all shows that the patients who had high mallampatti score were at greater risk of developing obstructive sleep apnea. Berlin score was not associated with any risk of obstructive sleep apnea or high Mallampatti score. Females were more in number in high mallampatti score class but the difference was not statistically significant in between both the genders.

The relationship of berlin score with obstructed sleep apnea was studied by Thurtell MJ et al.[10] and they found it to be statistically significant. For emergency screening, Berlin score questionnaire and Epworth sleep scale are very important parameters[11]. A quick idea about the condition of the patient can be made before any emergency intervention requiring anesthesia. A study conducted by Lee SJ et al.[12] showed that the Epworth sleep scale was 93.4% sensitive and is a useful scale to assess the risk of obstructive sleep apnea.

In contrast to current study, Bins S. et al[13] conducted a study in 2011 and put forth the conclusion that Mallampatti score was no significant enough to be used for the prediction of risk of obstructive sleep apnea syndrome. A few surveys, which were conducted after this time, opposed the results of above mentioned study. Naqvi SU et al[14] conducted a study in 2016 which was published in 2018. It was observed in that study that the Berlin score risk and Epworth sleep scale score was negatively associated with high Mallampatti score. But Mallampatti score was significant to rule out obstructive sleep apnea in low risk category patients of Berlin Score and Epworth sleep scale score. However, there was positive association of high Mallampatti score and snoring. Body mass index did not significantly affect the Mallampatti score.

Barceló X et al[15] in their study showed the modified Mallampatti score was useful in assessing the severity of obstructive sleep apnea syndrome, which can be estimated by simple oral examination. A positive predictive value of Mallampatti score was observed in a study by Myers KA et al[16] and it was 9.3. Rodrigues MM[17] studied 168 patients. All of these patients had undergone polysomnography test. When their modified Mallampatti score was plotted against obstructive sleep apnea score, there was strong association between high mallampatti score along with nasal obstruction and obstructive sleep apnea syndrome. However, nasal obstruction alone was not significantly associated with high mallampatti score.

CONCLUSION

We concluded that high Mallampatti score is greatly interrelated with snoring and high Epworth sleep score. This shows a strong relationship between high Mallampatti score and obstructive sleep apnea. Therefore, Mallampatti score can be used to predict the risk of obstructive sleep apnea**.**

Author's Contribution:

Concept & Design of Study:	Tariq Bashir
Drafting:	Saima Javaid Joyia
Data Analysis:	Iqra Batool
Revisiting Critically:	Tariq Bashir, Saima Javaid Joyia
Final Approval of version:	Tariq Bashir

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

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Original Article

Comparison of 2% Lignocaine with 50% Magnesium Sulfate in Reducing the Hemodynamic Stress Responses to Laryngoscopy and Endotracheal Intubation

Saima Javaid Joyia, Tariq Bashir and Iqra Batool

ABSTRACT

Objective: The comparison of 2% lignocaine with 50% magnesium sulfate in reducing the hemodynamic stress responses to laryngoscopy and endotracheal intubation in ASA (American Society of Anesthesiologists) grade I and II patients.

Study Design: A randomized control trail.

Place and Duration of Study: This study was conducted at the Anaesthesia department of Bahawal Victoria Hospital, Bahawalpur from July, 2017 to December, 2017.

Materials and Methods: Ninety two patients were divided randomly into two equal groups, Group-L for lignocaine and Group-M for magnesium sulfate. Age and weight of every patient was documented. Heart rate, systolic and diastolic blood pressures and mean arterial pressure were recorded before and after pre-medication, after injecting the drugs under study and at 1, 3 and 5 minutes after intubation. Variables were compared between the two groups and t-test was applied. SPSS v.23 was used to analyze the data. P value was taken as ≤ 0.05.

Results: The mean heart rate was significantly high in group-L at 1 minute ($p=0.006$), 3 minute ($p=<0.001$) and 5 minute ($p<0.001$) after the intubation. Mean systolic blood pressure, diastolic blood pressure and mean arterial pressure were also high in group-L at 1 minute, 3 minute and 5 minute after the intubation with statistically significant difference ($p<0.001$).

Conclusion: It was hereby concluded that significantly better and well-sustained control over hemodynamic stress responses to laryngoscopy as well as tracheal intubation, is obtained by the use of magnesium sulfate, as compare to lignocaine. This shows that magnesium sulfate is superior to lignocaine in offsetting the hemodynamic stress responses to laryngoscopy as well as endotracheal intubation.

Key words: 2% Lignocaine, 50% magnesium sulfate, hemodynamic, stress responses, laryngoscopy, endotracheal intubation

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INTRODUCTION

It is very well recognized fact that laryngoscopy and endotracheal intubation trigger the hemodynamic response by the activation of sympathetic nervous system, in the form of increased heart rate and raised blood pressure. This response is mediated by the enormous release of epinephrine and nor-epinephrine. Somatic as well as visceral somatic afferents of pharynx, epiglottis, larynx, peritracheal area, vocal cords and hypopharynx are stimulated by the laryngoscopy [1] and endotracheal intubation and the results are the occurrence of many cardiovascular as well as cerebrovascular hemodynamic responses such as raised blood pressure, intracranial pressure, intraocular pressure, increase in heart rate, dysrhythmias, cardiac asystole and sudden death [2-4]. In the patients who are elderly, or suffering from cerebrovascular diseases, cerebral aneurysms, ischemic heart disease, hypertension and diabetes mellitus, these responses can be excessively harmful, leading to increase in morbidity and mortality [5]. This problem was highlighted for the first time by King et al. [6] in the year 1951. Since then, many techniques have been tried to mitigate these unwanted hemodynamic reactions, which include the use of vasodilators such as nitroglycerin [7], topical or intravenous lidocaine [8,10], magnesium [8], beta-blocker drugs such as esmolol [9], calcium channel blockers [9,10], opiates in large doses especially alfentanil and fentanyl [11] and gabapentin. All of these techniques work either by reducing the input stimuli or by blocking the adrenergic responses. There is no direct blockade of

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release of catecholamines and these procedures have drawbacks of cardiovascular and respiratory depression. Lignocaine is the most commonly used drug to mitigate the stress responses which occur during and after laryngoscopy and endotracheal intubation. It is an aminoethylamide and belongs to the amide group of local anesthetics. It acts via membrane stabilization, due to which it is also used frequently as an anti-arrhythmic agent n patients having ventricular ectopics. When given intravenously, lignocaine has the ability to reduce the pressor response to laryngoscopy and endotracheal intubation 12. Sufficient effects of lignocaine on pressor response have been observed at an intravenous of 1.5mg/kg body weight. It is also used to perform nerve blocks and to control ventricular tachycardia. The commonly encountered side effects of lignocaine are arrhythmias, bradycardia, hypotension, raised defibrillator threshold, respiratory depression, venous insufficiency, flushing, nausea, vomiting, urticaria, angioedema and visual disturbances.

In the human body, magnesium is the fourth most common cation and it activates many enzyme systems. Magnesium sulfate impedes the discharge of epinephrine and nor-epinephrine from the adrenal medulla as well as adrenergic nerve endings. It is very effective in decreasing the hemodynamic responses to laryngoscopy and the tracheal intubation [13]. Different researchers have found different doses to be effective in obtaining the desired results. Magnesium sulfate at a dose of 50mg/kg body weight can prevent the pressor response to the laryngoscopy and the tracheal intubation, when administered before the procedure. This agent is known to cause a few cardiovascular adverse effects. Magnesium sulfate causes respiratory depression and has the ability to aggravate the effect of non-depolarizing neuromuscular blocking agents.

Lignocaine, to attenuate the pressor effects of intubation and laryngoscopy, has been studied for long but the use of magnesium sulfate in this respect has been studied very poorly. Current study is aimed as comparing the efficacy of 2% lignocaine and 50% magnesium sulfate in decreasing the hemodynamic reactions occurring during laryngoscopy as well as endotracheal intubation required for general anesthesia.

MATERIALS AND METHODS

It is a randomized control trail. After attaining the approval from the Department ethical committee, total of ninety two patients of ASA (American society of Anesthesiologists) grade I and II were selected and written informed consent was obtained. The data was collected from July, 2017 to December, 2017 in the Anaesthesia department of Bahawal Victoria Hospital, Bahawalpur. Sample size was calculated after taking the study by Padmawar S. [8] as our reference research and was selected by applying the non-probability consecutive sampling technique. The patients who were planned to undergo planned surgical procedure requiring general anesthesia or laryngoscopy were included in the study.

Ninety two patients were divided randomly into two equal groups, Group-L for lignocaine and Group-M for magnesium sulfate, each consisting of forty six patients with equal male to female ratio. Age and weight of every patient was documented. Complete history, examination and related investigation were performed prior to the induction of anesthesia. We excluded those patients from our study who were having electrolyte imbalance, preeclampsia, eclampsia, neuromuscular diseases, arrhythmias, ischemic heart disease, cerebrovascular conditions, allergic to drugs, already on magnesium sulfate, requiring longer than thirty seconds or multiple attempts for laryngoscopy. Inside the operation theatre, the devices to monitor heart rate, non-invasive blood pressure, and SpO2 were attached to the patients. The baseline heart rate, systolic and diastolic blood pressures and mean arterial pressure were recorded before any type of pre-medication. Wide bore intravenous lines were secured and intravenous infusion of ringers lactate was started. Pre-medication included 0.3mg/kg dose of pentazocine, 0.03mg/kg dose of midazolam, 1mg/kg of ranitidine and 0.2mg/kg of metoclopramide. All the patients were injected with these agents intravenously, ten minutes before inducing the anesthesia. Pre-oxygenation was performed with 100% oxygen for a minimum of 3 minutes. Heart rate, systolic and diastolic blood pressures and mean arterial pressure were recorded after pre-medication. Lignocaine injection at a dose of 1.5mg/kg body weight was given to group-L, intravenously. Group-M received a 40mg/kg dose of magnesium sulfate as an intravenous injection. Heart rate, systolic and diastolic blood pressures and mean arterial pressure were recorded, again. Propofol was used to induce anesthesia which was followed by succinylcholine injection to ease the endotracheal intubation. Cuffed endotracheal tube was used in all the patients and the process of intubation was completed in less than 30 seconds. Vecuronium bromide was used to maintain muscle relaxation. Heart rate, systolic and diastolic blood pressures and mean arterial pressure were recorded at one minute, three minutes and five minutes after the intubation and other surgical interpolations such as incision and catheterization were performed after recording the data. At the end of surgery, the patients were sifted to the recovery room after extubation and were monitored for at least half an hour.

Age, weight, heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure was compared between the two groups and t-test was applied. SPSS v.23 was used to analyze the data. Confidence interval was taken as 95%.

RESULTS

Ninety two patients were divided into two equal groups, having male to female ratio of 33:13, each. Both the groups were comparable in terms of age (42.09±6.86 years of group-L and 42.59±6.97 years of group-M) and weight (49.22±6.27Kg of group-L and 50.06±6.05Kg of group-M) with a p-value of 0.730 and 0.511, respectively. (Table-I)

Before and after the premedication the observed heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure was not significantly different in between both the groups. Just after administering the drugs under study, there was a significant rise in heart rate (p=0.007) and systolic blood pressure (p=0.017) in the group receiving Magnesium sulfate. Diastolic blood pressure and mean arterial pressure did not alter significantly (p-value 0.590 and 0.351, respectively). (Table-II)

The mean heart rate 1 minute, 3 minute and 5 minute after the intubation was 104.76±12.63 beats /min and 97.76±11.39 beats /min (p=0.006); 102.09±10.79 beats /min and 91.80±8.87 beats /min (p<0.001); and 93.13±10.07 beats /min and 86.21±5.05 beats /min (p<0.001) in group-L and Group-M, respectively. Mean systolic blood pressure 1 minute, 3 minute and 5 minute after the intubation was 133.59±6.91mmHg and 120.83±8.68 mmHg (p<0.001); 129.48±7.18 mmHg and 115.63±4.70 mmHg (p<0.001); and 123.19±9.55 mmHg and 115.96±4.43mmHg in group-L and Group-M, respectively. The difference was statistically significant. Mean diastolic blood pressure 1 minute, 3 minute and 5 minute after the intubation was 90.50±5.80 mmHg and 83.67±7.70 mmHg (p<0.001); 87.50±8.17 mmHg and 76.48±4.22 mmHg (p<0.001); and 83.24±6.54 mmHg and 78.28±4.62 mmHg (p<0.001) in group-L and Group-M, respectively. Similar trend was seen in mean arterial pressure 1 minute, 3 minute and 5 minute after the intubation with p<0.001 at every time. (Table-2)

Table No.1: Demographic Details

Variable	Group-L	Group-M	p-value
Age	42.09±6.86	42.59±6.97	0.730
weight	49.22±6.27	50.06±6.05	0.511
Male: Female	33:13	33:13	

Data are mentioned as Mean ± S.D or Number

Table No.2: Comparison of Observed Parameters between Two Groups

Variable	Groups	Before Premedication	After Premedication	After the Drug	1 minute after Intubation	3 minutes after Intubation	5 minutes after Intubation
Heart Rate (Beats/ min)	Group-L	84.15±6.07	81.41±6.96	82.28±6.40	104.76±12.63	102.09±10.79	93.13±10.07
	Group-M	86.22±5.05	80.61±7.18	86.15±7.03	97.76±11.39	91.80±8.87	86.21±5.05
	p-value	0.079	0.587	0.007	0.006	<0.001	<0.001
Systolic Blood Pressure (mmHg)	Group-L	117.06±3.73	112.43±3.28	110.61±5.26	133.59±6.91	129.48±7.18	123.19±9.55
	Group-M	116.17±5.20	111.80±4.87	113.24±5.06	120.83±8.68	115.63±4.70	115.96±4.43
	p-value	0.348	0.469	0.017	<0.001	<0.001	<0.001
Diastolic Blood Pressure (mmHg)	Group-L	75.84±5.76	74.43±4.55	76.37±4.48	90.50±5.80	87.50±8.17	83.24±6.54
	Group-M	76.78±4.65	75.39±3.47	75.91±3.55	83.67±7.70	76.48±4.22	78.28±4.62
	p-value	0.394	0.260	0.590	<0.001	<0.001	<0.001
Mean Arterial Pressure (mmHg)	Group-L	79.80±3.37	77.41±4.48	79.63±4.06	95.28±5.08	92.24±7.36	86.22±5.64
	Group-M	80.69±3.75	76.89±4.04	80.46±4.38	89.50±5.04	83.17±3.61	80.89±5.37
	p-value	0.234	0.559	0.351	<0.001	<0.001	<0.001

Data are mentioned as Mean ± S.D

DISCUSSION

We witnessed in the current study that there was a rise in heart rate and blood pressure levels when the patients were intubated but the rise was significant in the group which was given lignocaine. The blood pressure level and heart rate in the magnesium sulfate group were relatively much stable and returned to the baseline levels five minutes after the intubation. Similar results were seen in the study conducted by Padmawar S et al 8. They also observed that magnesium sulfate effectively controlled the fluctuations in the heart rate and blood pressure as compared to lignocaine. Also there was some change in the hemodynamics in the group which received magnesium sulfate but it was very mild and returned to the baseline quickly.

Kiaee MM et al. [14] compared the efficacy of both these drugs in the patients who were undergoing elective coronary artery bypass graft. They observed that lidocaine (lignocaine) caused hemodynamic instability in the patents while magnesium sulfate improved the hemodynamic status. When lignocaine was compared

with other drugs such as dexamethasone and esmolol, there was no effect of lignocaine over the stress responses and increase in heart rate, blood pressure and mean arterial pressure was observed [15,16]. Kord Valeshabad A. et al.[17] also observed in his study that a significant rise in heart rate and mean arterial pressure is seen in patients receiving lidocaine. They compared the effects of lidocaine against propacetamol.

Hirmanpour A. et al [18] observed in pregnant women that 60mg/kg dose of magnesium sulfate, when given intravenously at the time of induction of anesthesia, was sufficient to minimize the hemodynamic variations occurring after laryngoscopy and endotracheal intubation. Kotwani MB et al. [19] concluded in their study that a 30mg/kg dose of magnesium sulfate was adequate to attenuate the hemodynamic variations but higher doses were associated transitory tachycardia. Honarmand A. [20] concluded from his study that different doses of magnesium sulfate (30mg/kg, 40mg/kg, and 50mg/kg) were equal in efficacy when used to control the hemodynamic changes following laryngoscopy and endotracheal intubation. There witnessed no significant effect over the heart rate fluctuations.

