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Editorial

Breast Cancer: An Overview

Mohsin Masud Jan
Editor

Every year about 90,000 women are diagnosed with the disease and some 40,000 lose their lives to it; Pakistan has the highest rate of breast cancer occurrence in Asia; one in nine woman is at the risk of contracting it, whereas in India one in every 22 gets it, while in USA it accounts for 29% of all cancers. These statistics are based on the number of women that have accessed treatment at hospitals in Pakistan. We do not know how many more women are out there with breast cancer who have not reached hospitals due to social stigma or any other reason.

In Pakistan, the average age of women getting this disease is 40, in the West it is 50. The disease is being diagnosed among very young girls as well, even as young as age 18.

Another reason hindering the collection of accurate statistics is that women in our culture do not talk about this disease. They hesitate to even mention the word 'breast'. It's just too private. Typically, in Pakistan a woman will not disclose even to her dearest ones that she's been detected with breast cancer. And if the dear ones know, they will try to hide her condition from the outside world. This prevents them from accessing treatment.

This mindset is prevalent even in the educated, elite class of the society. The worst is they'd rather marry off their daughter than treat her. They believe ignorance is bliss.

We are told everything and nothing causes breast cancer. Women who are childless have a higher chance, so do women who have not breastfed, are obese and have had children late, have a family history or are on hormone replacement therapy. And so do women who've had late menopause, been on contraceptive pill and started periods too late or too early. Then the bra factors creep in — wearing a bra for too long during the day or selecting a wrong one can increase the risk of getting breast cancer.

Latest studies suggest that injecting steroids in cows and buffalos during lactation is directly impacting the estrogen levels in women. Estrogen is linked to breast cancer. Additionally, sugar is highly cancerous.

The lack of research in Pakistan on breast cancer is a real problem. Research in bits and pieces is only giving out wrong signals. We need to do something on large scale. We know occurrence of breast cancer among Polish jews is high because of their genetic mutation. We do not know what is causing the disease in Pakistan. We need to look at our nutrition and for any genetic mutations.

Because of this ambiguity, early detection has become the recommended method to prevent a fatality. Breast cancer responds to treatment very well. There's a 90 per cent recovery chance in early cases, and even in cases of last stage treatment can help them live a comfortable life.

Self-detection is the first and a very important step. Girls as young as 18 must conduct breast examinations periodically. At any age, a lump cannot go unnoticed, even if you're breastfeeding. By age 40 you are supposed to get mammograms every two years. Mammography helps identify growth at a stage when it is not even palpable.

Over the years, the treatment of breast cancer has come a long way. The decision about treatment depends on the doctor who determines the stage of cancer and then goes ahead with the treatment. The staging process depends on different factors, including the size of the tumour, the number of lymph nodes affected and whether the cancer has spread to other parts of the patient's body.

The patients have to go for biopsy followed by surgery and, if required, chemotherapy and radiation. Quite often, all these processes have to be followed to ensure there is no recurrence of this disease. Radiation therapy is hardly available in the government sector as most of the radiation machines are non-operational and out of order.

Not addressing this disease in an organised manner is the main culprit here. Screening of women living in far off areas must be conducted through satellite setups or at family planning institutions. At an average, the treatment of breast cancer cost Rs.400,000 to 500,000 and so, as a matter of fact, early detection is the only solution to cost-effective treatment.

A dearth of training of medical practitioners further complicates the situation. We may have women trained to conduct physical examinations and mammography but the number of female surgeons is very low. Women often hesitate in getting surgeries done by male surgeons.

We should have an organised cancer control programme in the country.

Breast cancer diagnosis is mostly made at advanced stages in Pakistan as very few women go for regular self-checks or screening for breast cancer. Treatment is available according to the stage of the disease.

If detected at an early stage, the lump can be removed through surgery and without doing mastectomy or chemotherapy. But what happens is that most of the women diagnosed with breast cancer are at a stage where they have to get specialised and expensive medical treatment.

Cancer treatment facilities in the country are far less than what is required. According to international standards, there should be a cancer hospital for every 5 million people in a country but in Pakistan there are few.

Pakistan Atomic Energy Commission (PAEC) also has 18 cancer hospitals but these have a limited capacity. Of these 18 hospitals, there are two each in Karachi and Lahore and one each in Islamabad, Gujranwala, Faisalabad, Bahawalpur, Multan, Larkana, Nawabshah, Jamshoro, Quetta, D I Khan, Bannu, Peshawar, Abbottabad and Swat.

We need to address the treatment of breast cancer in an organized manner.

Original Article

UTI with Cerebral Palsy

Frequency of Urinary Tract Infection in Children with Cerebral Palsy

Rahida Karim[1], Jahanzeb Khan Afridi[1], Ahmad Saud Dar[1] and Muhammad Batoor Zaman[2]

ABSTRACT

Objectives: To study Frequency of urinary tract infection in cerebral Palsy Children.
Study Design: Descriptive / cross sectional study.
Place and duration of study: This study was conducted in the Department of Pediatrics, Hayatabad Medical Complex, Peshawar from 01.01.2016 to 31.12.2016.
Materials and Methods: Total of 113 children with cerebral palsy, selected in a consecutive sampling and mid-stream urine specimen was collected for urine culture to detect UTI. Cerebral Palsy children aged 3years to 15 years of both genders were included in the study. Those cerebral palsy children not fulfilling criteria were excluded
Results: The mean age group of the sample was 7.8 $\pm$ 3.6 years. 68.1% of the sample was male and 31.9% were female gender. In our study, UTI was recorded in 32.7% of patients with more propensities towards age group above 5 years ($p < 0.001$)
Conclusion: The present study points to a high prevalence of urinary tract infections (UTI) among in children with cerebral Palsy, which may be due to severe immobility. Therefore, rigorous efforts should be put in place for effective physiotherapy aimed at achieving the greatest possible mobility and independence among children with cerebral Palsy.
Key Words: Cerebral Palsy, Pyrexia, Urinary Tract Infection, Urine Culture.

Citation of articles: Karim R, Afridi JK, Dar AS, Zaman MB. Frequency of Urinary Tract Infection in Children with Cerebral Palsy. Med Forum 2018;29(2):3-6.

INTRODUCTION

Incidence of cerebral Palsy is 2-25/1000 live[1]. In the last 40 years this rate has not changed. LBW and prematurity are major risk factors for cerebral palsy. Very low birth weight infants are 20-80 times more prone to cerebral palsy than those infants having birth weight of 2.5 kg[2.] Risk factors must not be confused with etiology as cause is unknown in majority of cases. Motor damaged occur in CP subjects after series of insult[3].

Yearly incidence of CP in United States is 1 out of 278 infants[4.] To find the frequency of CP in Pakistan a trial was done on a sample of 160 cases with abnormality of tone, posture and movement, 120 out of the had CP[5.] Initially hypoxic ischemic encephalopathy was considered to be the cause of CP. In recent studies multiple factors are responsible for CP. Prenatal, and postnatal injury to developing brain due to any of determinant i.e genetic factors, low birthrate, prematurity and multiple gestation result in CP[6.]

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Mental retardation mental retardation, seizure disorders, abnormalities of vision, respiratory problems and lower A cerebral palsy child had injury to brain before it was fully matured. It is a non-progressive injury and they have difficulty in neuromuscular control. urinary tract dysfunctions or associate morbidities with cerebral palsy[7] urgency frequency hesitancy, urinary incontinence and urinary tract infection or manifestation or lower urinary tract dysfunctions[7].

The possibility of UTI in CP subjects may be due to Vesicoureteral reflux and incomplete bladder emptying resulting from detrusor hyperreflexia and detrusor sphincter dyssynergia. They have impaired cognition and are immobile, therefore cannot communicate regarding bladder fullness and need to micturate, as a result of urinary retention are prone urinary tract infections is reported in a study in 38.5% of CP children in a study by Anígilájé EA et al[8].

The present study is designed to determine the frequency of UTI in children presenting cp. As mentioned above, the CP children are very prone to Urinary tract abnormalities and neurogenic bladder if leads to reflux can cause UTI among children with CP. This study will highlight the magnitude of the problem and the results of this study will be shared with other local pediatricians and suggestions will be given regarding future research or screening of children presenting with CP for UTI.

MATERIALS AND METHODS

This study is descriptive / cross-sectional study, conducted in Department of Pediatrics Hayatabad Medical Complex, Peshawar. The duration of study was one year, sample size was 113, using proportion of 38.5% of UTI among children with CP, with 95% confidence interval and 9% margin of error using WHO sample size calculate sampling technique was non probability consecutive.

Children of both genders with ages 3 years to 15 years having Cerebral Palsy were included in the study.

Children with history of complicated UTI, history of antibiotic or steroid use in last one month were not enrolled in the study.

Data Collection Procedure: Hospital ethical research committee approved the study to be conducted. Those CP children who had fever and were fulfilling inclusion criteria were included in the study. Written informed consent was taken from parents after explaining them purpose and benefit of the study.

History and clinical examination was carried on all patients to be studied. From all the children, a two specimen of clean mid stream urine (02 hours apart) was obtained and sent to hospital laboratory to detect UTI. All the laboratory investigations was done under supervision of same consultant microbiologist having minimum of five years of experience.

A predesigned proforma was used to record all the information according to inclusion criteria and avoid confounders and bias by strictly adhering to exclusion criteria.

Data Analysis Procedure: SPSS version 20 was used to store data and analyse it quantitative variables like age were calculated by mean+-SD categorical variables like gender and UTI were calculated via frequencies and percentages. To see the effect modifications UTI was stratified among age and gender. Tables and graphs were used to present the results.

RESULTS

The study was conducted on 113 children with cerebral palsy who presented with fever.

The mean age of the sample was 7.8 $\pm$ 3.6 years. Minimum age of 3.5years to maximum 13.5 years with mean 10 years were age ranges in our study. Sample was grouped in different age groups, it was observed that patients in the age group up to 5 years were 33.6%, patients in the age group > 5 to 10 years were 36.3% and patients in the age group > 10 to 15 years were 30.1%. (Table 1).