CONCLUSION

It is hereby concluded that significantly better and well-sustained control over hemodynamic stress responses to laryngoscopy as well as tracheal intubation, is obtained by the use of magnesium sulfate, as contrast with lignocaine. This shows that magnesium sulfate is superior to lignocaine in offsetting the hemodynamic stress responses to laryngoscopy as well as endotracheal intubation.

Author's Contribution:

Concept & Design of Study:	Saima Javaid Joyia
Drafting:	Tariq Bashir
Data Analysis:	Iqra Batool
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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

Whether Hematological Parameters are Predictor of Pregnancy Induced Hypertension

Afshan Rasheed[1], Muhammad Ali Mahota[2] and M Asif[2]

ABSTRACT

Objective: To find role of hematological parameters in predicting hypertension in pregnant women.
Study Design: Case control study.
Place and Duration of Study: Department of Gynecology and Obstetrics, Nishtar Hospital Multan from October 2017 to January 2018.
Materials and Methods: The sample size of this study was 125 patients. They were divided in three groups as 60 patients in pre-eclamptic group, 20 patients in severely pre-eclamptic and 45 pregnant women in control group. . One way ANOVA was used to calculate mean and standard deviation of given data. In all the statistical calculation, the p value of ≤ 0.05 was considered to be significant.
Results: A total number of 125 patients were included in this study. All the pregnant women were divided into three groups. 48% (n=60) pregnant women were in pre-eclamptic group, 16% (n= 20) women in severe pre-eclamptic group and 36% (n=45) pregnant women were in control group. In pre-eclamptic group, the mean cell value, mean cell Haemoglobin, mean cell Haemoglobin concentration, RBC distribution width, mean platelet value and MPV / platelet count was 82.62±4.99, 27.52±2.68, 34.12±1.85,14.22±2.30, 225.96±36.50, 8.9±1.03 and 0.0415±0.018 respectively. In severe pre-eclamptic group, the mean cell value, mean cell Haemoglobin, mean cell Haemoglobin concentration, RBC distribution width, mean platelet value and MPV / platelet count was 83.67±9.43, 29.63±2.81,34.20±0.83,15.02±2.89, 9.15±1.23 and 0.0481±0.010 respectively. When pre-eclamptic and severely pre-eclamptic patients were compared with control group, the difference was statistically insignificant according to CBC, platelet count, and MPV.
Conclusion: From this study, we have concluded that hematological parameters like CBC, platelet count and mean platelet volume (MPV) values are not predictor of pregnancy induced hypertension.

Key Words: Hematological parameters, pregnant women, Pre-eclampsia, hypertension

Citation of articles: Rasheed A, Mahota MA, Asif M. Whether Hematological Parameters are Predictor of Pregnancy Induced Hypertension. Med Forum 2018;29(4):56-59.

INTRODUCTION

Pre-eclampsia is multisystem, heterogeneous disorder characterized by onset of proteinuria, peripheral oedema and hypertension that usually arises in third trimester of gestation period. It influences almost 3-6% of pregnant women worldwide[1]. It is highly related to intrauterine growth restriction, Preterm delivery, Placental abruption and perinatal mortality. It also affects maternal mortality and morbidity[2]. Hypertension may cause raise of intraocular pressure and visual abnormalities. It also causes abnormality of maternal-fetal vascular interface in the placenta and it could only be resolved by delivery[3,4].

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Seizures associated with Pre-eclampsia leads to onset of Eclampsia[5,6]. It is also associated with HELLP syndrome and pre-eclamptic liver dysfunction. Hypertension, oliguria, Edema, proteinuria and seizures all characteristics of pre-eclampsia and severe pre-eclampsia, they often cause intrauterine growth retardation, perinatal mortality, mental abnormalities, placental abruption and preterm delivery of baby[7,8]. There is very little knowledge about the pathophysiological mechanism of pre-eclampsia but its association with hematological parameters like platelet count, complete blood count (CBC), white blood cells (WBCs), hemoglobin and hematocrit has been explained in many past studies[9]. A clinical trial by T Ceyhan at el; in which they have observed blood pressure, platelet count, CBC and mean platelet volume of mild pre-eclamptic, severe pre-eclamptic and normotensive pregnant women. They wanted to find that lowered platelet count has any indication of hypertension in pregnant women. But they had not found any significant difference in platelet count in normotensive and pre-eclamptic women[10].

There is no local study to find out that low platelet count and other CBC parameters are indication of hypertension in pregnant women. So, this clinical trial was organized to find low platelet count in pregnant women.

MATERIALS AND METHODS

This case control study was organized in Department of Gynecology and Obstetrics, Nishtar Hospital Multan from October 2017 to January 2018. The ethical approval was granted by department and informed consent was taken from all patients before start of the study. The sample size of this study was 125 patients. They were divided in three groups as 60 patients in pre-eclamptic group, 20 patients in severely pre-eclamptic and 45 pregnant women in control group. Pregnant women who were suffering from blood pressure over baseline > 140/90 mmHg with or without proteinuria after 20 weeks of gestation period were in inclusion criteria. Those pregnant women who had previous history of Diabetes, hypertension, ITP, renal diseases, pheochromocytoma, and hepatic diseases during non-pregnant state were in exclusion criteria.

Complete medical history of all patients was recorded and it was normal. Blood pressure was recorded in sitting position. Blood pressure of all pregnant women was regularly measured after every 2 weeks throughout pregnancy. All the definitions and measurements used in this study were all according to International Society for the Study of Hypertension in Pregnancy[11]. The pregnancy was defined as normal in which a normotensive woman having no proteinuria delivered a normal weight healthy neonate after 36 weeks of complete gestation period. It was mentioned as pre-eclampsia in which patient had hypertension (blood pressure of 145/95 mmHg or more for 5 hours) and continuous proteinuria (350 mg/ day). Severe pre-eclampsia was defined as: 1) Blood pressure > 160mmHg systolic or >11o mmHg diastolic on different occasion a persistent for 6 hours. 2) Significant proteinuria (>5 + on dipstick random sample)

3) Oliguria having urinary output > 450 mg/day. In addition to this, any patient was suffering from Cyanosis, pulmonary edema, visual and cerebral disturbance, thrombocytopenia; liver dysfunction was included in severe pre-eclampsia. Automated blood counter Cell-Dyn 4000 was used to measure and calculate all parameters of CBC.

All the data was recorded and analyzed by using computer software SPSS version 20. One way ANOVA was used to calculate mean and standard deviation of given data. In all the statistical calculation, the p value of < 0.05 was considered to be significant.

RESULTS

A total number of 125 patients were included in this study. All the pregnant women were divided into three groups. 48%(n=60) pregnant women were in pre-eclamptic group, 16% (n= 20) women in severe pre-eclamptic group and 36% (n=45) pregnant women were in control group. In pre-eclamptic group, the mean cell value, mean cell Haemoglobin, mean cell Haemoglobin concentration, RBC distribution width, mean platelet value and MPV / platelet count was82.62±4.99, 27.52±2.68, 34.12±1.85,14.22±2.30, 225.96±36.50, 8.9±1.03 and 0.0415±0.018 respectively. In severe pre-eclamptic group, the mean cell value, mean cell Haemoglobin, mean cell Haemoglobin concentration, RBC distribution width, mean platelet value and MPV / platelet count was 83.67±9.43,29.63±2.81,34.20±0.83, 15.02±2.89, 9.15±1.23 and 0.0481±0.010 respectively. When pre-eclamptic and severely pre-eclamptic patients were compared with control group, the difference was statistically insignificant according to CBC, platelet count, and MPV. That had been shown in (Table No. 1).

Table No. 1: CBC Parameters of Pre-eclamptic, Severely Pre-eclamptic and control cases

Parameters	**Pre-eclamptic (n=60)**	**Severely Pre-eclamptic (n=20)**	**Control (n=45)**	**P-value**
Age (years)	31.31±6.69	24.84±4.36	27.75±3.32	0.000
White blood cell	10.09±2.0	14.77±4.19	10.59±2.93	0.091
Red blood cell	4.49±0.20	3.89±0.49	4.27±0.39	0.167
Haemoglobin	11.07±2.08	11.10±1.19	11.91±0.977	0.090
Haematocrit	34.33±3.83	32.80±2.57	35.78±3.01	0.101
Mean cell value	82.62±4.99	83.67±9.43	83.96±3.40	0.483
Mean cell Haemoglobin	27.52±2.68	29.63±2.81	28.64±2.03	0.324
Mean cell Haemoglobin concentration	34.12±1.85	34.20±0.83	34.07±0.83	0.936
Red cell distribution width	14.22±2.30	15.02±2.89	14.26±2.22	0.347
Platelet	225.96±36.50	207.95±68.03	225.10±50.16	0.269
MPV	8.9±1.03	9.15±1.23	9.88±1.34	0.389
MPV/PLT	0.0415±0.018	0.0481±0.010	0.0602±0.00319	0.196

DISCUSSION

Pregnancy induced hypertension (PIH) is one of the main causes of maternal death all around the world. It is highly related with intrauterine fetal death (IUD) and intrauterine growth retardation (IUGR).There are still no hematological parameters to predict PIH that leading to IUD and IUGR[12].

A study by Makuyana et al; that showed no significant differences of CBC parameters and platelet count between normotensive and pre-eclamptic pregnant women[13]. Platelet count, Haemoglobin level, WBC and mean cell volume of 72 normotensive and 38 pre-eclamptic women were same. The results of above mention study are completely similar to our results.

Neiger at el[14]; they had stated that they observed the significant different between CBC parameter and platelet count of pre-eclamptic women and control group. In their study normal non pregnant healthy women were in their control group. But they also reported that there was no difference of platelet count, WBC and Haemoglobin in mild and severe pre-eclamptic women. So, in our study we have concerned about platelet count only. That is same in mild and severe pre-eclamptic women.

Jaremo et al, had reported that elevate mean plasma value (MPV) and lowered platelet count was observed in pre-eclamptic women[15]. But in our study such lowered platelet count was not significant.

Boriboonhirunsarn et al; had declared that elevated MPV value is very important to differentiate between normotensive and pre-eclamptic pregnancy[16]. But we did not find any significant difference in MPV in our study. Von Dadelszen et al; they explained that MPV and platelet count ratio is very useful indicator of maternal health in pre-eclamptic women[17]. But, Calvert et al; have reported that MPV and platelet count are not useful indicator in clinical progress of 336 women[18]. Similarly, in our study, no significant difference was observed in MPV and platelet count between mild and severe pre-eclamptic women. There is another very important study by Temel Ceyhan et al; this study explains that there is no significant difference of CBC parameters and platelet count between mild, severe pre-eclamptic and normotensive pregnant women[10].

A study by Edelstam G et al, in which they had specified the platelet count and other CBC parameters in all non-pregnant and pregnant women[19]. They had compared the CBC values and platelet count of pregnant women with men and non-pregnant women. There was great difference in many CBC parameters between pregnant women blood sample and non-pregnant women. During pregnancy the WBC (white blood cell count) was increased, platelet count was reduced during third trimester and hemoglobin level was decreased. The results of their study are according to our results. Due to this reason, we have pregnant women in our control group instead of normal non pregnant women.

A study conducted in India by DIPTI Mohapatra et al, to find association of hematological parameters with pregnancy induced hypertension. This study reported that increased thrombocytopenia had been observed during moderate and severe pre-eclampsia than normotensive pregnant women[7].

Dominique Mannaerts et al, reported in their study that mean platelet value (MPV) raised in pregnant women suffering from moderate ad severe pre-eclampsia[20]. All the above studies explain that CBC parameters and platelet count do not show any significant difference in normotensive and pre-eclamptic pregnant women. So, platelet count, mean platelet volume (MPV) and CBC parameters do not help to indicate about hypertension in pregnant women.

CONCLUSION

From this study, we have concluded that hematological parameters like CBC, platelet count and mean platelet volume (MPV) values are not predictor of pregnancy induced hypertension.

Author's Contribution:

Concept & Design of Study:	Afshan Rasheed
Drafting:	Muhammad Ali Mahota
Data Analysis:	M Asif
Revisiting Critically:	Afshan Rasheed, Muhammad Ali Mahota
Final Approval of version:	Afshan Rasheed

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

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Original Article

Atrial Fibrillation

Frequency of Atrial Fibrillation and its Common Clinical Outcomes among Patients Presenting with Acute Myocardial Infarction

Muhammad Inam Qureshi[1], Afzal Qasim[2], Nadeemuddin[3] and Muhammad Umar Khan[4]

ABSTRACT

Objective: To determine the outcome of acute myocardial infarction associated with a trial fibrillation.
Study Design: Observational study.
Place and Duration of Study: This study was conducted at the Karachi Institute of Heart Diseases and Dow University Hospital OJHA Campus Karachi, from July 2017 to December 2017.
Materials and Methods: 311 patients aged >30 years, both gender presented with acute myocardial infarction were included in the study through Outpatient department or Emergency Room. Hospital admitted patients to CCU due to acute myocardial infarction (ST elevation MI and Non ST elevation MI) were also included. Patients with severe comorbid conditions like malignancies, renal failure, COPD, or decompensated liver cirrhosis, patients already on treatment on ventricular dysfunction, AF, stroke were excluded from this study.
Results: Out of 311 patients, 203(65.27%) were having STEMI, and 108(34.72%) patients were admitted with NSTEMI. Atrial Fibrillation was found in 38 (12.21%) patients. The most common clinical outcome in patients with AF was Ventricular Fibrillation, followed by Ventricular Tachycardia (VT), patients death and stroke. Among 3 patients who died, 6(15.78%) patients had VF and 4(10.52%) patient had stroke, so clinical outcome occurred in 19 out of 38 patients who developed AF.
Conclusion: Rate control therapy and oral anti coagulants should be offered to patients at risk for development of atrial fibrillation, This can result in significant reduction of mortality.
Key Words: Atrial fibrillation, Acute Myocardial Infarction, STEMI, NSTEMI

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INTRODUCTION

Atrial fibrillation is the most common arrhythmia found in patients with acute myocardial infarction. The predominant cause for development of atrial fibrillation includes myocardial ischemia. Some other causes can include hemodynamic disturbances, pericarditis, left ventricular dysfunction and catecholamine surge[1]. A population-based study showed that Atrial fibrillation status in acute myocardial ischemia usually increases by 13.3% over the last ten years. Atrial fibrillation between acute myocardial ischemia has a serious impact on the clinic and disease prediction[2].

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Atrial fibrillation was found at 10.4-12% of cases with acute myocardial ischemia treated with thrombolytics or primary percutaneous interventions, with higher levels of risk of LV dysfunction [3].

It has been estimated that atrial fibrillation complicates around 6-21% of acute myocardial infarction. It is associated with higher in hospital mortality (13.8 vs 5.8%). The development of ventricular fibrillation and ventricular tachycardia are also more evident among patients who experienced atrial fibrillation compared to those with sinus rhythm (14.7%,14.8% vs 5.8%, 5.2%). There is an increased risk of subsequent stroke among these patients (9.2% vs 2.6%) [4].

The cause for development of atrial fibrillation is ischemia however during the arrhythmia the blood supply to the myocardium is further compromised leading to devastating outcomes . The associated loss of atrial contraction leads to reduced stroke volume and subsequent elevation of filling pressures with atrial dilation[5]. Atrial fibrillation alone is an independent risk factor for adverse clinical outcomes among patients with myocardial infarction. It can further precipitate tachyarrhythmias due to further loss of blood supply, varying R-R intervals. Atrial fibrillation can also be associated with activation of sympathetic nervous system[6,7].

Some other predictors for development of atrial fibrillation after myocardial infarction include advanced heart failure (as demonstrated by Killip Class), advanced age (>65), elevated heart rate at presentation, no history for use of beta blockers or thrombolytic therapy in the past [8].

MATERIALS AND METHODS

This study was carried out at Karachi Institute of Heart Diseases and Dow University Hospital OJHA Campus Karachi, from July 2017 to December 2017. Patients aged >30 years, both gender present with acute myocardial infarction were included in the study through Outpatient department or Emergency Room. Hospital admitted patients to CCU due to acute myocardial infarction (ST elevation MI and Non ST elevation MI) were also included. Patients with severe comorbid conditions like malignancies, renal failure, COPD, or decompensated liver cirrhosis, patients already on treatment on ventricular dysfunction, AF, stroke were excluded from this study.