Table No.1: Age-Wise Distribution of Sample (n=113)

Age Groups		Frequency	Percent
	Up to 5 years	38	33.6
	> 5 to 10 years	41	36.3
	>10 to 15 years	34	30.1
	Total	113	100.0

Table No.2: Gender-wise distribution of sample (n=113)

Gender		Frequency	Percent
	Male	77	68.1
	Female	36	31.9
	Total	113	100.0

Table No.3; Frequency of urinary tract infection (n=113)

UTI		Frequency	Percent
	Yes	37	32.7
	No	76	67.3
	Total	113	100.0

Table No.4; Age group wise stratification of UTI (n=113)

		Urinary Tract Infection		P Value
		Yes	No	
Age Groups	Up to 5 years	0	38	< 0.001
		0.0%	100.0%	
	> 5 - 10 years	29	12	
		70.7%	29.3%	
	>10 - 15 years	8	26	
		23.5%	76.5%	
Total		37	76	
		32.7%	67.3%	

Table No.5; Gender group wise stratification of UTI (n=113)

		Urinary Tract Infection		P Value
		Yes	No	
Gender of the patient	Male	23	54	0.34
		29.9%	70.1%	
	Female	14	22	
		38.9%	61.1%	
Total		37	76	
		32.7%	67.3%	

It was observed that in our study 68.1% of the sample was male and 31.9% were female gender, when the patients were distributed on the basis of their gender. (Table 2)

Form all the patients, a mid stream specimen of urine was collected in sterile container and was sent to hospital laboratory for detection of UTI which is defined where Urine analysis showed greater than or equal to 2-5 WBCs or 15 bacteria per high power field (HPF) in centrifuged urine sediment and the urine culture yielding growth of more than 10^5 organisms per ml of urine. In our study, UTI was recorded in 32.7% of patients. (Table 3).

We observed that the difference was statistically significant after applying chi square test with a p value of < 0.001, when UTI was stratified with respect to age group. (Table 4)

We observed that difference was statistically insignificant after applying chi square test with a p

value of 0.34, when UTI was stratified with respect to gender. (Table 5).

DISCUSSION

Acute urinary tract infection (UTI) is common problem of childhood. 8.4% of girls and 1.7% of boys experience at least one episode of UTI till they are seven years old[9]. Mortality is rare but morbidity is common. 40% of the patients need hospital admission particularly infants. Transient renal damage occurs in 40% patients and 5% get permanent damage[10]. This can occur even after a single infection. Younger children suffer from systemic symptoms such as fever, letchargi, anorexia and vomiting, localized symptoms are real. More than 80% of cases have UTI due to Escherichia coli[11], and are treated with a course of antibiotics.

Even those who had experienced single UTI are at risk for further infections, 30% children get recurrent UTI. Vesicoureteric reflux (VUR), previous infection and unstable bladder are risk factors for recurrent UTI[11, 13]. Girls are more prone to recurrent UTI than boys.

Febrile urinary tract infection is more common both sexes in first year of life, where as girls older than 3 years are more prone to nonfebrile UTI[14]. Localized symptom occur in urinary tract infections confined to bladder, they are common after infancy and are easily treatable in contrast febrile urinary infection increases probability of renal involvement (sensitivity 53 to 84%; specificity, 44 to 92%)[15]. This is usually associated abnormalities of urological system and greater risk of renal scarring[16]. Urinary tract infection leading to renal scarring has been considered as a cause of long term morbidity.[16] Children with proven urinary tract infections are intensively evaluated and treated. They receive antibiotic prophylaxis and often undergo surgery[15]. Such approaches have questioned[17,18]. Various studies and trials have been done, for assessment and management of febrile urinary tract infections and subsequent interventions for them.

In our study, we studied the frequency of UTI in children presenting with cerebral palsy and fever. We observed it to be 32.7% with equal propensity of either gender towards UTI. Studies that reported the epidemiology of UTI's in children have varied them by population, sampling method, and diagnostic criteria. Rates vary widely, from 0.25% in a small UK - GP study[19] to 13.5% in a hospital-based study of febrile infants[20].

In our study frequency of UTI is 32.7% which is comparable to Ozturk et al. in Turkey. Who reported 32.5%[21] but it is not comparable with Reid and Borzyskowski in London 7.4%[22]. And Hellquist et al in North Carolina 2.2%[23]. The differences in frequency of UTI in latter two studies[22, 23] may be due to the prior use of antibiotics, although not reported in our study. CP usually have repeated urinary symptomatology, constipation, enuresis and recurrent UTI confirmed by laboratory in comparison to age and sex matched non CP subjects. Ozturk et al. in also reported same findings.

CP children have difficulty in mobility, parents and siblings have to carry them from one place to another. Their families need manually propelled or electrically powered wheelchairs, for which they don't have access. These are neglected children who stay supine for long period of time resulting in development of pressure source on dependent body parts. They have poor personal hygiene and remain soil most of the time in their feces resulting in increase risk of UTI. Few of them may be continent but because of immobility retain urine, as are unable to attend the toilet resulting in UTI. Poor water intake due to immobility results in kidney stones which may predispose to UTI[24]. In addition some of these children have high burden of pinworms[25] which may be linked to higher risk of UTI. Poorly mobile CP children had propensity to develop constipation which also contributes to higher risk of UTI in this group of children.

We found that all the CP children with UTI are over-five in our study. These findings in our studies resulted due to recruitment bias as 65% patients included were over 5 years. When CP patients come for follow up in our clinics we should review symptoms of UTI as it presents symptomatically, it should be confirmed and treated in order to prevent its potential complications.

CONCLUSION

We concluded from this study that severe immobility in CP children is responsible for high prevalence of UTI, therefore efforts should be made for effective physiotherapy, so that CP children can attain maximum mobility and independence.