RESULTS

A total of 311 patients with acute myocardial infarction were enrolled in this study. There were 188(60.45%) male and 123(39.54%) female patients. Out of 311 patients, 203(65.27%) were having STEMI, and 108(34.72%) patients were admitted with NSTEMI (Table No.1).

Atrial Fibrillation was found in 38 (12.21%) patients. Among these 38 patients12 were male, and 26 were female. The age of the study population ranged from 30 years to 71 years, with mean age of the patients was 51.12±6.21 years. The most common clinical outcome in patients with AF was Ventricular Fibrillation, followed by Ventricular Tachycardia (VT), patients death and stroke. Among 3 patients who died, 6(15.78%) patients had VF and 4(10.52%) patient had stroke, so clinical outcome occurred in 19 out of 38 patients who developed AF (Chart No.1).

Table No.1: Clinical outcome of patients

Variable	Patients	Percentage
Age groups (n=311)		
31 – 40 years	65	20.90%
41 – 50 years	88	28.29%
51 – 60 years	109	35.04%
> 60 years	49	15.72%
Gender (n=311)		
Male	188	60.45%
Female	123	39.54%
STEMI and NSTEMI		
STEMI	203	65.27%
NSTEMI	108	34.72%

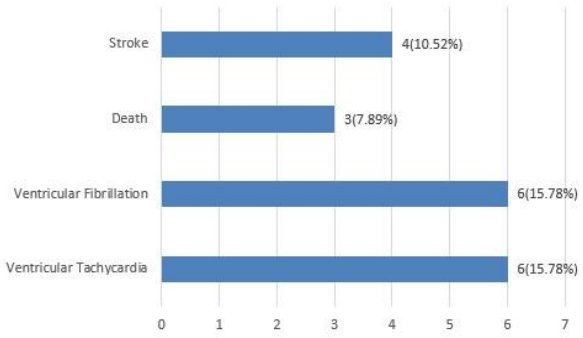

Chart No.1: Clinical outcome of acute myocardial infarction with Atrial Fibrillation (n=38)

DISCUSSION

There are various predictors of atrial fibrillation in patients with acute myocardial infarction. Some of them include advanced age, presence of heart failure and inadequate left ventricular function[4]. Studies predicting in-hospital mortality have suggested that development of atrial fibrillation among patients with acute myocardial infarction is an independent predictor of mortality. This can be explained as atrial fibrillation can be described as a demonstrator of heart failure. Atrial fibrillation can also represent elevated filling pressures or volume overload. Similarly lone AF is not associated with mortality and morbidity due to the absence of these markers[9].

Atrial fibrillation can also trigger other ventricular tachyarrythmias. This can be due to variable R-R intervals, widespread sympathetic activation or ischemia[8]. In our study, 12.2% patients developed atrial fibrillation after acute MI. Crenshaw et al's study shows 10.4% patients with atrial fibrillation after acute myocardial infarction. Crenshaw et al's study has demonstrated that age is an independent predictor for development of atrial fibrillation after acute myocardial infarction[10]. Zahoor et al's study shows 9.1% patients with atrila fibrillation after acute myocardial infarction[4]. 7.5% patients developed atrial fibrillation after myocardial infarction in Lopes et's study. Lopes et al catergorized his study participants into two categories. Those with STEMI whereas those with NSTEMI. Atrial fibrillation was more prevalent among patients with STEMI than NSTEMI (8% vs 6.4%)[11]. A meta-analysis was conducted which included 20 different studies. The results report that upto 6-21% patients with acute myocardial infarction develop atrial fibrillation during the acute phase[12,13].

In our study death occurred in 7.89% patients whereas Zahoor et al's study showed a mortality rate of 18.2% patients[4]. Lopes et al and his collegues demonstrated a mortality rate of 5.1% among myocardial infarction patients who developed atrial fibrillation compared to

1.6% among those who were in sinus rhythm. In our study ventricular fibrillation developed in 15.78% patients whereas ventricular tachycardia also in 15.78% patients. Stroke developed in 10.52% patients. These results are similar to that seen in GUSTO I trial[10,11].

It has been seen that with the development of thrombolytic therapies, the rate of atrial fibrillation has significantly declined. A study has reported that oral anti-coagulants particularly warfarin has resulted in significant reduction in mortality. Around 29% decrease in relative mortality risk whereas 7% reduction in absolute mortality risk at 1 year interval [14]. Patients at risk of atrial fibrillation are usually offered beta blockers for rate control however use of beta blockers or calcium channel blockers in ischemic myocardium can further compromise cardiac function. In this case digitalis can be offered. Amiodarone can also be added to the regime[15,16].

CONCLUSION

Patients at risk for development of atrial fibrillation should be offered rate control pharmacologic therapy to prevent devastating outcomes. Other options include anti-arrthymic agents and prophylaxis for thromboembolism. Patients with older age, advanced heart failure, elevated heart rate and not using rate control therapy should be given attention as they are more prone to developing atrial fibrillation which can precipitate further devastating clinical outcomes.

Author's Contribution:

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Original Article

A Study of Risk Factors of Diabetic Foot Ulcers

Risk Factors of Diabetic Foot

Anam Shafi, Maaz-Ul-Hassan and Sidra Tufail

ABSTRACT

Objectives: To determine the risk factors associated with development of diabetic foot ulcers
Study Design: Descriptive / cross-sectional
Place and Duration of Study: This study was conducted at the Department of Internal Medicine, Services Hospital, Lahore from 1st January 2017 to 31st July 2017.
Materials and Methods: One hundred and fifty diabetics aged between 20-75 years presenting to surgical OPD / emergency with diabetic foot ulcers were enrolled. Patients with comorbidities like congestive cardiac failure, chronic renal failure and chronic liver disease were excluded from the study. The complete history was taken regarding duration of diabetes and its management. A detailed general physical examination was performed in each case along with sensory examination and ABI testing using Doppler ultrasound. Blood sample was sent for HbA1c to check for glycemic control. Ulcer debris was sent for culture and sensitivity.
Results: There were 90 males and 60 females. Peripheral neuropathy was present in 53.3% patients, 64% had absent or diminished peripheral pulses, 46.7% had poor glycemic control. Underlying infection was seen in upto 90% of the patients. Footwear trauma was present in 40% of the cases. Thirty (20%) of the patients had to undergo amputation eventually while rest were managed conservatively.
Conclusion: Prolonged diabetes, presence of underlying infection, peripheral vascular disease and peripheral neuropathy are the major risk factors responsible for development of diabetic foot ulcer. There is a dire need to educate diabetic regarding strict glycemic control and meticulous foot care.

Key Words: Diabetes mellitus, Diabetic foot ulcer, Amputation

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INTRODUCTION

Diabetes mellitus (DM) is a chronic metabolic illness which can lead to multiple complications in the long run.[1,2] Diabetic foot ulcer is one of the common complications associated with long running poorly controlled DM.[3] It is associated with severely impaired health related quality of life (HRQOL) in both physical and mental health domains.[4] A recent meta-analysis by Zhang et al[5] reported a global prevalence of 6.3% for diabetic foot ulcer. This proportion is much higher in Pakistan. In fact, a recent local study by Khan et al[6] estimated an overall prevalence of 13.9%.

Diabetic foot ulcer presents a major public health challenge.[7] WHO has ranked Pakistan 7th on diabetes prevalence list.[8] Due to lack of awareness regarding diabetes self management techniques, people are at increased risk of developing various complications. Diabetic foot is particularly challenging as its management frequently involves amputation thus limiting the limb functionality. Once the gangrene sets in, there is no viable alternative other than to amputate the limb.[9] It has been estimated that diabetic foot is responsible for upto 40,000 amputations yearly in Pakistan.[10]

There are various risk factors associated with an increased risk of developing diabetic foot ulcers. These include diabetes present for more than 10 years, male sex, presence of associated microvascular complications, peripheral neuropathy, peripheral vascular disease and local bone deformity or trauma.[11] It is important to be able to recognize these risk factors early on in the disease so as to limit and delay the complications. A recent local study by Jan et al[12] reported poor glycemic control (HbA1c >8%), peripheral neuropathy and peripheral vascular disease in 65.3%, 40% and 53.3% of the patients respectively. Accidental or footwear trauma was also present as a risk factor in upto 44% of the patient.

These risk factors can be controlled by proper health education of the patients regarding the illness. In addition, there is a dire need to educate the diabetics regarding foot care. In fact a recent survey by Ali et al[13] reported that only 36.7% of doctors told their patients regarding diabetic foot care. A rigorous approach at primary healthcare level is needed to educate the public. Therefore, we decided to conduct this study with the principal aim of elucidating the risk factors associated with development of diabetic foot ulcers.

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MATERIALS AND METHODS

This descriptive cross sectional study was carried out from 1st January 2017 to 31st July 2017 at Department of Internal Medicine, Services Hospital, Lahore. One hundred and fifty diabetic patients were included. Consequently, diabetics aged between 20-75 years presenting to surgical OPD / emergency with diabetic foot ulcers were enrolled in the study. Non probability consecutive sampling technique was employed. Patients with comorbidities like congestive cardiac failure, chronic renal failure and chronic liver disease were excluded from the study. A complete history was taken regarding duration of diabetes and its management. A detailed general physical examination was performed in each case along with sensory examination and ABI testing using Doppler ultrasound. Blood sample was sent for HbA1c to check for glycemic control. Ulcer debris was sent for culture and sensitivity. The data was entered and analyzed through SPSS-20.

RESULTS

Out of 150 patients, 90 (60%) were males and 60 (40%) were females. Right foot only was involved in 96 (64%) patients, left foot only was involved in 48 (32%) patients, and both feet were involved in just 6 (4%) patients. (Table 1). Mean age of the patients was 55.35±7.12 years. The mean duration of diabetes mellitus was 12.3±3.2 years with upto 96% of the patients having type II diabetes. Mean HbA1c was 9.1±2.9 % (Table 2). No treatment had been received by half of the patients while 40% were on oral anti-diabetics and the remaining 10% patients were on insulin.

Table No.1: Demographic information of the patients

Variable	No.	%
Gender		
Male	90	60.0
Female	60	40.0
Involvement of foot		
Right foot	96	64.0
Left foot	48	32.0
Both feet	6	4.0

Table No.2: Baseline characteristics of the patients

Variable	Mean±SD
Age (years)	55.35±7.12
Duration of diabetes (years)	12.3 ± 3.2
HbA1c	9.1±2.9

Peripheral neuropathy was present in 53.3% patients, 64% had absent or diminished peripheral pulses, 46.7% had poor glycemic control. Underlying infection was seen in upto 90% of the patients; staphylococcus aureus being the most commonly isolated organism. Osteomyelitis was seen in 43.3% patients. Footwear trauma was present in 40% of the cases (Table 3). Thirty (20%) of the patients had to undergo amputation eventually while rest were managed conservatively.

Table No.3: Risk factors for diabetic foot ulcer

Risk factor	No.	%
Poor glycemic control	70	46.7
Peripheral neuropathy	80	53.3
Peripheral vascular disease	97	64.7
Prolong diabetes (>5 years)	140	93.3
Accidental/Footwear trauma	60	40.0
Underlying infection on C/S	135	90.0
Osteomyelitis	65	43.3

DISCUSSION

Diabetic foot ulcer is routinely seen on the surgical floor. Elderly patients are a common victim and the associated morbidity is high amongst them. What is alarming regarding diabetic foot is the fact that its management may require amputation of the affected limb. The number of diabetics is on the rise and poses a serious public health concern. Creating awareness regarding foot care amongst diabetics is of utmost significance.

We conducted this study with aim of elucidating the risk factors associated with development of diabetic foot ulcers. Our study identified prolonged diabetes i.e. diabetes >5 years duration and underlying infection to be commonest prevailing risk factors present in upto 93.3% and 90% of the patients respectively. This was consistent with the findings of Ahmad et al.[7] We reported a mean age of 55.35±7.12 years. The average duration of disease was 12.3±3.2 years. This was in line with the result of Ahmad et al[11] and Jan et al[12] who reported a mean duration of 11.4 years and 11 years respectively. A longer duration is associated with increased risk of developing diabetic foot ulcers. In our study, peripheral vascular disease and peripheral neuropathy was present in 64% and 53.3% of the patients respectively. This was in line with findings of Ahmad et al[11] who reported prevalence of 62.8% and 51% respectively. Our study identified footwear trauma as risk factor present in upto 40% of the patients. This was consistent with results of Jan et al[12] who reported that 44% of the patients showed evidence of footwear trauma. The amputation rate following diabetic foot ulcers is quite high. Ahmad et al[11] reported an amputation rate of 20.9% amongst patients with diabetic foot ulcer. This was in line with our results as we observed an amputation rate of 20%. However Rashid et al[14] reported a much higher amputation rate of a staggering 35.8%.

There is a need to initiate a countrywide health education campaign detailing the patients on the particulars of diabetes and how to ensure strict glycemic control. Only then we can hope of tackling this huge public health challenge.

CONCLUSION

Prolonged diabetes, presence of underlying infection, peripheral vascular disease and peripheral neuropathy are the major risk factors responsible for development of diabetic foot ulcer. There is a dire need to educate diabetic regarding strict glycemic control and meticulous foot care.

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

Somatic Symptoms in Depression; A Teaching Hospital Based Cross Sectional Study

Somatic Symptoms in Depression

Javeria Ali Asghar, Aqsa Faiz-ul-Hassan, Rana Mozammil Shamsher Khan and Saba Tabbasum

ABSTRACT

Objective: The objective of the current study was to assess somatic symptoms in patients who were suffering from depression.

Study Design: Cross sectional study.

Place & duration of study: This study was conducted at the Department of Psychiatry & Behavioural Sciences, AIMTH affiliated to KMSMC Sialkot during October 2017.

Material and methods: Adult consenting new patients of depression coming through OPD were included. Exclusion criteria were patients suffering from any other physical or psychiatric illness, minors or those refusing consent. In phase 1 clinical assessment was done according to ICD-10 criteria and Urdu version of Beck Depression Inventory- II (BDI- II) was administered. In the 2nd phase presenting complaints were noted. If the main presenting complaint was one or more somatic symptoms, they were recorded along with the demographic details on a sheet. The data was analyzed by SPSS v 21.

Results: Majority of the patients of depression coming to our hospital were young married females from middle and lower income class with no or little education. 151 (63.71%) reported somatic symptoms. Headache was the most common 131 (22.05%) followed by muscle pain 86 (14.48%) and decreased appetite 85 (14.315%) generalized weakness 77 (12.96%) joint pains 71 (11.95%) gastrointestinal disturbances 59 (9.93%) tingling and burning sensations 38 (6.39%) and other symptoms by 47 (7.91%).

Conclusion: Majority of the patients were young married females from middle and lower income class with no or little education. 151 (63.71%) reported somatic symptoms. Headache was the most common 131 (22.05%) followed by muscle pain 86 (14.48%) and decreased appetite 85 (14.315%).

Key Words: somatic symptoms, physical symptoms, teaching hospital, depression

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INTRODUCTION

Depression is a major illness. Although mortality associated with depression may not be high but morbidity is very high. It is a disease which has high prevalence. According to W.H.O. it was the 4th leading cause of morbidity and also mortality but it was projected that in 2020 depression will become number 2 among all diseases as far as GBD is considered.[1] Prevalence and burden of depression is increasing in the world but there are many obstacles in its recognition. It is missed or under diagnosed in various settings. In primary care, in general health care, by doctors in general practice and also by specialists working in other fields of medicine than psychiatry.

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One of the reasons may be that depression does not always present with typical symptoms for example low mood. Many a times it presents with somatic symptoms. Doctors are usually trained to listen to somatic or physical symptoms and think of medical or surgical illnesses. There is deficiency in their training to recognize these symptoms. They go on and order laboratory and other unnecessary investigations. The patient who is already suffering also goes through these unnecessary investigations leading to waste of money, time and human resources. It also burdens the diagnostics departments of any hospital.[2]

The patient on the other hand may go in to more distress. He may ruminate [3] and not satisfied with care in the hospital.[4] Depression is also common after surgery.[5] It may lead to inappropriate referrals [6], inappropriate operations leading to keloids [7] and burden on the patient and family.[8] Distress can lead to battering in women [9] and depression in students of medicine[10] and inappropriate hospital admission getting infections[11] and other complications.