Author's Contribution:

Concept & Design of Study:	Rahida Karim, Jahanzeb Khan Afridi
Drafting:	Rahida Karim, Ahmad Saud Dar, Muhammad Batoor Zaman
Data Analysis:	Rahida Karim, Ahmad Saud Dar
Revisiting Critically:	Ahmad Saud Dar, Jahanzeb Khan Afridi, Muhammad Batoor Zaman
Final Approval of version:	Rahida Karim, Jahanzeb Khan Afridi

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

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Original Article

Fibroids of the Uterus and Outcome of Pregnancy

Outcome of Pregnancy in Fibroids

Anila Ansar[1], Ashba Anwar[2] and Neelam Saba[2]

ABSTRACT

Objectives: To study the outcome of pregnancy in Fibroids of the Uterus.
Design of Study: Prospective / Experimental Study.
Place and Duration of Study: This study was conducted at the Idris Teaching Hospital, Sialkot & Islam Teaching Hospital, Sialkot from August 2013 to August 2016.
Materials and Methods: This study was carried to seek out the result of maternity related to female internal reproductive organ fibroids and to find out the actual fact that each pregnant female should be screened for female internal reproductive organ fibroids (UF). If the fibroids diagnosed along with pregnancy, these patients want alert prenatal care and therefore the maternity ought to be treated as high risk maternity. Fifty pregnant females with fibroids of the uterus were enrolled during this Prospective Experimental Study. Performa was designed to record age, socio economic standing, area, complications in early, late maternity and delivery. Written informed consent was taken from every patient. Permission was additionally taken from ethical committee of the institutes. The data was analyzed on SPSS version ten for results.
Results: In this study it was observed that incidence of pregnancy with fibroids uterus was higher(54%) n=27 at the age of 31-35 years as compared to other age groups. The women of middle socio economic group had higher incidence of pregnancy with Fibroids of the Uterus (46%) n=23 as compared to other socio economic group of women. The women from rural areas had double incidence of pregnancy with Fibroids of the Uterus (68%) n=34 as compared to women having pregnancy with Fibroids of the Uterus from urban areas (32%) n=16. The incidence of miscarriage of pregnancy with Fibroids of the Uterus was maximum (28%) n=14 and patients of fetal growth restriction was minimum (04%)n=02 in complications of pregnancy. The incidence of Postpartum hemorrhage was maximum (46%) n=23 and minimum (08%) n=04 in case of retained placenta during delivery.

Key Words: Fibroids, Miscarriage, Preterm labor, Placenta disruption, fetal anomalies, Myomectomy, arterial blood vessel embolism.

Citation of articles: Ansar A, Anwar A, Saba N. Fibroids of the Uterus and Outcome of Pregnancy. Med Forum 2018;29(2):7-10.

INTRODUCTION

Fibroids are benign smooth muscle fiber tumors of the female internal reproductive organ. Though they are extraordinarily common, with associate degree overall incidence of forty to sixty percent at age of thirty five and seventy to eighty percent by age fifty, the precise etiology of female internal reproductive organ fibroids remains unclear[1]. The designation of fibroids in physiological condition is neither straight forward nor simple. solely forty two percent of huge fibroids (> five cm) and twelve. Five percent of smaller fibroids (3–5 cm) may be diagnosed on physical examination[2].

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The ability of ultrasound to find fibroids in physiological condition is even a lot of restricted (1.4%–2.7%) primarily because of the issue of differentiating fibroids from physical thickening of the smooth muscle[3,6]. The prevalence of female internal reproductive organ fibroids throughout physiological condition is so seemingly under-estimated. Reflective the growing trend of delayed childbearing, the incidence of fibroids in older girls undergoing treatment for physiological condition is reportedly twelve-tone system to twenty fifth[7]. Despite their growing prevalence, the connection between female internal reproductive organ fibroids and adverse physiological condition outcome isn't clearly understood.

Prospective studies exploitation ultrasound to follow the dimensions of female internal reproductive organ fibroids throughout physiological condition have shown that the bulk of fibroids (60%–78%) don't demonstrate any vital amendment in volume throughout physiological condition[8,9]. Of the twenty two percent to thirty two percent of fibroids that did increase in volume, the expansion was restricted nearly completely to the first trimester, particularly the first ten weeks of gestation, with little if any growth within the second and third trimesters. The mean increase in volume during

this cohort was solely twelve percent ± 6 tone system ± 6 June 1944, and therefore the most growth was solely twenty fifth of the initial volume[8]. Some studies have shown that little fibroids square measure even as seemingly to grow as massive fibroids,[8] whereas different studies have steered that little {and massive and enormous and huge} fibroids (≥ six cm) have totally different growth patterns within the trimester (small fibroids grow whereas large fibroids stay unchanged or decrease in size), however all decrease in size within the trimester (9,10). the bulk of fibroids show no amendment throughout the time period, although 7.8% can decrease in volume by up to 100%[8,9].

Most fibroids square measure well. However, severe localized abdominal pain will occur if a fibroid undergoes questionable "red degeneration," torsion (seen most ordinarily with a pedunculated sub serosal fibroid), or impaction. Pain is that the commonest complication of fibroids in physiological condition, and is seen most frequently in girls with massive fibroids (> five cm) throughout the second and third trimesters of physiological condition[3,11].

MATERIALS AND METHODS

This study was carried to find out the result of maternity related to female internal reproductive organ fibroids and to findout the actual fact that each pregnant female should be screened for female internal reproductive organ fibroids (UF). If the fibroids size measure & diagnosed along with pregnancy, these patients want special prenatal care and therefore the maternity ought to be treated as high risk maternity. Fifty pregnant females with fibroids of the uterus were enrolled during this Prospective Experimental Study. Performa was designed to record age, socio economic standing, area, complications in early, late pregnancy and delivery.