The two classification systems in Psychiatry DSM and ICD fail to incorporate somatic symptoms in the diagnostic category of depression. There is a debate for a long time that somatic symptoms do not get enough attention by the two major systems of classification

used world over for many years. One criticism is that they address psychological symptoms of depression only. Cognitive symptoms are also included in the diagnostic systems. Since these two major classifications do not adequately address the issue of somatic systems of depression, major books of medical and other curriculum taught at medical schools lacks integration. Medical students who graduate and then become doctors who come in practice and see patients have little or no understanding or knowledge of somatic symptoms. They miss cases or misdiagnose them altogether. They may embark upon the journey of unnecessary investigations and prescribing wrong medicines. DSM-V1TR has added some significance to somatic symptoms in the diagnosis of depression by adding unnecessary worry and concern about physical health in the new version of the classification.[2]

To address this issue of under diagnosis and diagnosing depression when it does not present with typical psychological or cognitive symptoms we planned to conduct a study in our hospital. Up till now, to our knowledge no research has been done on this topic in our hospital. The objective of the current study was to assess somatic symptoms in patients who were suffering from depression.

MATERIALS AND METHODS

The cross sectional study was conducted at AIMTH affiliated to KMSMC Sialkot Pakistan during the calendar month of October 2017. Ethical guidelines in the Declaration of Helsinki were followed. Approval was taken from ethics review committee. All patients coming to OPD during working hours were approached. Inclusion criteria were adult new patients of depression coming to the OPD of Psychiatry and Behavioral Sciences department for the first time. Exclusion criteria were patients suffering from any other physical or psychiatric illness, minors or those refusing consent. Purpose and title of the study was explained to all patients and written informed consent was taken.

The study was conducted in two phases. In phase 1 a Psychiatrist or senior medical officer in Psychiatry conducted the clinical assessment according to inclusion and exclusion criteria to confirm the presence of depression according to ICD-10 criteria. Then data collectors administered Urdu version of Beck Depression Inventory- II (BDI- II) [12] to confirm the presence of depression. The cronbach's alpha for this study was .87. For illiterate patients data collectors read out the questions and responses were recorded according to patient's answers. The cut off score was taken as 14. 243 patients were diagnosed to be depressed after clinical assessment however 6 scored below 14 on BDI- II. These 6 patients were excluded and final sample size was 237 patients. The demographic and other variables of these 6 patients were not very different from the final sample.

In the 2nd phase presenting complaints of the patients were noted. If the main presenting complaint was one or more somatic symptoms, they were recorded along with the demographic details on a sheet which was already prepared for this purpose. Data was analyzed by SPSS v 21.

RESULTS

237 patients were included in the study. 141 (59.49%) patients were females and 96 (40.51%) patients were males. The mean age of female patients was 29.33±14.29 years with range from 18-69 years. The mean age of male patients was 30.77±12.47 years with range from 18-71 years. Majority of patients 108 (45.57%) were in age bracket 18-30 years. While 97 (40.93%) were in age bracket 31-55 years and 32 (13.50%) had age more than 55 years. Majority 131 (55.27%) were married while 72 (30.38%) were single and 34 (14.35%) were either divorced or widowed. Majority of the patient belonged to lower and middle income class. With lower income there were 65 (27.43%) patients and middle income 134 (56.54%) patients. only 38 (16.03%) patients belonged to upper income class. 79 (33.33%) patients were illiterate. The majority 107 (45.15%) had less than 10 years of education while 51 (21.52%) had more than 10 years of education. Table 1

Table No.1. Demographics of the patients N=237

Variable	Frequency	%age
Gender		
Female	**141**	**(59.49%)**
Male	**96**	**(40.51%)**
Age in years		
18-30	**108**	**(45.57%)**
31-55	**97**	**(40.93%)**
> 55	**32**	**(13.50%)**
Marital status		
Single	**72**	**(30.38%)**
Married	**131**	**(55.27%)**
Divorced/widowed	**34**	**(14.35%)**
Monthly income in (Pak Rupees)		
<15000	**65**	**(27.43%)**
16000-60000	**134**	**(56.54%)**
>60000	**38**	**(16.03%)**
Education		
Illiterate	**79**	**(33.33%)**
Less than 10 years	**107**	**(45.15%)**
More than 10 years	**51**	**(21.52%)**

Out of the total 237 patients 151 (63.71%) reported somatic symptom as chief presenting complaint. Patients had one or more than one somatic symptoms. Patients with each somatic symptom were counted checked and added to the total list of symptoms. Headache was the most common symptom 131

(22.05%). Muscle pain as symptom was reported by 86 (14.48%). Decreased appetite was another important symptom to be reported 85 (14.315%). Generalized weakness was common. 77 (12.96%) times it was reported. Joint pains were reported 71 (11.95%) times. Gastrointestinal disturbances were reported 59 (9.93%). Tingling and burning sensations were also reported by the patients 38 (6.39%). Other symptoms were reported by 47 (7.91%). Table 2.

Table No.2. Somatic symptoms in depression N=237

Symptom	Frequency= n	%age
Headache	**131**	**22.05**
Generalized weakness	**77**	**12.96**
Muscle pain	**86**	**14.48**
GI disturbance	**59**	**9.93**
Joint pains	**71**	**11.95**
Tingling and burning	**38**	**6.39**
Decreased appetite	**85**	**14.31**
Others	**47**	**7.91**
Total	**594**	**100**

DISCUSSION

The results of our study show that majority of the patients of depression coming to our hospital were young married females from middle and lower income class with no or little education. 151 (63.71%) reported somatic symptoms. Headache was the most common 131 (22.05%) followed by muscle pain 86 (14.48%) and decreased appetite 85 (14.315%).

In another study somatic symptoms were also reported to be present in majority of the patients who were suffering from depression. In this study female were 260 and male were 239. 80% of these patients reported somatic symptoms. Our figures are not very far away from this study and corroborate findings from our study. The somatic symptoms as authors argued were mainly concerned with psychopathology. The main themes were hypochondriacal in nature and physical or somatic manifestations of stress were common. Depression and stressful factors are common in the psychopathology of somatic symptoms. They are not only present in patients coming to OPD but also are present in patients who are admitted in the hospital.[13]

Another study carried out by W.H.O. included 1146 patients. It was a large study. It was multi center reporting findings from patients who were suffering from depression. This large study reported that 2/3 of patients of depression presented with somatic symptoms. These findings are also similar to findings from our study. More than half of the patients reported symptoms which were somatic but not explained by medical reasons. These might be due to psychological factors.[14]

In another study in U.S. conducted on 573 patients 69% had somatic complaints. The most frequent being general body aches along with pain. There may be an association of pain or symptoms of pain with depression.[15] Depression and pain may have link or pathway that is common. Painful symptoms occur in depression and it is seen that in painful conditions or illnesses which are chronic depression is present in significant percentage of patients. This is more than what statistics and other confounding variables could count. If the impact of other factors is removed even than painful symptom in depression are common and depression is common in chronic painful disorders. It was shown from all tiers of health care that symptoms which were distressing and painful and somatic in nature were present in 2/3 of the patients.[15]

Differences in somatic symptoms in male and female gender have also been reported. From a large sample in which depressed patients were assessed, data was divided in to depressed patients who had somatic symptoms and who had "pure" symptoms of depression. It was found that in female patients there was majority of patients who reported somatic rather than pure type of depression and these female patients had their illness started in young and adolescent age and the main symptoms were body aches along with pains. The findings are very similar to findings from our study. We also had young female patients more than male patients, reporting somatic symptoms in depression.[16,17]

Our study has strengths and limitations. The strengths of the study are easy and cost effective methodology. Data was easily collected from hospital. It was a hospital based study and patients from OPD were included. Patients coming after OPD timings through emergency were missed. In future, studies with more robust methodology and in community setting are needed.

CONCLUSION

It can be concluded that majority of the patients of depression coming to our hospital were young married females from middle and lower income class with no or little education. 151 (63.71%) reported somatic symptoms. Headache was the most common 131 (22.05%) followed by muscle pain 86 (14.48%) and decreased appetite 85 (14.315%).

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Original Article

Evaluation of Marginal Integrity in Posterior Teeth

Longevity of Posterior Restorations in Terms of Marginal Integrity: A Clinical Study Evaluating the Marginal Integrity Between the Resin Composite and Silver Amalgam in Posterior Teeth

Nadeem Tarique[1], Faisal Izhar[3], Rabia Awan[2] and Kalsoom Tariq[3]

ABSTRACT

Objective: To evaluate the marginal integrity of silver amalgam and resin composite restorations in posterior teeth having Black's class 1 carious lesion.

Study Design: Perspective study

Place and Duration of Study: This study was conducted at the Department of Operative Dentistry, Dental Section, Punjab Medical College Faisalabad and Fatima Memorial Hospital College of Dentistry, Lahore from October 2016 to March 2017.

Patients and Methods: One hundred and sixty patients were selected having class 1 cavity in any of the mandibular molars. Radiographs were taken to assess the depth of cavity and periodontal status.78 patients got resin composite restorations while 86 patients received silver amalgam fillings. All the restorations were performed following standard isolation protocols. The success of the restorations was assessed after six months by considering the marginal integrity. This was checked by Cvar and Ryge criteria.

Results: The Chi square statistic value that we observed with our statistical data with degree of freedom (df) 1 is 10.3385. The p-value captured by the analysis is 0.001. The result is significant at $p<0.05$.

Conclusion: In perspective of successful restorations, good marginal integrity among all the restorations had predilection for the resin composite.

Key Words: Resin composite, Amalgam, Marginal integrity, Hybrid composite, Micro gaps, Hydrophobic

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INTRODUCTION

Dental restorations are subjected to failures and dislodgemen. These are amongs the main problem in the dentistry.[1] Amalgam being an old restorative material has been used extensively in the posterior dental fillings. It has also limited use in the anterior teeth having class III cavities in the areas which are not visible during smile or talking. The development of resin composite has made it possible to be used successfully in the anterior as well as posterior teeth.[2] The longevity of the resin composite has been considered as greater than amalgam. During amalgam restoration, only the macromechanical means and measures are responsible for the retention of restorative material into the cavity. While in case of resin composite the micro mechanical retention helps to retain the composite.[3] The amalgam is successful equally in the smaller as well as larger complex tooth preparations. Amalgam being a hydrophobic material provide ease for the manuplation even in the areas where the field isolation is difficult to achieve. While resin composite requires strict field isolation. Although the longevity of the restoration depends upon a number of factors like skills of the operator, type of restorative material used and the basic techniques applied to prepration yet the *m*ain reasons for the restoration failures are the recurrent caries, tooth fracture and the fracture of the main bulk of the restorative material.[2]

A number of restorative materials have been developed with improved strength and aesthetics. Although the amalgam has been used as a restorative material in the posterior teeth since long yet there has always been a focus of the investigators to develop a material having good strength as well as esthetically acceptable suiting all the requirements. Such types of materials that are esthetically acceptable, have and good acceptance by the patients and are materials of cf choice for restoration. There are certain controversies that are being related to the amalgam. One of them is mercury

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toxicity and esthetically non appealings.[4] The other disadvantage include the lack of bonding to the tooth surface, weakining of the tooth structure and need for the lining material. The currently available other restorative materials not only have the bonding capabilities but they also seldom require a lining.[5] Resin composites are tooth coloured and have good strength. They are used extensively as fissure sealant, direct and indirect restorations and bonding certain ceramic restorations.[5,6] Despite the merits of resin composite the polymerization shrinkage is still considered a major issue.[6,7] Bonding to the enamel is a positive point regarding to success. The same is also true for the dentine. There are certain problems associated with dentine due to its wet nature. However the enamel margin is important for the restorative adhesion, because most of the retention is achieved by the enamal margins.[8] In case of amalgam restorations there is no bond and micro gaps are created between the tooh restoration interface. These gaps are responsible for the colonization of the bacteria and caries recurrence. The behaviour of the resin composite is better as compared to the amalgam in terms of micro gaps.[3] These newly emerged resin composites represent a groundbreaking alternate to amalgam.

MATERIALS AND METHODS

This perspective study was carried out at Department of Operative Dentistry, Dental Section, Punjab Medical College Faisalabad and Fatima Memorial Hospital College of Dentistry, Lahore from October 2016 to March 2017. Total 164 outdoor patients were selected having age between 20-30 years. 110 patients were males and 54 patients were females. The study proceeds the following steps outlined below. A complete medical and dental history was recorded before the operational procedures. The radiographs were taken to assess the depth of the carious lesions and periodontal health. Only mandibular molars were selected having Black's class 1 carious lesion. All the restorations were performed following standard parameters of isolation. 78 patients received the resin composite restoration while 86 patients got silver amalgam fillings. The cavity was prepared with the high speed air turbine using copious irrigation of water. Isolation was achieved by the use of cotton rolls and wafers. For resin composite, etching was done, washed and then adhesive was applied. Then restorative composite was packed into the cavity and light cured. The design of cavity was made considering the C-factor to avoid polymerization shrinkage. For silver amalgam fillings, the outline of the cavity was prepared following Black's rule of cavity preparation. All the unsupported enamel was removed to avoid marginal fracture of the tooth. After the restorations, the follow up was made after six months to evaluate the marginal integrity and thus restoration success. The marginal integration of the restorations was assessed by the criteria used by Cvar and Ryge. This criteria has three categories i.e. Alpha, bravo and Charlie. Statistical significance was analyzed by using SPSS 16.

RESULTS

The Chi square statistic value obtained with degree of freedom (df) 1 is 10.3385. The p- value is 0.001303. The result is significant at $p<0.05$. The value in the chi square chart is 3.841.While our statistical value is 10.3385 which is remarkably higher than the value in the chi square table. So we can say that there is significant difference among two modes of treatment (Tables 1-2).

Table No. 1: Frequency and percentage of procedures

Restorative material	Successful (Alpha)	Failure (Bravo/ Charlie)	Total
Resin composite	67	11	78
Silver amalgam	55	31	86
Total	122	42	164

Table No.2: Contingency table with expected values and Chi square statistic for each cell

Restorative material	Successful	Failure
Resin composite	58.02 (1.39)	19.98 (4.03)
Silver amalgam	63.98 (1.26)	22.02 (3.66)

DISCUSSION

The resin composite has been used extensively due improved marginal integrity and the esthetics. It almost fulfils the esthetic demands of the patient. This quality of the material ensures a good patient satisfaction. There is a little failure observed with this material. There is vast amount of literature available on this material. This failure is mostly due to the wear and is related to the bruxismic patients.[9,10] These demerits have drawn the attention of researchers towards a new better innovation. In the study the first group of resin composite restoration showed a good marginal adaptibility i.e. 85.89% fell into Alpha criteria after six months. The other 14.10% restorations categorized as having compromised marginal integrity. It is plausible that a number of limitations could have influenced this category. Out of these, 7 patients (63.30%) were in Bravo and remaining 4 patients(36.36%) were in Charlie category.

According to Gianordoli et al[11] the resin composites showed acceptable marginal integration even after two years. current study supports this practical outcome being not a far cry. The same researcher also concluded that two different resin composites were clinically

satisfactory after one year.[12] The cavity margins were bevelled slightly to improve the sealing effect of the adhesive. But at the same time maximum conservation of the tooth structure was preserved. However unsupported enamel is liable to fracture and on account of this fact it was removed. Soliman et al[13] is correct to argue that in the larger class II cavities bevelling should not be done and is no longer recommended. Perhaps this is due to the increased bulk of the restorations that failed to reproduce a well integrated margin. However in the smaller class I cavities a slight bevelling is allowed to enhance the marginal integrity.