Written informed consent was taken from every patient. Permission was additionally taken from ethical committee of the institutes. The data was analyzed on SPSS version ten for results.

RESULTS

In this study it was observed that incidence of pregnancy with fibroids uterus was higher(54%) n=27 at the age of 31-35 years as compared to other age groups as shown in table 1. The women of middle socio economic group had higher incidence of pregnancy with Fibroids of the Uterus (46%) n=23 as compared to other socio economic group of women as shown in table 2. The women from rural areas had double incidence of pregnancy with Fibroids of the Uterus (68%) n=34 as compared to women having pregnancy with Fibroids of the Uterus from urban areas (32%) n=16 as shown in table 3. The incidence of miscarriage of pregnancy with Fibroids of the Uterus was maximum (28%) n=14 and patients of fetal growth restriction was minimum (04%)n=02 in complications of pregnancy as shown in table 4. The incidence of Postpartum hemorrhage was maximum (46%) n=23 and minimum (08%) n=04 in case of retained placenta during delivery as shown in table 5.

Table No. 1: Age distribution in Fibroids of the Uterus and outcome of Pregnancy

Sr No	Age (Years)	Cases	Percentage%
1	25-30	10	20%
2	31-35	27	54%
3	36-40	13	26%
	Total	50	100%

Table No. 2: Socio economic status distribution in Fibroids of the Uterus and outcome of Pregnancy

Sr No	Socio economic status	Cases	Percentage%
1	High	10	20%
2	Middle	23	46%
3	Low	17	34%
	Total	50	100%

Table No. 3: Area distribution in Fibroids of the Uterus and outcome of Pregnancy

Sr.No	Area	Cases	Percentage%
1	Urban	16	32%
2	Rural	34	68%
	Total	50	100%

Table No. 4: Complications of pregnancy in Fibroids of the Uterus

Sr No	Complications	Cases	Percentage%
1	Miscarriage	14	28%
2	Bleeding in early pregnancy	03	06%
3	Preterm labor	11	22%
4	Placental abruption	10	20%
5	Placenta previa	10	20%
6	Fetal growth restriction	02	04%
	Total	50	100%

Table No. 5: Complications of delivery in Fibroids of the Uterus

Sr. No	Complications	Cases	Percentage%
1	Malpresentation	13	26%
2	Postpartum hemorrhage	23	46%
3	Retained placenta	04	08%
4	Cesarean delivery	10	20%
	Total	50	100%

DISCUSSION

In our study it had been seen that incidence of physiological state with fibroids female internal reproductive organ was higher (54%) n=56 at the age of 31-35 years as compared to other age groups. The women of middle socio economic class had higher incidence of physiological state with Fibroids of the female internal reproductive organ (46%) n=23 as compared to other socio economic group of women. The women from rural areas had double incidence of physiological state with Fibroids of the female internal reproductive organ (68%) n=34 as compared to women having physiological state with Fibroids of the female internal reproductive organ from urban areas (32%) n=16[7]. In our study the incidence of Placental gap was (10%). The relationship between fibroids and pregnancy outcome was seen in number of studies, each of that counsel that the presence of fibroids is related to a 2-fold augmented risk of maternity even when adjusting for previous surgeries like cesarian section or Myomectomy[4,7,12]. However in our study it had been (10%) cases of maternity. Fetal growth doesn't seem to be suffering from the presence of female internal reproductive organ fibroids. Though accumulative knowledge and a population-based study urged that ladies with fibroids at slightly augmented risk of delivering a growth-restricted baby. In our study the incidence of foetal growth restriction was (2%). The risk of foetal malpresentation will increase in ladies with fibroids compared with managed women (13% vs 4.5%, severally[7,12]. Large fibroids, multiple fibroids, and fibroids within the lower female internal reproductive organ phase have been at risk factors for malpresentation[4,10,12], In our study the incidence of foetal malpresentation was (26%).

Numerous studies have shown that female internal reproductive organ fibroids is a single risk factor for cesarean section[3,7,10,12]. during a systematic review, ladies with fibroids were at a 3 to 7 fold augmented risk of cesarean section (48.8% vs 13.3%, respectively)[7]. This is due partly to a rise abdominal dystocia, that is augmented 2-fold in pregnant ladies with fibroids[7,12]. Malpresentation, massive fibroids, multiple fibroids, sub mucosal fibroids, and fibroids within the lower female internal reproductive organ are thought-about predisposing factors for cesarean section [5,10,12]. In our study the incidence of cesarean section was (10%) that is opposite to other studies. Reports on the association between fibroids and postnatal hemorrhage area unit conflicting[2,10,12]. Pooled accumulative knowledge counsel that postnatal hemorrhage is considerably a lot of possible in ladies with fibroids compared with management subjects (2.5% vs 1.4%, severally[7] Fibroids could distort the female internal reproductive organ design and interfere with myometrial contractions resulting in female internal reproductive organ status and postnatal hemorrhage[12]. In our study the incidence of postnatal hemorrhages (46%) that was higher as compared to alternative complications of delivery with fibroids of female internal reproductive organ.

One study reported that preserved placenta was a lot of common in ladies with fibroids, however as long as the fibroid was settled within the lower female internal reproductive organ phase[10] but, pooled accumulative knowledge counsel that preserved placent a is a lot of common altogether ladies with fibroids compared with management subjects, despite the placement of the fibroid (1.4% vs 0.6%, severally[7]. In our study the incidence was (08%) that was very low as compared to other complications of delivery with fibroids of the uterus.

CONCLUSION

Uterine fibroids are very common in women of reproductive age.

Pain is the most common complication of fibroids during pregnancy. The symptoms can usually be controlled by conservative treatment such as bed rest, hydration, and analgesics.

Author's Contribution:

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Data Analysis:	Ashba Anwar & Neelam Saba
Revisiting Critically:	Ashba Anwar & Anila Ansar
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Original Article

Stroke Rehabilitation

Length of Hospital Stay During Stroke Rehabilitation at a Tertiary Care Rehabilitation Center in Saudi Arabia

Ahmad Zaheer Qureshi[1], Sami Ullah[1], Randolph Mitchell Jenkins[2] and Saquib Hanif Janjua[1]

ABSTRACT

Objectives: To analyze the factors associated with length of inpatient stay of individuals with stroke at a tertiary care rehabilitation hospital in Saudi Arabia.

Study Design: Retrospective Cohort Study.

Place and Duration of Study: This study was conducted at the Inpatient Department of Physical Medicine & Rehabilitation, King Fahad Medical City, Riyadh Saudi Arabia at King Fahad Medical City, Riyadh from June 2010 to June 2011.

Materials and Methods: The rehabilitation data of sixty stroke patients discharged from inpatient stroke rehabilitation unit was collected retrospectively. Patients who were not able to complete their rehabilitation either due to death or discharge against medical advice, were excluded from the study. Patients who were difficult to be discharged or who were shifted to other medical service due to medical instability were not included in the study. Complex Statistical analysis was carried out using SPSS version 17.

Results: Our study included 60 patients with 62% males and 38% females. Mean descriptive analysis for age, Length of stay in acute (LOSa), Length of stay in rehab (LOSr), Functional status at admission (FIMa) and Functional status at discharge (FIMd) are 63.4 years, 22.1 days, 48.8 days, 59.7 and 80.8 respectively. LOSr was more in hemorrhagic stroke patients. FIMd has a strongly positive correlation with FIMa and has a negative correlation with age and LOSa. LOSr has a negative correlation with FIMa and age. In a multivariate linear regression model the only significant variable was age.

Conclusion: Earlier rehabilitation interventions during acute stroke care should be emphasized as it can not only improve the functional outcomes of patient during inpatient rehabilitation but also shorten the length of stay in rehabilitation unit.

Key Words: Stroke, Length of Stay, Rehabilitation, Outcome Measures, Saudi Arabia

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INTRODUCTION

Cerebrovascular accident (stroke) is one of the major causes of disability in human beings. With an incidence of 600,000 new cases per year in the U.S., stroke stands out as the third leading cause of death, the leading cause of paralysis, and a major cause of disability.[1] As a result, identifying factors that predict functional recovery after stroke has been the subject of much research. It has been argued that certain subgroups of the stroke population may benefit more than others from comprehensive rehabilitation. Hence it is important to identify predictors that discriminate between stroke patients with good and poor prognoses.

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One such factor is length of stay (LOS) which has been repeatedly used as an indicator of efficiency for inpatient care, probably due to its clear meaning as one of the main sources of hospital costs and because LOS can be also deemed an indicator of quality.[2,3] The prediction of inpatient rehabilitation outcome is relevant for rehabilitation specialists to maximize the preparation of stroke patients for a return home.

From previous studies done in Saudi Arabia, the incidence and prevalence of strokes were low when compared to those reported from Western countries, but this was mainly due to the younger age of the population.[4] The overall distribution of stroke types was not different from that reported in other communities with some exceptions.[4] Data suggests that stroke is not an uncommon neurological problem in Saudi Arabia. Al Rajeh reported that the annual crude incidence rate of stroke was 43.8 per 100 000 population.[5] This was similar to preliminary results of an ongoing stroke registry in the Eastern Province of Saudi Arabia, in which the crude stroke incidence rate was approximately 40 per 100 000 per year with a male female ratio of approximately 2:1. In two community-based studies in the Eastern Province of Saudi Arabia, the prevalence rate for stroke was found to be

178/100,000.[6] The demand of acute management followed by inpatient rehabilitation as an active medical service continues to grow in Saudi Arabia. Hence determination of risk factors for stroke remains an important consideration. The results of one study suggest that gender, age, and ethnic differences were risk factors of LOS of stroke patients in Saudi Arabia.[7] Prediction of LOS has become increasingly important for policy makers in health care administration. Fourteen studies reported that age negatively correlates with function on or after discharge, and four studies showed no correlation.[8] Brosseau et al. found that the LOS for stroke rehabilitation also involved the process of functional recovery in stroke patients.[9] Galski et al. revealed that higher-order cognitive impairment is important in extended LOS.[10] Lin et al. reported that the functional independence measure score at admission was useful in the prediction of functional outcome for the stroke survivors after rehabilitation therapy.[11] Keeping in view all the previously cited variables for LOS and importance of the topic, we decided to conduct a study of LOS in inpatient rehabilitation after stroke at a tertiary care rehabilitation centre in Saudi Arabia, where there were no such studies conducted earlier.

The objective of this study was to analyze the factors associated with length of stay at a tertiary care rehabilitation hospital in Saudi Arabia. This will help to predict the rehabilitation outcome of patients after stroke and suggest measures in improving rehabilitation strategies for stroke patients.

MATERIALS AND METHODS

The medical rehabilitation data of 60 stroke patients discharged from inpatient stroke rehabilitation unit at King Fahad Medical City was collected retrospectively from medical records during the period from June 2010 to June 2011. This excluded patients who were not able to complete their rehabilitation either due to death or discharge against medical advice. Patients who were difficult to be discharged or who were shifted to other medical service due to medical instability were not included in the study.