In case of silver amalgam restorations 55 patients (63.95%) were declerad as successful and 31 patients (36.05%) were having compromised marginal integrity. Out of these unsuccessful restorations, 19 patients (61.29%) were in Bravo category and the rest 12 patients (38.70%) were in Charlie category.Any significant difference was not observed in compliance to the gender basis. A review of the literature shows that the longevity of the restoration depends on quality and technique of operator, socioeconomic factors such as income, type of dental service and demographic factors.[14,15] Recent research has also shown the satisfactory results of the hybrid materials and that the composites can be used successfuly in the posterior teeth.[16]

It has been widely observed that the failure of the restorations is mainly due to the recurrent caries. This recurrence is the main etiology of the restorations to fall to pieces. There is further progression of caries with the invasion of bacteria into the crevice and so responsible for the decay of tooth. The past research pertaining to the restoration failures in resin composites exhibits secondary caries, caries risk factors the presence of lining and bruxism.[17] Repair of the composite restoration has also been gaining popularity these days. This repair is able to increase the longevity of the restoration provided the patient, operator and the material is taken into account.[18,19]

There are a number of factors that influence the performance of the restorations. These include experience of the operator, position of the tooth in the arch, restoration design, size and age of the patient.[20,21] The use of amalgam is mainly indicated in the larger cavities and where the isolation is difficult to achieve. As far as the composite restoration is considered, it is cumbersome, costly and highly technique sensitive. In these conditions the amalgam can be used effectively.[22] The onset of the caries along the margins of the amalgam is more as compared resin composite due to the non adhesive behaviour of the material. Despite these amalgam is successful in the smaller restorations and allows more tooth conservation.[23]

CONCLUSION

Composite restorations are evidently more successful in terms of marginal integration and restoration longevity as compared to the conventional silver amalgam restorations. This feature and thus the whole restorative technique is not a brain surgery. The material has an adhesive nature which makes less chances of caries recurrence and restoration fracture. Despite certain demerits of the adhesive restorations, the next decade is likely to see further advancements in the bio materials.

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Original Article

Macrosomia in Pregnant

To Determine Association of Macrosomia in Pregnant Women Who Have Altered Glycemic Control

Anila Rehman, Asifa Khuwaja, Fozia Unar and Jahan Ara

ABSTRACT

Objective: To determine association of macrosomia in pregnant women who have altered glycemic control.
Study Design: Prospective cohort study
Place and Duration of Study: This study was conducted at the Department of Obstetrics and Gynaecologic Unit 2, Civil Hospital, Dow University of Health Sciences, Karachi from 04-09-2013 to 04-02-2014.
Materials and Methods: Two thirty eight pregnant women were included in this study. 119 women who had abnormal HbA1c were in exposed group and 119 Women who had a normal HbAlC were taken as Non-Exposed Groups. Information from all patients were gathered through a pre- designed Proforma which include socio-demographics such as age, height weight as well as other study variables including booking status, gestational age, parity, history of macrosomic infants, history of diabetes in family, weight of baby.
Results: Macrosomia was 2 time (Approximate of 1.59) more common in exposed than non-exposed group (RR: 1.59 95%CI: 1.29 to 2.02).
Conclusion: We conclude that in this study woman with GDM mean HbA1c are significant predictors of newborn macrosomia. Early diagnosis and appropriate treatment of GDM aimed at tight control over maternal glucose levels positively influence the perinatal outcome and it prevents macrosomia.
Key Words: Gestational diabetes mellitus, Macrosomia, Altered glycemic control, HbA1c.

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INTRODUCTION

Gestational diabetes mellitus is associated with increased risk of macrosomia, development of impaired glucose level and diabetes after delivery. Previous pregnancy that resulted in large for gestational age infant is often considered to be a risk factor for gestational diabetes mellitus in subsequent pregnancy[1]. Macrosomia is associated with a higher incidence of cesarean delivery (double that of control subjects) and with birth canal lacerations associated with vaginal delivery[2]. Macrosomic neonates are at risk for shoulder dystocia and birth trauma. This risk is directly related to neonatal birth weight and begins to increase substantially when birth 5 weight exceeds 4500g. Brachial plexus injury is rare, with an incidence of fewer than 2 cases per 1000 vaginal deliveries. This risk is approximately 20 times higher when the birth weight is more than 4500g[3]. Gestational diabetes mellitus affects approximately 4% of all pregnant women in the US, complicates 4-14% of pregnancies[6].

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Glucose crosses the placental barrier, and the resulting higher levels of foetal glucose in gestational diabetic pregnancy induce hyperinsulinaemia, which is associated with an increased risk of large-for-gestational age (LGA) infants, shoulder dystocia and neonatal hypoglycemia[7,8]. Glycocylated hemoglobin, as measured by hemoglobin Al C (HbA1C), can potentially identify pregnant women at high risk for adverse outcomes associated with. GDM including macrosomia and post-postpartum glucose intolerance[9]. Early diagnosis and appropriate treatment of GDM aimed at tight control over maternal glucose levels positively influence the perinatal outcome[10] and it prevents macrosomia. Macrosomia is a complication of poor glycemic control in pregnancy. The purpose of my study is to estimate burden of impaired glucose tolerance and gestational diabetes who might benefit from life style modification and 6 pharmacological intervention, thus we can decrease the morbidity and prevent macrosomia in our population.

MATERIALS AND METHODS

After Approval from Hospital's Ethics Review Committee and competitive authority (College of Physicians and Surgeons of Pakistan),written as well verbal informed consent from patient, before commencing the study. All patients who fulfilled the eligibility criteria were included in this study. Information from all patients were gathered through a

pre- designed Proforma which include demographics such as age, height weight as well as other study variables including booking status, gestational age, parity, history of macrosomic infants, history of diabetes in family, weight of baby. Patient was seen in labour room venous blood was drawn for HbAlC. Patient were divided into two groups one in whom HbA 1 C is abnormal are exposed and others in which HbA 1C is normal are non-exposed was followed delivered to see the outcomes of those patients.

RESULTS

Two thirty eight pregnant women were included in this study. 119 women who had abnormal HbA1c were in exposed group and 119 Women who had a normal HbAlC were taken as Non-Exposed Groups. The average age, gestational age, parity and BMI of the women were not significant between exposed and non-exposed group.[7] Regarding parity status of the women, 30(12.6%) had nulli parity, 96(40.3%) had Primiparous and 112(47.1%) had multi parity (parity>2). Diabetic was observed in 19(8%) cases as shown. Out of 238 women, 77(32.4%) were delivered cesarean and 161(67.6%) were spontaneously. Mode of delivery with respect to exposed and non-exposed groups . History of macrosomic was noted in 18(7.6%) cases and high in exposed group. In this study, rate of macrosomia was observed in 26.9% (64/238) cases. Macrosomia was 2 time (Approximate of 1.59) more common in exposed than non-exposed group (RR: 1.59 95%CI: 1.29 to 2.02) . Stratification analysis showed that macrosomia was 2time more likely in exposed than non-exposed group for the age below 25 and 26 to 30 years of age women while it was not significant for 31 to 35 years of age women. Macrosomia was significantly high and also two times more likely in exposed group than non-exposed group in those women who had nullipara and multipara. Similarly with respect to mode of delivery, rate of Macrosomia was high in exposed groups in those women who delivered spontaneously and cesarean. Association of Macrosomia and HbA1c was also observed with respect to history of Macrosomia and diabetic women history of macrocosmic according to groups 8 n= 238T.

Table No.1: Association of macrosomia and glycemic control

Macro-somia	Exposed Group n=119	Non-Exposed Group n=119	Total	P-Value	RR (95% CI)
Yes	44 (37%)	20 (16.8%)	64 (26.9%)	0.0005	1.59 (1.29 to 2.02)
No	75 (63%)	99 (83.2%)	174 (73.1%)		

Chi-Square= 5.25 OR: Relative Risk; CI: Confidence Interval
RR= (44/64)/ (75/174) = 1.59

Table No. 2: Association of macrosomia and glycemic control by mode of delivery.

Mode of Delivery	n	Macrosomia	Exposed Group	Non-Exposed Group	P-Value	RR (95%CI)
Spontaneous	161	Yes	26(31.3%)	13(16.7%)	0.03	1.42 (1.06 to 1.91)
		No	57(68.7%)	65(83.3%)		
		Total	83	78		
Caesarean Section	77	Yes	18(50%)	7(17.1%)	0.003	2.08 (1.33 to 3.25)
		No	18(50%)	34(82.9%)		
		Total	36	41		

Chi-square test and Fisher exact test were applied according to condition

Table No. 3: Association of macrosomia and glycemic control by history of macrosomia.

History of Macrosomia	n	Macrosomia	Exposed Group	Non-Exposed Group	P-Value	RR (95%CI)
Yes	18	Yes	6(40%)	0(0%)	0.18	1.61 (1.23 to 2.09)
		No	9(60%)	3(100%)		
		Total	15	3		
No	220	Yes	38(36.5%)	7(17.1%)	0.001	1.59 (1.25 to 2.02)
		No	66(63.5%)	34(82.9%)		
		Total	104	41		

Chi-square test and Fisher exact test were applied according to condition

Table No. 4: Association of macrosomia and glycemic control by diabetic mellitus.

Diabetic Militus	n	Macrosomia	Exposed Group	Non-Exposed Group	P-Value	RR (95%CI)
Yes	19	Yes	4(36.4%)	0(0%)	0.05	2.14 (1.24 to 3.68)
		No	7(63.6%)	8(100%)		
		Total	11	8		
No	219	Yes	40(37%)	20(18%)	0.002	2.67 (1.44 to 4.98)
		No	68(63%)	91(82%)		
		Total	108	111		

Chi-square test and Fisher exact test were applied according to condition

DISCUSSION

Maternal gestational diabetes (GDM) and hyperglycemia in pregnancy have long been related to excessive fetal growth[11,12]. Maternal obesity before pregnancy and excessive weight gain during pregnancy are additional, potentially modifiable, independent risk factors of excessive fetal growth[13] and often occur in conjunction with GDM or hyperglycemia in pregnancy. There is a worldwide consensus that delivery of a macrosomic or large-for-gestational-age (LGA) infant is associated with increased frequencies of prolonged labor, operative delivery, shoulder dystocia and brachial plexus trauma[14]. In the particular case of the macrosomia that is due to gestational diabetes mellitus (GDM), maternal hyperglycemia – and its consequence, fetal hyperinsulinemia – are positively correlated to neonatal excess body mass[15]. However, tight glucose control seems not to be enough to prevent macrosomia in GDM, as other variables have emerged as independent factors of excessive fetal growth, particularly maternal overweight and obesity (body mass index [BMI] of 25 or greater)[16]. HbA1c is widely used as a measure of metabolic control during pregnancy, and it has been documented that it is associated with diabetes-related pregnancy complications in type 1 diabetes[17]. 14 In this study abnormal HbA1c (>6%) were in exposed group and women who had a normal HbAlC (6.0%[4]). Gonzalez Quintero VH et al found Macrosomia incidence with 15.7% compared to non-controlled which was 9.3 % in diabetic patients in his study[5].

CONCLUSION

We conclude that in this study woman with GDM mean HbA1c are significant predictors of newborn macrosomia. Thus, without ceasing in our efforts to improve glycemic control during GDM pregnancies, patients with overweight/obesity need to be treated prior to becoming 15 pregnant. Early diagnosis and appropriate treatment of GDM aimed at tight control over maternal glucose levels positively influence the perinatal outcome and it prevents macrosomia.

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Original Article

Tumor Necrosis

Tumor Necrosis Factor Alpha, Obesity and Polycystic Ovarian Syndrome

Imrana Ihsan, Asma Tehreem Kazi and Shafia Rasool Qazi

ABSTRACT

Objective: To determine the level of tumor necrosis factor alpha in polycystic ovarian syndrome and to find out correlation of TNF- α with BMI in obese and non-obese females.

Study Design: Cross sectional study

Place and Duration of Study: This study was conducted at the outpatient Department of Lady Aitcheson Hospital Lahore 1st July 2016 to 31st December 2016.

Materials and Methods: Eighty female patients diagnosed with PCOS were selected. Their height in meters (m) and weight in kg was determined and they were divided into cases with BMI> 25kg/m^2 and controls with BMI<25kg/m^2. 5ml of blood was taken from antecubital vein to measure serum TNF-alpha by ELISA kit.

Results: The mean age of cases and controls was 25.42±4.16 years and 22.98±3.35 years, with significantly lower mean age in controls, p-value < 0.001. The mean BMI was 27.59±5.72 kg/m2 in cases and 22.74±4.44 kg/m2 in controls with significantly higher mean BMI in cases, p-value < 0.001. Mean TNF-α was statistically higher in cases (66.14±122.37 pg/ml) when compared to controls (19.98±37.10 pg/ml), p-value < 0.05.

Conclusion: Serum TNF-alpha was increased in females with PCOS in both cases and controls but levels are significantly higher in cases. No significant correlation was found between TNF-alpha and BMI in either cases and controls. TNF- α level can be used as a molecular marker of disease.

Key Words: Tumor necrosis factor alpha (TNF-α), Body mass index (BM)I, Polycystic Ovarian syndrome (PCOS)

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INTRODUCTION

TNF-α, also named as cachexin, is a 157 amino acid unglycosylated polypeptide cytokine that is synthesized as a trans-membranous monomeric form with molecular weight of 26 kDa (m-TNF-α).[1-,3] It is produced majorly by activated macrophages (monocytes). On its cleavage by enzyme (TACE) a 17 kDa soluble TNF-α is obtained.[4] Both the forms have biological activity but activity of m TNF-α is different as it mediates paracrine and autocrine activity and STNF-α produces endocrine effects.[4,5] For mediation of endocrine effects high concentration of s TNF-α must be maintained in blood.[6]

Levels of TNF α are raised in conditions septic shock, graft rejection, parasitic infection cancer, post-hemofiltration, during in vivo cytokine therapy. Its role is both diagnostic as well as prognostic in systemic diseases.[6]

Scientific literature proves that both chronic inflammation and PCOS are associated with each other.[7]

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Pro-inflammatory mediators, e.g. tumor necrosis factor α (TNF-α), interleukin (IL)-6, and IL-1, mediate inflammation and are found to be elevated in women with PCOS.[8-10] Women with PCOS have increased levels of inflammatory cells as well as inflammatory markers. This oxidative stress and chronic inflammation contributes to insulin resistance and ovarian dysfunction.[11]

The corpus luteum secretes TNF-α and its levels changes with different phases of menstrual cycle.[12] The inflammatory mediators especially TNF-α, are believed to play crucial role in reproductive physiology. Biosynthesis of steroid in ovaries, maturation of ovarian follicles, ovulation, fertilization, and implantation etc. are influenced by TNF-α.[13,14] PCOS being a pro-inflammatory condition, promotes chronic low-grade inflammation which also leads to metabolic disturbances and ovarian dysfunctions.[15] In addition to this, genes which code pro-inflammatory mediators or their ligands are also linked with the genes for obesity, insulin resistance, diabetes and PCOS.[16,17] TNF–α performs several functions such as regulation of the ovulation, fertilization, and implantation, which are usually affected in females with PCOS.[18]

Females with PCOS show hyperandrogenism, infertility, anovulation, obesity, insulin resistance and high levels of TNF-α in their serum. The levels of TNF-α is raised in all the chronic inflammatory diseases and as discussed earlier PCOS is one such disease.[17]

It is commonly seen that that women diagnosed to have PCOS are usually overweight or have high BMI. With

the increase in worldwide prevalence of obesity the incidence of PCOS is also increasing in susceptible individuals.[19]

Obesity is now considered as a condition in which there is systemic sub-clinical inflammation. There is increased infiltration of CD-4 and CD-8 cells into adipose tissue that further causes release of mediators of inflammation including CRP and TNF-α. There is evidence of visceral adiposity in PCOS patients.[20-22] The fat cell increase in size and produce many hormones namely TNF-α, IL-6, resistin and leptin. It has also been noted that in obesity related disorders the levels of both MTNF-α as well as STNF-α are raised especially in adipose tissues .This adipose tissue derived TNF-α is also involved in regulation of biochemical processes e.g. glucose homeostasis in adipocytes, promotes lipolysis in cultured adipocytes and potently inhibits adipocyte differentiation and lipogenesis.[6]

To summarize PCOS patients have hormonal disturbances that results in insulin resistance and chronic inflammation that results in infertility in young females. Taking into account the role of TNF-α in chronic inflammatory conditions it can be regarded as a diagnostic and therapeutic marker whose levels must be regulated in order to get long term benefits especially in impaired glucose tolerance and dyslipidemia.[23] Thus, obesity can also flare up pre-existing clinical, endocrinological, and metabolic features in women with PCOS.[19]

MATERIALS AND METHODS

This cross-sectional study was done at outpatient department of Lady Aitcheson Hospital Lahore from 1st July 2016 to 31st December 2016. Eighty patients with diagnosis of PCOS based on the operational definition were selected. Patients with co-morbid conditions, other endocrinological abnormalities, menstrual abnormalities, history of smoking or NSAIDs consumption were excluded. Informed and written consent was taken and a complete history and general physical examination was performed. Height in meters and weight in kg was recorded. Body mass index was calculated by formula weight (kg)/height(m^2). On the basis of BMI they were divided into Controls (BMI< 25kg/ m^2) and Cases (overweight: BMI>25kg/ m^2). Patients were called again after an overnight fast on day 3 of menstrual cycle. Fasting glucose was determined by the glucometer. For laboratory parameters TNF-alpha, testosterone, and fasting insulin levels 5ml of blood was taken from antecubital vein under aseptic conditions and after centrifugation stored in 3 aliquots in the chemical Pathology laboratory K.E.M.U at -40 degree celcius. All information collected was entered in a specially designed performa. Serum insulin was detected by Diasourse Insulin Elisa Kit (Kap 125). Diasourse TNF-alpha kit was used for determination of TNF-alpha levels. It is a solid phase enzyme amplified sensitivity immunoassay performed on microtiter plate. Monoclonal antibodiies against the specific epitopes of TNF-alpha are used. Calibrators and samples react with antibodies coated on microtiter wells (Mab2). After incubation a sandwich of MAb-1MAb2-HRP is formed. Microtiter plate is washed and enzyme labelled antibodies is measured by chromogenic reaction by adding chromogenic solution. Incubation done and stop solution added. Microtiter plate is than read at appropriate wavelength. the substrate turnover is measured calorimetrically and by finding absorbance which is proportional to TNF-alpha concentration.