Variables included in the study were age of the patient, length of stay in acute care (LOSa), length of stay in rehabilitation (LOSr), functional independence measure on admission (FIMa) and discharge (FIMd).[13] FIM data was taken from the first and last case conferences for each patient. Patients were grouped by impairments defined by cause as ischemic or hemorrhagic stroke, and right or left body side deficit. No identifiable patient information was included. Complex Statistical analysis was carried out using SPSS 17.0 statistical package. Descriptive analysis was done for continuous as well as categorical variables. Pearson correlation coefficient was used to see association between the continuous variables. Regression analysis was performed to see predictor variables for dependent variable (LOSr). A p value of 0.05 was considered to be a statistically significant level.

RESULTS

The study included 60 stroke patients with an age range of 20-95 years. The distribution of qualitative characteristics is shown in Table 1. 62% of our patients were males and left side of body was mostly affected. Though 80% of patients had ischemic strokes, but LOS in rehab was greater for hemorrhagic stroke patients, who had a mean stay of 60 days. Nearly one-third of patients were retired, while only 16% of patients had paid jobs. 95% of patients were married and 22 out of 23 females were housewives. The descriptive statistics of variables included in the study are shown in Table 2. Mean length of stay in both acute stay and inpatient rehabilitation is shown along with mean FIM at admission to rehab and at discharge from rehab.

Table No.1: Distribution of Qualitative Characteristics in the Sample (N=60)

Variables	Category	N
Gender	Male	37
	Female	23
Side of body affected	Right	20
	Left	37
	Bilateral	3
Cause	Hemorrhage	12
	Ischemia	48
Occupation	Paid employment	10
	Self-Employed	5
	Student	2
	Homemaker	22
	Retired	18
	Unemployed	3
Marital Status	Married	57
	Single	3
	Separated	0
	Divorced	0

Table No.2: Descriptive Statistics of Included Variables in the Study

	Mean + SD
Age (years)	63.4 + 14.5
FIMa (%)	59.7+ 19.6
FIMd (%)	80.8 + 24.2
LOSa (days)	22.7 + 21.3
LOSr (days)	48.8 + 21.3

Associations of FIMa with other variables is presented in Table 3 which shows that there was a strongly positive correlation between FIMa and FIMd and a weakly negative correlation between FIMa and age. Associations of LOSr with different variables is shown in Table 4. It was found that there is a strong negative correlation between LOSr and age and a weakly negative correlation between LOSr and FIMa. Data

analysis did not demonstrate any association between LOSr and age. In a multivariate linear regression model the only significant variable was age as shown by a negative correlation between age and LOSr.

Table No.3: Association of FIMa with Different Variables in the Study

Variables	r	p(Two Tailed)
FIMd	0.764	0.00
LOSa	- 0.167	0.203
Age	- 0.223	0.086

Table No.4: Association of LOSr with Different Variables in the Study

Variables	r	p(Two Tailed)
FIMa	- 0.229	0.079
Age	- 0.307	0.017

DISCUSSION

Determination of prognosis and an expected length of rehabilitation stay is of critical importance for management of stroke patients. It is also a major concern for the patients and their families. In this study, the functional status upon discharge has a strongly positive correlation with the functional status upon admission to rehabilitation. Hence, patients entering rehabilitation initially with greater amounts of function tended to leave rehabilitation with greater total function at the end of the rehabilitation course. It is reported that patients who are admitted for comprehensive stroke care within thirty days of their stroke were both admitted and discharged with higher functional scores than those admitted after thirty days, and the length of stay was significantly shorter. [13]

There was also a negative correlation between the length of stay in rehabilitation and FIMa, indicating that patients with higher function on admission had shorter LOS in the rehabilitation unit. A study reports that a high ADL measure identifies patients who will be home at one month post inpatient rehabilitation.[14] Given this, the functional status upon admission of the patient to the rehabilitation unit is the most outstanding variable in our study as a prognostic factor and determinant of length of stay in rehabilitation. It could also serve as a parameter for improving outcomes for our patients. Meiner reported that the mean FIM values at admission and at discharge were significantly higher in stroke patients after inpatient rehabilitation program. Rehabilitation therapy services are routinely provided upon referral from the stroke unit during the acute hospitalization phase. Considering the importance of FIM upon admission to a rehabilitation unit, initiating the comprehensive integrated interdisciplinary rehabilitation program in the acute stroke unit could be of significant benefit. A rehabilitation physician can assess and initially screen the acute stroke patients so that effective earlier rehabilitation interventions can help in improving the functional prognosis. Later, upon transfer to the rehabilitation unit, the patient will continue the rehabilitation care under the same team. This may not only facilitate appropriate selection, transfer and discharge planning, but also may lead to higher functional outcomes and decreased length of stay.

Another important consideration for outcomes and length of stay is patient age. The care of elderly stroke patients constitutes a major bulk in stroke rehabilitation in our patient group. Mean age of the patients is around 63 years and one third of the patients were retired. Functional status on discharge had a negative correlation with age, indicating that older individuals tended to leave rehabilitation at a lower functional level. Interestingly, our analysis shows that there is also a negative correlation between age and LOSr, as older patients tended to have a shorter length of stay on the rehabilitation unit. This is a unique finding; as generally older patients are reported to stay longer in rehabilitation post stroke.[16] This may be due to cultural reasons, as older patients are uncomfortable in the hospital setting, seek earlier discharges because there is considerable caregiver support available at home.