All data was entered and analyzed using SPSS version 20. Mean ± S.D was used to present quantitative data. Normality of data was checked by one sample Kolmogorov Simonov test. Independent sample t-test was applied to compare quantitative data if assumption fulfilled otherwise we used Mann-Whitney U test. Pearson correlation was applied to see relationship between insulin and TNF-α. P-value ≤ 0.05 was considered as significant.

RESULTS

The mean age of cases and controls was 25.42 ± 4.16 years and 22.98 ± 3.35 years, with significantly lower mean age in controls, p-value < 0.001 (Table 1).

Table No.1: Comparison of age in both cases and controls

Group	Mean±SD	P value
Case	25.42±4.16	<0.001
Control	22.98±3.35	

Table No.2: Comparison of BMI in both cases and controls

Group	Mean±SD	P value
Case	27.59±5.72	<0.001
Control	22.74±4.44	

Table No.3: Comparison of TNF- α in both cases and controls

Group	Mean±SD	P value
Case	66.14±122.37	0.001
Control	19.98±37.10	

Table No.4: Correlation between TNF-α with BMI in cases and controls

		Cases	Controls	Overall
TNF-α with BMI	Correlation (r)	-0.104	0.278	0.095
	p-value	0.525	0.082	0.403

The mean BMI was 27.59 ± 5.72 kg/m2 in cases and 22.74 ± 4.44 kg/m2 in controls with significantly higher mean BMI in cases, p-value < 0.001 (Table 2). Mean TNF-α was statistically higher in cases (66.14 ± 122.37 pg/ml) when compared to controls (19.98 ± 37.10 pg/ml), p-value < 0.05 (Table 3).

No significant correlation was found between TNF-α with BMI in cases, controls nor overall, p-value > 0.05 (Fig.1).

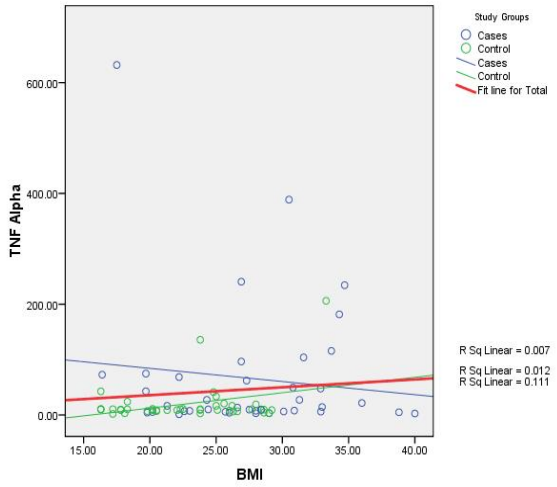

Figure No. 1: Scatter diagram of TNF-α and BMI

DISCUSSION

In our study, mean BMI was 27.59±5.72 kg/m2 in cases and 22.74±4.44 kg/m2 in controls with significantly higher mean BMI in cases, p-value < 0.001 (Table 2) Mean TNF-α was statistically higher in cases (66.14±122.37 pg/ml) when compared to controls (19.98±37.10 pg/ml), p-value < 0.05 (Table 3).

Victor et al[24] found that level of TNF–α is more in PCOS females as compared to control and a potential correlation exist between IR and inflammatory markers such as TNF-α and IL-6 in females with PCOS. Gonalez et al[25] also reported raised TNF-α in females with PCOS. Gonalez et al[25] further developed a positive correlation between TNF-α and BMI in females with PCOS. They also confirmed with his finding that the levels of TNF-α were higher in both normal and raised BMI females with PCOS and value is even higher in high BMI obese patients.

Cristiano et al[17] reported that no significant difference in TNF-α was observed in females of PCOS with normal BMI or high BMI. Randeva et al[26] also found no difference in levels of circulating cytokines including TNF-α in females with PCOS, whether thin lean or obese.

A meta-analysis study of women with PCOS reported no difference in TNF-α levels in women with PCOS and controls.[27] Another study found that no difference in levels of TNF-α exist in normal weight and overweight females.[28]

Seyam et al[29] in their analysis related TNF–α with BMI in PCOS patients and found that as BMI increases so does the level of TNF-α. In comparison to his study Mohlig et al[30] proved that PCOS is not associated with chronic inflammation. He in his studies argued that BMI is the strongest parameter related to chronic inflammation in in females with PCOS. The endocrinological parameters which are important in relation to PCOS do not result in low grade chronic inflammation and are not the risk factor for type II diabetes or metabolic syndrome. They also related BMI and IR with chronic inflammation not the disease itself. The risk of diabetes is linked to obesity and metabolic alterations and is encountered in such patients only.

Araya et al reported raised TNF–α levels in PCOS and found a positive correlation with BMI. TNF-α is implicated in affecting ovarian function and producing hyperandogeneamia.[31]

Several studies have reported raised TNF–α levels in PCOS but what is triggering this increase is not confirmed.[29-31] If only obesity is regarded as a key factor taking part in producing PCOS in females than lean individual should never suffer from the syndrome. It is established that PCOS is affecting both lean and obese subjects although obese individuals are more likely to have disease. So overweight and obesity are a risk factor for PCOS. Literature is also available showing contrary results. Possible explanation to contrary results is that not only BMI matters but also the pattern of obesity as well.[32,33]

Last but not the least is role of inflammation particularly TNF-α in PCOS and its relation with BMI. As mentioned level of TNF–α rises as BMI increases in females with PCOS. So inflammation also affects all the aspect of disease pathogenesis as well as its complications. Inflammation, insulin resistance and BMI play hand in hand in PCOS progression and complication but none can be regarded as a causative factor. By limiting and controlling these factors we can decrease the symptoms and eliminate morbid complications but cannot eliminate the disease.

CONCLUSION

Serum levels of TNF–α are raised in females with PCOS in both cases as well as controls but levels are significantly higher in cases so it can be regarded as a molecular marker for diagnosis of PCOS. No significant correlation was found between TNF-α and BMI in females with PCOS.

Author's Contribution:

Concept & Design of Study:	Imrana Ihsan
Drafting:	Asma Tehreem Kazi
Data Analysis:	Shafia Rasool Qazi
Revisiting Critically:	Imrana Ihsan, Asma Tehreem Kazi
Final Approval of version:	Imrana Ihsan

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

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Original Article

Risk Factors for Cardiovascular Diseases among Young Office Workers

Sidra Tufail, Iram Imran and Anam Shafi

ABSTRACT

Objective: To determine the frequency of risk factors associated with development of cardiovascular disease amongst young office workers.

Study Design: Descriptive / cross-sectional study.

Place and Duration of Study: This study was conducted at the Medical Outdoor Department of Services Hospital Lahore from 1st January 2017 to 31st July 2017.

Materials and Methods: A total of 150 office workers aged 25-35 years and either gender were included. Those employees that did not complete the proforma were excluded from the final analysis. The demographic details of family history, past history regarding diabetes, hypertension, hypercholesterolemia and MI were recorded. Other risk factors that were investigated included physical inactivity, smoking and occupational stress were also recorded.

Results: There 120 males and 30 females with mean age of the patients was 31.2±3.9 years. .Occupational stress was identified as the most important risk factor found in upto 80% of the employees. Other common risk factors included smoking prevalent in 45.8% of workers and lack of physical activity reported by 40% of the employees. Diabetes was prevalent in only 6.7% of the workers.

Conclusion: Occupational stress, physical inactivity and smoking are the common risk factors prevalent among young employees. These potentially modifiable risk factors need to be controlled in order to reduce the incidence of cardiovascular disease.

Key Words: Cardiovascular diseases (CVD), Occupational stress, Hypercholesterolemia

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INTRODUCTION

Cardiovascular diseases are a major cause of mortality and morbidity worldwide.[1] It is estimated that nearly seven million people are diagnosed with myocardial infarction (MI) each year.[2] Numerous risk factors have been identified in the past. These include both modifiable and non modifiable risk factors. Non-modifiable risk factors include advancing age, gender, family history of CVD and ethnicity. These are to be taken for granted and nothing can be done about them. Modifiable risk factors include hypertension, diabetes, physical inactivity, obesity, unhealthy diet, smoking and dyslipidemias.[3] These are extremely important to recognise and understand as these can be controlled in order to reduce the risk of developing CVD.

Millions of people go to office daily around the world. Office routine usually involves sitting for long hours in front of a screen. Moreover there are deadlines to meet every other week and this makes office job quite stressful.

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This sedentary lifestyle increases the risk of developing CVD in the long run.[4] In fact a recent review by Kivimaki et al[5] concluded that work stressors, such as job stress and long working hours, are associated with increased risk of coronary heart disease and stroke. An earlier meta-analysis[6] found out that lowering office stress can reduce the incidence of coronary heart disease (CHD).The main reason for a increased risk of CVD secondary to office job is the excessive sedentary time spent. In fact a study by Parry et al[7] showed that sedentary time accounted for 81.8% of work hours which was significantly higher than sedentary time during non-work time (68.9% $p < 0.001$).In addition to the risk factors identified above, young office workers are under increased stress especially in our setup. Unemployment rate is quite high and even if they find job after months of distress, the jobs are usually low paying and working hours are long. Moreover, additional responsibilities are suddenly put on their shoulders and sooner stressors of married life come into play. All this leads to increased stress on the individual.

Only a few local studies are available discussing the risk factors of CVD amongst office workers. Sultana et al[8] identified smoking, age, family history, high cholesterol levels and occupational stress as the important risk factors amongst office workers. They did not conducted their study solely on young workforce rather only 35% of the patients belong to 25-35 years age bracket. Owing to scarcity of literature regarding the topic, we decided to conduct this study with

objective of determining the frequency of various risk factors associated with CVD amongst young office workers.

MATERIALS AND METHODS

This descriptive cross sectional study was conducted from January 2017 to July 2017 in Medical Outdoor Department of Services Hospital Lahore where all these young office workers visited for these problems. A total of 150 office workers aged 25-35 years and either gender were included. Those employees that did not complete the proforma were excluded from the final analysis. The proforma included demographic details, family history, past history regarding diabetes, hypertension, hypercholesterolemia and MI. Other risk factors that investigated and included physical inactivity, smoking and occupational stress. Smokers were operationally defined as those that even smoke a single cigarette per day. Those who had never smoked or had quit smoking ≥5 years ago were classified as non-smokers.

SPSS version 21.0 was used to analyze data. Mean and standard deviation was calculated for all quantitative variables like age etc. Frequency and percentage was calculated for all qualitative variables like gender and the various risk factors etc. Data was represented as bar graphs and pie charts.

RESULTS

There were 120 males (80%) and 30 females (20%). Occupational stress was identified as the most important risk factor found in upto 80% of the employees. Half of the patients reported moderate stress whereas extreme stress was found in approximately 16.7% of the workers (Table 1). Mean age of the patients was 31.2±3.9 years.12% of the office workers were found to be obese with a BMI of 30 or above while 40% were found to be overweight (BMI = 25-29.9).

Table No.1: Demographic information of the patients

Variable	No.	%
Gender		
Male	30	20.0
Female	120	80.0
Occupational stress		
Extreme stress	25	16.7
Moderate stress	75	50.0
Mild stress	20	13.3
No stress	30	20.0

Other common risk factors included smoking prevalent in 45.4% of workers and lack of physical activity reported by 40% of the employees. Diabetes was prevalent in only 6.7% of the workers (Table 2).

Table No.2: Risk factors for cardiovascular disease

Risk factor	No.	%
Occupational stress	120	80.0
Physical activity	60	40.0
Smoking	68	45.4
Family history of CVD	35	23.3
Diabetes	10	6.7
Hypertension	25	16.7
Hypercholesterolemia	30	20

DISCUSSION

Cardiovascular diseases are responsible for millions of deaths each year around the globe. In 2013 alone, more than 17 million people died as a result of various cardiovascular diseases.[9] Modern life is becoming increasingly stressful with little room for healthy activities such as exercise. As young people are emotionally vulnerable, they are more prone to develop anxiety and stress.[10] Stress triggers the person to start smoking.[11] All this eventually translates into increased risk of developing CVD.

We conducted this study with the aim of elucidating the various risk factors associated with CVD prevalent among young employees. Unlike us, Sultana et al[7] conducted their survey amongst office workers in general irrespective of a particular age bracket. This could account for the variation in trends observed by us. We identified occupational stress as the commonest risk factor prevalent in upto 80% of the employees. This was consistent with the findings of Sultana et al[7] who found out that occupational stress was present in 85% of the employees. Upto 50% of employees in our study had moderate degree of stress with only a small minority having mild stress (13.3%). In contrast, majority of employees in Sultana et al's[7] study had mild stress (37%).This could be due to fact that that young people are much more emotionally vulnerable.[12,13] Smoking was recognized as a risk factor in 45.8% of the cases in our study whereas only 19% of employees were smokers in Sultana et al's[8] study. This was also higher compared to a survey amongst healthcare professionals that showed smoking to be prevalent in 29% of the study population.[14] Diabetes, hypertension and hypercholesterolemia was reported in only 6.7%, 16.7% and 20% of the employees respectively. We observed a male to female ratio of 4:1 which was in line with the male predominance observed by Sultana et al. We only included patients aged 25-35 years as other age groups were beyond the scope of our study.

There were certain limitations to our study. Effect modifiers and confounders (gender, degree of stress) were not controlled. Ideally they should have been controlled via stratification and post stratification chi square test applied. Secondly, we used a non probability consecutive sampling technique. Lastly but most importantly our study was conducted amongst those office workers who for some reason visited the hospital

OPD. These patients might not be the true representative of a young office workforce as they were visiting hospital for some health related issue. But due to feasibility issues we had to conduct our study on those office workers attending OPD rather than reaching out in various offices for the survey.

Young employees are the backbone of a country's economy. It is important to be able to recognize these risk factors especially the ones that are modifiable. Controlling these modifiable risk factors will help reduce the incidence of CVD in the long run. Moreover, future surveys are warranted determining the knowledge of various risk factors of CVD amongst office workers as the knowledge of CVD risk factors is essential in bringing out the necessary lifestyle changes that will result in reduction in overall cardiovascular risk of an individual.[15,16]

CONCLUSION

Occupational stress, physical inactivity and smoking are the common risk factors prevalent among young employees. These potentially modifiable risk factors need to be controlled in order to reduce the incidence of CVD.

Author's Contribution:

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Revisiting Critically:	Sidra Tufail, Iram Imran
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Original Article

Associations Between Artificially Sweetened Beverages and Obesity Among UK Children

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ABSTRACT

Objective: to examine the association between artificially sweetened beverage (ASB) consumption and obesity/overweight in a large, nationally representative sample of UK children.

Study Design: Observational / cross-section study.

Place and Duration of Study: This study was conducted at Avicenna Medical & Dental College, Lahore December 2017 to February 2018.

Materials and Methods: Data came from the UK Millennium Cohort Study sweep 5. The sample included 13,287 children aged 10-12 years. Multinomial regression models were run to examine the associations between ASB consumption and obesity, after adjusting for socio-demographic factors and physical activity.

Results: A significant association between ASB consumption and obesity was detected in multinomial regression models. After adjusting for socio-demographic factors and physical activity, children who frequently consumed ASB had a 59% (CI: 1.36-1.85) increased relative risk of being overweight and a 2.39 times (CI: 1.82-3.13) greater relative risk of being obese than those with no ASB consumption.

Conclusion: ASB consumption was found to be significantly associated with obesity. Further research is needed on the role of added sugars and artificial sweeteners in beverages for childhood obesity. A further comprehensive research with intervention design is recommended.

Key Words: Artificially Sweetened Beverages, Obesity, Obesity among children, Childhood Obesity, Weight Gain in childhood.

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INTRODUCTION

Obesity is a world-wide phenomenon[1] and a major public health problem[2]. It is a huge burden on the worldwide economy, affecting a significant proportion of the world population. The harmful aspects of obesity also affect overall general health, quality of life of individuals, as well as the economy of communities and countries[3]. The global rise in obesity is universal in high income, middle income and many low income countries[4].

Childhood obesity is also becoming a major problem and a pandemic.Sugar is one of the major causes of obesity and sugar added into commercial beverages are thought to pose a risk to obesity and weight gain[5]. The role of Artificially Sweetened Beverages (ASB) on health and weight status has so far been controversial and the evidence on the association between obesity and ASB is inconsistent in its findings. This study will therefore examine the role played by the consumption of artificially sweetened beverages in childhood overweight and obesity.

Artificially sweetened beverages (ASB) have emerged as a substitute to Sugar-sweetened Beverages (SSB) with the aim of providing the appetency of sweetness without adding calories. But, their role still remains questionable.

Epidemiological studies and large-scale surveys, reviewing on metabolic effects of artificial sweeteners in young people have found associations between artificial sugar intake and weight gain[6].

Some of the studies have reported that ASB consumption was positively associated with obesity in epidemiological studies but no association was found in interventional studies[7]. Some Studies concluded a strong cross-sectional association between diet soda consumption and weight gain in young adults[8]. Consumption of sugar containing beverages is a behaviour influenced by socio-economic determinants[9]. Socio-economic factors like maternal education, family income, child's ethnicity, social class play important role in developing hazardous behaviours for health[10, 20]. Moreover, physical activity is an important confounder to be considered. These socio-demographic and

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confounding covariates were not always included in previous studies.

Artificially sweetened beverages (ASB) have emerged as a substitute to SSB with the aim of providing the appetency of sweetness without adding calories. But, their role still remains questionable.

MATERIALS AND METHODS

This study is based on the secondary data analysis of data from the Millennium Cohort Study (MCS). The MCS is housed by the Centre for Longitudinal Studies (CLS).

The data used in this study came from the 5th sweep (MCS5), when the children were 11 years old.

The total number of cohort members[11] was 13,469 but after taking out those with missing values, total number of study participants were 13,287.

In MCS, data were collected through house-hold questionnaire along with face-to-face interviews. The outcome measure among children was Obesity having 3 categories namely not overweight (including underweight), overweight and obese. Exposure to the outcome was frequency of ASB consumption. It has 7 categories: More than once a day, once a day, 3-6 days a week, 1-2 days a week, less often but at least once a month, Less than once a month, Never. The association between the risk and outcome was adjusted for age, sex, ethnic background, education level of mothers, socio-economic status and physical activity.

The statistical analyses were carried out using STATA 12.0 (StataCorpLP).

Multinomial regression was used to examine the associations with overweight and obesity, a variable with 3 categories. Relative Risk Ratios (RRR) for being overweight/obese with 95% confidence intervals were estimated for association of obesity with ASB consumption using multinomial regression models. The regression analysis had 3 models. Model A showed unadjusted or crude association. Model B showed adjusted results only with demographic and socio-economic association. Model C was fully adjusted model with socio-demographic and confounding factors.

RESULTS

The sample characteristics are shown in Table 1. Of 13,287 total participants, 51% were males.

Most of the children in the sample (67%) were 11 years old. Of all children, 21% were overweight and 7% were obese. In relation to the consumption of artificially sweetened drinks (ASB), 20% of children reported no ASB consumption. About 35% of mothers in the sample had a university degree or higher, while 14% of mothers reported no educational qualifications. The majority of the sample (83%) belonged to White ethnicity. 23% of children reported no regular physical activity while 9% of children recorded physical activity of 5 or more days a week.

Table No. 1. Sample characteristics N: 13,287

Variable	N	%
Sex: Male	6,713	50.52
Female	6,574	49.48
Missing	0	
ASB Consumption: Never	2,654	19.97
<Once a month	860	6.47
Once a month at least	1,074	8.08
1-2 days/week	1,900	14.30
3-6 days/week	1,135	8.54
Once a day	2,268	17.07
>Once a day	2,743	20.64
Missing	653	4.91
Child's Age		
10 Years	4,378	32.95
11 Years	8,843	66.55
12 Years	66	0.50
Obesity Flag		
Not overweight+ under-weight	9,294	69.95
Over-weight	2,717	20.45
Obese	860	6.47
Missing	416	3.13
Mother's Education		
Level 5	1,053	7.93
Level 4	3,627	27.30
Level 3	1,146	8.62
Level 2	3,883	29.22
Level 1	1,214	9.14
Overseas only	449	3.83
None of above	1,865	14.04
Missing	50	0.38
Child Ethnicity		
White	10,992	82.73
Mixed	383	2.88
Indian	340	2.56
Pakistani & Bangladeshi	948	7.13
Black	431	3.24
Other Ethnic groups	190	1.43
Missing	3	0.02
Equivalised Income Quintiles		
Top Quintile	2,366	17.81
2nd Quintile	2,578	19.40
3rd Quintile	2,751	20.70
4th Quintile	2,778	20.91
Bottom Quintile	2,814	21.18
Parental Social Class (Current job)		
Managerial & Professional	3,351	25.22
Intermediate	2,014	15.16
Small employer	797	6.00
Low Supervisory & Technical	266	2.00
Semi-routine & routine	2,135	16.07
Missing	4,724	35.55
Frequency of Physical Activity		
5 or more days/week	1,101	8.29
4 days/week	1,001	7.53
3 days/week	1,932	14.54
2 days/week	2,564	19.30
1 day/week	2,776	20.89
<1 day/week	247	1.86
Not at all	3,024	22.76
Missing	642	4.83

Table 2. Multinomial Regression Analysis for ASB consumption and overweight/obesity. (No. of observations = 12,205)

Variables	Model A	Model B	Model C
	RRR (95% CI)	RRR (95% CI)	RRR (95% CI)
	Baseline Outcome = not overweight (Ref RRR: 1)		
	Overweight		
ASB Consumption: Never	Ref RRR: 1	Ref RRR: 1	Ref RRR: 1
<Once a month	1.02 (0.80-1.30)	1.05 (0.82-1.35)	1.07 (0.83-1.37)
Once a month	1.16 (0.94-1.43)	1.21 (0.98-1.49)	1.21 (0.98-1.50)
1-2 days/week	1.38 (1.16-1.64)***	1.41 (1.18-1.68)***	1.42 (1.19-1.70)***
3-6 days/week	1.45 (1.17-1.79)***	1.45 (1.16-1.80)***	1.45 (1.16-1.81)***
Once a day	1.38 (1.16-1.65)***	1.42 (1.18-1.70)***	1.41 (1.18-1.70)***
>Once a day	1.55 (1.33-1.80)***	1.58 (1.35-1.85)***	1.59 (1.36-1.85)***
Sex: Male		Ref RRR: 1	Ref RRR: 1
Female		1.28 (1.14-1.43)***	1.24 (1.11-1.39)***
Child age: 10 years		Ref RRR: 1	Ref RRR: 1
11 Years		0.93 (0.83-1.04)	0.93 (0.83-1.03)
12 Years		1.60 (0.71-3.59)	1.66 (0.74-3.73)
Mother's Education: Level 5		Ref RRR: 1	Ref RRR: 1
Level 4		1.04 (0.84-1.28)	1.04 (0.84-1.29)
Level 3		1.35 (1.04-1.74)*	1.33 (1.02-1.72)*
Level 2		1.40 (1.11-1.78)**	1.38 (1.08-1.75)**
Level 1		1.36 (1.04-1.78)*	1.31 (1.00-1.72)
Overseas only		1.27 (0.87-1.88)	1.25 (0.85-1.85)
None of above		1.39 (1.06-1.81)*	1.34 (1.02-1.75)*
Child's Ethnicity: White		Ref RRR: 1	Ref RRR: 1
Mixed		1.34 (0.99-1.82)	1.32 (0.98-1.80)
Indian		1.36 (0.99-1.88)	1.30 (0.95-1.79)
Pakistani & Bangladeshi		1.50 (1.23-1.83)***	1.43 (1.18-1.74)***
Black		1.97 (1.50-2.60)***	1.91 (1.45-2.52)***
Other Ethnic groups		1.03 (0.57-1.83)	0.97 (0.54-1.74)
Equivalised Income Quintiles			
Top Quintile		Ref RRR: 1	Ref RRR: 1
2nd Quintile		1.03 (0.86-1.23)	1.03 (0.86-1.22)
3rd Quintile		1.09 (0.91-1.30)	1.07 (0.90-1.27)
4th Quintile		1.10 (0.91-1.33)	1.06 (0.87-1.28)
Bottom Quintile		0.87 (0.71-1.08)	0.84 (0.68-1.04)
Parental Social Class			
Managerial & Professional		Ref RRR: 1	Ref RRR: 1
Intermediate		0.88 (0.73-1.05)	0.87 (0.72-1.05)
Small employer		1.09 (0.85-1.41)	1.08 (0.84-1.39)
Low Supervisory & Technical		1.09 (0.72-1.65)	1.08 (0.71-1.62)
Semi-routine & Routine		1.04 (0.86-1.25)	1.02 (0.84-1.23)
Missing		1.04 (0.89-1.21)	1.02 (0.87-1.18)
Frequency of Physical Activity			
5 or more days/week			Ref RRR: 1
4 days/week			0.99 (0.75-1.30)
3 days/week			1.08 (0.86-1.37)
2 days/week			1.08 (0.87-1.34)
1 day/week			1.46 (1.20-1.78)***
<1 day/week			1.70 (1.14-2.52)**
Not at all			1.33 (1.08-1.63)**
Constant	0.22 (0.20-0.25)***	0.11 (0.09-0.15)***	0.10 (0.07-0.14)***
	Obese		
ASB Consumption: Never	Ref RRR: 1	Ref RRR: 1	Ref RRR: 1

<Once a month	0.73 (0.44-1.24)	0.76 (0.45-1.29)	0.77 (0.46-1.31)
Once a month	1.26 (0.86-1.84)	1.43 (0.97-2.10)	1.41 (0.96-2.09)
1-2 days/week	1.77 (1.25-2.51)***	1.83 (1.29-2.60)***	1.86 (1.31-2.64)***
3-6 days/week	1.76 (1.17-2.64)**	1.71 (1.16-2.53)**	1.71 (1.15-2.52)**
Once a day	1.95 (1.45-2.63)***	2.04 (1.50-2.77)***	2.03 (1.49-2.76)***
>Once a day	2.41 (1.86-3.13)***	2.40 (1.84-3.14)***	2.39 (1.82-3.13)***
Sex: Male		Ref RRR: 1	Ref RRR: 1
Female		1.18 (1.00-1.39)*	1.12 (0.95-1.33)
Child age : 10 Years		Ref RRR: 1	Ref RRR: 1
11 Years		0.89 (0.74-1.09)	0.90 (0.74-1.09)
12 Years		0.93 (0.29-3.05)	0.98 (0.30-3.16)
Mother's Education: Level 5		Ref RRR: 1	Ref RRR: 1
Level 4		1.09 (0.70-1.70)	1.08 (0.69-1.69)
Level 3		1.17 (0.68-2.00)	1.14 (0.66-1.95)
Level 2		1.57 (0.95-2.60)	1.52 (0.92-2.52)
Level 1		2.32 (1.35-3.96)**	2.17 (1.26-3.72)**
Overseas only		1.74 (0.89-3.41)	1.72 (0.89-3.35)
None of above		2.13 (1.23-3.71)**	2.00 (1.15-3.50)**
Child's Ethnicity: White		Ref RRR: 1	Ref RRR: 1
Mixed		1.85 (1.19-2.87)**	1.81 (1.17-2.80)**
Indian		0.87 (0.44-1.72)	0.82 (0.42-1.61)
Pakistani & Bangladeshi		1.61 (1.18-2.20)**	1.51 (1.10-2.07)*
Black		3.39 (2.10-5.49)***	3.25 (2.01-5.24)***
Other Ethnic groups		0.85 (0.30-2.45)	0.79 (0.27-2.29)
Equivalised Income Quintiles			
Top Quintile		Ref RRR: 1	Ref RRR: 1
2nd Quintile		1.10 (0.76-1.58)	1.08 (0.75-1.56)
3rd Quintile		1.45 (0.97-2.16)	1.39 (0.94-2.06)
4th Quintile		1.81 (1.20-2.74)**	1.68 (1.10-2.55)*
Bottom Quintile		1.17 (0.77-1.76)	1.09 (0.72-1.65)
Parental Social Class			
Managerial & Professional		Ref RRR: 1	Ref RRR: 1
Intermediate		0.95 (0.68-1.33)	0.95 (0.68-1.32)
Small employer		1.48 (1.00-2.20)	1.44 (0.97-2.14)
Low Supervisory & Technical		1.30 (0.71-2.38)	1.25 (0.68-2.28)
Semi-routine & Routine		1.02 (0.73-1.42)	1.00 (0.71-1.39)
Missing		1.21 (0.90-1.62)	1.17 (0.87-1.57)
Frequency of Physical Activity			
5 or more days/week			Ref RRR: 1
4 days/week			1.25 (0.70-2.23)
3 days/week			1.25 (0.76-2.03)
2 days/week			1.71 (1.06-2.78)*
1 day/week			2.03 (1.29-3.17)**
<1 day/week			2.88 (1.53-5.41)***
Not at all			2.02 (1.26-3.23)**
Constant	0.05 (0.04-0.07)***	0.02 (0.01-0.03)***	0.01 (0.00-0.02)***

*p<0.05 **p<0.01 ***p<0.001

Table 2 presents the multinomial regression models for the association between ASB consumption and overweight/obesity. Total observations in this model were 12,205 after excluding observations with missing data.

In model A, the frequency of ASB consumption was associated with overweight and obesity risk. Children consuming ASB more than once a day were 55% more likely to be overweight as compared to non-consumers (RRR=1.55; CI: 1.33-1.80). Further, more than once a day ASB consumption was associated with a more than 2 times increased risk of being obese (RRR=2.41; CI: 1.86-3.13). The association with obesity was linear and with overweight almost linear, meaning that the risk of being overweight or obese increased the more frequently ASB were consumed.

Model B adjusted for demographic and socioeconomic factors. Adjustment for aforementioned factors did not lead to any substantial changes in the association between ASB consumption and overweight/obesity. As before, being female, low maternal education, Pakistani, Bangladeshi and Black ethnicities were significantly associated with both overweight and obesity risks.

Model C additionally adjusted for the frequency of physical activity, which as before was associated with both overweight and obesity. However adjusting for physical activity did not affect the association with ASB consumption.

DISCUSSION

This study analysed data from UK's Millennium Cohort study to explore the association between beverages' consumption and obesity. The survey gathered the information about the frequency of drinking artificially sweetened beverages among UK children. This study provided evidence of an association between ASB consumption and overweight/obesity. After adjustment for socio-demographic variables and physical activity, children who consumed ASB more than once a day had a 1.59 times increased risk of being overweight and a 2.39 times increased risk of being obese, compared to non-consumers. These findings are consistent with previous studies on the effects of artificial sugars[6, 17]. This association is attributed to multiple plausible behavioural mechanisms such as sweet taste dissociation from caloric consumption may enhance appetite resulting in increased food consumption and weight gain[4,18]. Moreover, poor diet quality is associated with raised uptake of added caloric sweeteners[12,13]. Multinomial models of ASB consumption showed that females were more susceptible to be overweight and obese and this phenomenon is observed and confirmed by other studies as well[19]. Mother's education appeared to be a significant protective factor in all multinomial analyses. Children whose mothers had no qualifications were at higher risk of being overweight or obese compared to those with high maternal education. The analyses showed that children doing physical activity for less than one day a week had an almost 3 times higher risk of being obese than those involved in physical activity of 5 or more days. This impact was supported by evidence from other studies[14, 15, 16].

Strengths of this study was analysis on a large study data and adjustment and controlling for confounding factors that play important role in the development of various unhealthy behaviours among children. This study used a large sample from Millennium cohort study sweep 5 which included nationally representative data of UK children. The sampling methods were standardized so that every region of the country shows equalized representation. Weaknesses of this study include cross-sectional study design that is insufficient to make an inference between exposure and outcome. This study also did not look at the dietary habits of the children that may act as a confounding factor in being over-weight/obese. Further research is recommended on the associations between artificially sweetened beverages and obesity among children as well as adults.

CONCLUSION

Analyzing UK children at the age of 11, this study provided evidence of a significant association between artificially sweetened beverages and obesity keeping in consideration the confounding factors like Socio-economic status, maternal education and physical activity.

Author's Contribution:

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Original Article

Is the Lung Recruitment and Titrated Positive End Expiratory Pressure a Better Strategy as Compare to Low PEEP on Mortality in Patients with Acute Respiratory Distress Syndrome

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ABSTRACT

Objective: To establish whether lung recruitment maneuver with PEEP titration reduces 28-day mortality in patients with moderate to severe ARDS in comparison to low PEEP strategy.

Study Design: A Randomized Control Trial.

Place and Duration: This study was conducted at the Intensive Care Unit Nishtar Hospital, Ibn e Sina Hospital, City Hospital, Multan from February 2016 to January 2018.

Materials and Methods: A total of 490 patients were divided in two equal groups on the base of technique use as Lung recruitment maneuver with PEEP titration RP Group and in patents low PEEP (LP Group) was used to treat ARDS. Primary outcome was all-causes mortality up till 28 days. Secondary outcome included length of ICU and hospital stay, ventilator-free days, pneumothorax or barotrauma within seven days. Chi square test and student T tests were used to analyze data. P value ≤ 0.05 was considered significant.

Results: Death ≤28 days was observed as (58%) and (51%) for lung recruitment maneuver with PEEP titration group and low-PEEP group respectively. The difference was statistically insignificant (p=0.058). Deaths in intensive care unit, in hospital and within 6 months was observed as (62%) and (51.8%), (59.6%) and (50.6%), (70.6%) and (58%) for lung recruitment maneuver with PEEP titration group and low-PEEP group respectively

Conclusion: There is no significant difference of 28-day survival and decrease hospital stay, ICU Stay, and on ventilator duration, so lung recruitment maneuver and PEEP titration is not a better and effective strategy as compare to low PEEP.

Key Words: Positive end expiratory pressure, Mechanical ventilation, Acute respiratory distress syndrome, PEEP titration, recruitment maneuver

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INTRODUCTION

One of the common and grave clinical conditions encountered by severely ill patients is acute respiratory distress syndrome (ARDS)[1]. It is correlated with increased levels of mortality and decreased levels of health-related quality of life[2.] There is reduction in functional lung size as a result of non-aeration or poor aeration of multiple lung units due to consolidation, flooding or collapse[3]. There is an increased risk of ventilator induced injury among such patients as a result of over expansion of lungs and rhythmic opening and closure of small alveoli [4].

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The target of recruitment strategies and positive end expiratory pressure (PEEP) is the opening of collapsed lungs and keep them opened, thereby reducing the atelectasis[5,6]. There were two randomized trials that compared analogous recruitment strategy following a decrease in PEEP versus well-adjusted reduced PEEP maneuver proves to be propitious with regards to oxygenation, inflammation, respiratory tree compliance in the absence of increasing risk of barotrauma or other adverse effects [7, 8]. Further systemic reviews showed a decrease in mortality rate in the absence of barotrauma[9,10]. Thence, we conducted Alveolar Recruitment for ARDS Trial (ART) in order to determine if lung recruitment maneuver along with PEEP in accordance with best respiratory tree compliance versus well-adjusted low PEEP strategy ameliorates clinical outcomes in patients having moderate to severe ARDS.

MATERIALS AND METHODS

It was a randomized control trial conducted in Intensive Care Unit Nishtar Hospital, Ibn e Sina Hospital, City Hospital, Multan from February 2016 to January 2018.

A total of 490 patients were divided into two equal groups. Group RP in which lung recruitment maneuver and titration PEEP and group LP in which Low PEEP used.

Patients having invasive mechanical ventilation suffering from moderate to severe ARDS no more than 72 hours were included in the study. Exclusion criteria included less than 18 years of age, having mean arterial pressure lower than 65mmHg, vasoconstrictor drug usage in previous two hours, contraindicated to hypercapnia. Mechanical ventilation was given for three hours with low PEEP and low tidal volume.

The patients belonging to LP group received the low PEEP strategy. While the RP group received neuromuscular blocker in the form of a bolus and maintenance of hemodynamic status was done through IV fluids administration when the signs of fluid responsiveness were seen. Then the maneuver of lung recruitment was performed with increasing levels of PEEP, following decreasing levels of PEEP titrated in accordance with respiratory system compliance and secondary recruitment maneuver. The levels of PEEP were weaned once the PaO2:FIO2 became stable or kept on increasing within 24 hours. It was reduced by 2cmH2O in every eight hours. Other than PEEP titration and lung recruitment maneuvers, rest of the clinical care was similar for both the groups.

Primary upshot was 28-day mortality. Secondary outcome included duration of hospital and ICU stay, pneumothorax needing drainage within seven days, ventilator-free days, and mortality in hospital, ICU or 6-month mortality. The other exploratory outcomes included hypoxemia within seven days, death with barotrauma or refractory acidosis within seven days.

The effects of intervention on categorical variables were determined and presented as frequency and percentages. X2 test was used for the comparison among differences between two groups. P value equal or less than 0.05 was taken significant.

RESULTS

Base line findings for both groups were described in (Table **I**).

Table No. I: Baseline characteristics of the patients

Variables	RP Group n=245	LP Group - n=245	P Value
Age	45.88±4.89	48.34±3.99	0.000
Gender: Male	(60%) n=147	(61.6%) n=151	0.711
Female	(40%) n=98	(38.4%) n=94	
SAPS 3 score	62.76±9.64	62.19±8.64	0.493
No. of non-pulmonary organ failures	2.08±0.82	2.04±0.64	0.583
Septic shock	(63.3%) n=155	(63.7%) n=156	0.925
Cause of ARDS			
Pulmonary ARDS	(63.3%) n=155	(55.5%) n=136	0.081
Pneumonia	(52.7%) n=129	(49%) n=120	0.000
Gastric aspiration	(6.5%) n=16	(2%) n=5	0.014
Lung contusion	(4.1%) n=10	(1.6%) n=4	0.104
Near drowning	(5.7%) n=14	(2.0%) n=5	0.000
Extra pulmonary ARDS	(39.2%) n=96	(41.0%) n=100	0.000
Non-septic shock	(20%) n=49	(2.9%) n=7	0.000
Sepsis or septic shock	(19.6%) n=48	(19.6%) n=48	0.000
Trauma without lung contusion	(0.8%) n=2	(0%) n=0	0.156
Cardiac surgery	(9.0%) n=22	(7.3%) n=18	0.509
Other major surgery	(4.1%) n=10	(1.2%) n=3	0.049
Head trauma	(8.6%) n=21	(0.4%) n=1	0.000
Smoke inhalation	(9.4%) n=23	(6.1%) n=15	0.177
Multiple transfusions	(1.2%) n=3	(3.7%) n=9	0.079
Drug or alcohol abuse	(1.6%) n=4	(1.6%) n=4	0.000
Other	(5.7%) n=14	(4.1%) n=10	0.402
Prone position	(6.5%) n=16	(11.4%) n=28	0.058
time since onset of ARDS,	0.11±0.32	0.12±0.33	0.783
Days intubated prior to randomization	15.03±3.61	16.03±2.67	t0.000
Respiratory measures,			
PaO_2:FIO_2	1.97±0.94	1.97±0.67	1.0
Tidal volume, mL/kg predicted body weight	119.14±3.36	114.75±6.60	0.000
Plateau airway pressure, cm H_2O	5.78±1.18	5.65±2.03	0.398
Minute ventilation, L/min	25.78±3.23	27.13±2.98	0.000
Respiratory rate, breaths/min	8.87±2.42	8.87±2.98	0.991
Driving pressure, cm H_2O	25.22±3.12	25.97±2.93	0.006
Positive end-expiratory pressure, cm H_2O	13.41±2.25	14.13±3.96	0.014
Respiratory system static compliance, mL/cm H_2O	12.28±2.13	13.0±1.73	0.000

Table No.2: Outcomes among Patients Treated With Lung Recruitment Maneuver With Positive End-Expiratory Pressure (PEEP) vs Low-PEEP Strategy

Variables	Lung Recruitment Maneuver With PEEP Titration Group n=245	Low-PEEP Group n=245	P value
Primary Outcome			
Death ≤28 day	(58%) n=142	(51%) n=125	**0.058**
Secondary Outcome			
In intensive care unit	(62%) n=152	(51.8%) n=127	**0.023**
In hospital	(59.6%) n=146	(50.6%) n=124	**0.046**
Within 6 months	(70.6%) n=173	(58%) n=142	**0.003**
Length of stay			
Intensive care unit	20.42±14.58	22.35±10.81	**0.000**
Hospital stay	28.45±15.65	31.25±9.61	**0.000**
No. of ventilator-free d from d 1 to d 28	6.87±4.56	8.47±5.10	**0.000**
Pneumothorax requiring drainage ≤7 d	(6.9%) n=17	(1.0%) n=3	**0.235**
Barotrauma ≤7 d	(5%) n=12	(4%) n=10	**0.051**
Exploratory Outcomes			
Death			
Within 7 d	(7.3%) n=18	(2.4%) n=6	**0.012**
With refractory hypoxemia ≤7 d	(37.6%) n=92	(4.5%) n=11	**0.000**
With refractory acidosis ≤7 d	(10.6%) n=26	(11%) n=27	**0.884**
With barotrauma ≤7 d	(12.2%) n=30	(12.7%) n=31	**0.891**
Cardiorespiratory arrest on day 1	(2.0%) n=5	(2.4%) n=6	**0.760**
Need of commencement or increase of vasopressors or hypotension (MAP <65 mm Hg) within 1 h	(3.3%) n=8	(5.7%) n=14	**0.191**
Refractory hypoxemia (PaO2<55 mm Hg) ≤1 h	(36.3%) n=89	(29%) n=71	**0.083**
Severe acidosis (pH<7.10) ≤1 h	(0.4%) n=1	(2.0%) n=5	**0.100**

Table No.3: Effects of the Lung Recruitment Maneuver With Titrated PEEP vs the Low-PEEP Group on Mortality According to Subgroups

Variables	Lung Recruitment Maneuver With PEEP Titration Group n=245	Low-PEEP Group n=245	Test of Sig.
PaO_2:FIO_2			
≤100 mm Hg	(42%) n=103	(58%) n=142	**0.000**
>100 mm Hg	(58%) n=142	(42%) n=103	
Simplified Acute Physiology Score 3			
<50	(43.3%) n=106	(48.6%) n=119	**0.239**
≥50	(56.7%) n=139	(51.4%) n=126	
Type of ARDS			
Extrapulmonary	(43.3%) n=106	(55.9%) n=137	**0.005**
Pulmonary	(56.7%) n=139	(44.1%) n=108	
Duration of ARDS at randomization, hours			
≤36	(45.3%) n=111	(46.9%) n=115	**0.717**
>36 to <72	(54.7%) n=134	(53.1%) n=130	
Position 1 h after randomization			
Supine (dorsal decubitus) or lateral decubitus	(38%) n=93	(30.2%) n=74	**0.070**
Prone	(62%) n=152	(69.8%) n=171	
Duration of mechanical ventilation before randomization, day			
0-4	(49%)n=120	(47.3%) n=116	**0.718**
≥5	(51%) n=125	(52.7%) n=129	
Protocol modification			
Before	(38%) n=93	(53.5%) n=131	**0.001**
After	(62%) n=152	(46.5%) n=114	

The difference was statistically significant for age (p=0.000), pneumonia (p=0.000), near drowning (p=0.000), extra pulmonary ARDS (p=0.000), non-septic shock (p=0.000), sepsis or septic shock

(p=0.000), head trauma (p=0.000), drug or alcohol abuse (p=0.000), days intubated prior to randomization (p=0.000), tidal volume (p=0.000), minute ventilation (p=0.000), driving pressure (p=0.006), positive end-expiratory pressure (p=0.014) and respiratory system static compliance (p=0.000). (Table **1**).

The difference was statistically significant of secondary outcome in intensive care unit (p=0.023), in hospital (p=0.046), within 6 months (p=0.003), length of stay in intensive care unit (p=0.000), hospital (p=0.000) and no. of ventilator-free d from d 1 to d 28 (p=0.000). The difference was statistically significant death with refractory hypoxemia ≤7 d (p=0.000). (Table **2**). Effects of the lung recruitment maneuver with titrated PEEP versus the low-PEEP Group on mortality according to subgroups were shown in (Table **3)**. The difference was statistically insignificant simplified acute physiology score 3 (p=0.239), duration of ARDS at randomization, hours (p=0.717), position 1 h after randomization (p=0.070) and duration of mechanical ventilation before randomization, day (p=0.718) (Table. 3).

DISCUSSION

A recruitment maneuver by Povoa P et al [11] was performed in which effect of constant positive inspiratory pressure along with high PEEP was determined upon the static compliance and oxygenation in patients having severe ARDS. It was concluded that this recruitment maneuver was "safe and useful" in attempt to ameliorate the oxygenation and compliance static in patients having severe ARDS having lung ventilation added with lung protective strategy.

Neto AS et al [12] compared ventilation at various levels of PEEP in ICU patients without suffering from ARDS, it was observed that there was no difference between two levels of PEEP in seven RCTs as well as the duration of mechanical ventilation.

PEEP serves as protective role in preventing from atelectasis in patients undergone general anesthesia even when coupled with high inspired oxygen concentration, says Neumann P et al [13]. The results showed significant decrease in levels of atelectasis in patients where moderate levels of PEEP were maintained. There was a noteworthy relationship between PaO2 and atelectasis and similar study done by Martin JB et al [14] established the effect of PEEP and decreased levels of inspired oxygen and VC in preventing atelectasis in patients having general anesthesia.

With regards to arresting the postoperative pulmonary complications and reducing mortality in patients undergoing anesthesia, Barbosa FT et al [15] studied the effects of intraoperative PEEP. There were no complications reported. However, due to insufficient evidence, it cannot be said clearly if intraoperative PEEP ameliorates the postop complications and mortality.

The application of alveolar recruitment maneuver in patients with ARDS or acute lung injury is still controversial as said by Badet M et al [16]. There is no standard strategy in this regard. According to the results, the optimal levels of PEEP were found to be was 12 +/- 4 cm H(2)O., the other findings were as such "The measurements from the standardization periods were comparable between the 3 PEEP groups. In the optimal-PEEP-plus-sighs group the changes in P(aO(2)) (85 +/- 96%) and static compliance (14 +/- 20%) were significantly greater than in the 2 other groups".

Toth L et al [17] determined the hemodynamic and respiratory changes during lung recruitment maneuver and decreasing PEEP titration among patients suffering from ARDS. Whereas a negative correlation was found between CI and CVP and no correlation was present between mean arterial pressure and CI. After performing lung recruitment maneuver and decreasing PEEP titration, the levels of PaO2 ameliorates remarkably in the absence of variation in EVLW up till one hour. It shows that reduction in formation of atelectasis is due to the recruitment rather than due to reduction in EVLW. Although a change in CI is seen during the maneuver, however, CVP, MAP, or heart rate fail to show these changes.

Cruz S et al [18] compared high and low levels of PEEP in patients having ARDS or ALI on mechanical ventilation. The mortality as a result of ALI or ARDS can be reduced by mechanical ventilation. However, there is high risk of ventilator induced injury in these patients. It is assumed that higher levels of PEEP are helpful in reducing the injury and improving the survival of patient. PEEP is thought to improve the gaseous exchange as well as respiratory compliance but on the other hand, it may as well reduce the tissue injury and inflammation [19,20].

CONCLUSION

There is no significant difference of 28-day survival and decrease hospital stay, ICU Stay, and on ventilator duration, so lung recruitment maneuver and PEEP titration is not a better and effective strategy as compare to low PEEP.

Author's Contribution:

Concept & Design of Study:	Nadeem Ahmed Khan
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Conflict of Interest: The study has no conflict of interest to declare by any author.

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