The qualitative characteristics of the study show that the left side of the body is more commonly affected, which may be a good prognostic factor as most of the general population is right-handed. Ischemic strokes were more common, but hemorrhagic stroke patients were found to have a longer LOSr. This emphasizes secondary preventive measures for both types of strokes, with special measures to focus on decreasing the LOSr for hemorrhagic stroke patients. some studies found better functional prognosis in survivors with hemorrhagic CVA after inpatient rehabilitation.[17,18] Hypertension and diabetes were present in nearly half of our patients, which endorses the need for primary and secondary prevention of stroke. With exception of one female student, all other females were housewives and married. This highlights the occupational needs of these patients as homemakers.

Most of our patients were discharged home with moderate handicap requiring little assistance with ADLs. This may be due to a bias towards only allowing patients who continue to improve to stay longer in the inpatient stroke programme, which is reported in literature before.[19] This improves the impact of the LOSr on the functional outcomes Similarly, the majority of patients were able to walk with aids at the time of discharge, while the activities of significant percentage of patients (35%) were confined to bed or wheelchair at the time of discharge. This necessitates the early involvement of family in caregiver training for ensuring continued care of patients at home, and the substantial role that social workers need to play in our population.

Limitations in our study include some indistinctness in the term “length of stay.” The LOS for stroke

rehabilitation patients was around 48 days with standard deviation of 21.3, though we propose that the actual active days of rehabilitation may be less, as the length of stay in rehabilitation does not include the number of days that the patient was unable to participate in an active rehabilitation program. This endorses the importance of investigating the factors which could result in inactive days and add to the length of stay. In our opinion, 'difficult discharge' patients are a unique group of patients as they are not undergoing rehabilitation but still occupy a bed and receive nursing and medical care. Thus a separate study would be more appropriate to highlight factors involved in their length of stay. Another limitation in our study is the lack of discernment between patients with varying functional levels on admission. A patient's FIMa could vary depending on the severity of neurological insult, comorbid conditions, or the amount of rehabilitation obtained on the acute service. Further study would seek to determine factors influencing FIMa and their outcomes in rehabilitation. The sample size in this study was relatively small, and we recommend a similar study including a larger patient group with additional variables to explore further details and obtain pertinent data.

CONCLUSION

Earlier rehabilitation interventions during acute stroke care should be emphasized as it can not only improve the functional outcomes of patient when admitted on rehabilitation floor but also shorten the length of stay during rehabilitation. Specific rehabilitation interventions can be considered for hemorrhagic stroke patients as they tend to have a longer length of stay. Decreasing the length of stay in stroke unit during acute stroke management can reduce length of stay on the rehabilitation floor and improve functional outcomes after rehabilitation. These measure may help in reducing the cost of health care for stroke patients during acute and rehabilitation phase by decreasing their hospital stay and achieving better functional outcomes.

Author's Contribution:

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Data Analysis:	Randolph Mitchell Jenkins, Sami Ullah
Revisiting Critically:	Saquib Hanif Janjua, Rubina Ullah
Final Approval of version:	Ahmad Zaheer Qureshi and Sami Ullah

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Original Article

Side Effects of Cyclopentolate

Distribution of Side Effects of Cyclopentolate in Cycloplegic Patients (Age Group 1-8 Years) at Mardan Medical Complex

Muhammad Tariq, Haleema Zafar, Hira Ali and Bilal

ABSTRACT

Objective: To determine the possible side effects of cyclopentolate.
Study Design: Observational study.
Place and Duration of Study: This study was conducted at the Department of Ophthalmology, Mardan Medical Complex Mardan from May 2017- July 2017.
Materials and Methods: 96 patients of age group from 1-8 years were examined with instillation of one drop of 1% cyclopentolate three times at the interval of 10-15 minutes. The possible side effects were then observed.
Results: Most of the children were observed with more than one side effect like Blurred vision, Watering, Fever, Swelling of eye lids and Allergy etc to the drug. Bilateral swelling and laziness were also observed in few patients, not reported in previous literatures.
Conclusion: Patients compliance was very poor due to side effects of these cycloplegic drug. So to improve the patient compliance, so to minimize the side effects of cycloplegic drugs we need to use drugs with fewer side effects.
Key Words: Cyclopentolate, Side effects, Cycloplegic Patients

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INTRODUCTION

Cycloplegia is also refers to the pharmacological paralysis of the ciliary muscles, and is primarily results in inhibition of accommodation[1]. The time in which maximum cycloplegia can be achieved, may range from 10 to 60 minutes after instillation of cyclopentolate[2]. Difference in iris colors has also been reported to affect the timing in the adult people. Cycloplegic agents act on muscarinic receptor sites and block the action of acetylcholine. Due to their mechanism of action, cycloplegics are called anti-cholinergics, anti-muscarinics or parasympatholytic agents. Muscarinic receptors are extensively distributed in the human body, especially in the iris and ciliary body[3]. Instillation of a cycloplegic agent results in inhibition of accommodation and also mydriasis (due to paralysis of the pupillae sphincter muscle). However, many cycloplegics have been shown to cause mydriasis but very little accommodative suppression[4]. Mydriasis also occurs without accompanying cycloplegia when a sympathomimetic agent is used. This shows that mydriasis is not always evidence of accompanying cycloplegia.

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Because of the different time courses of mydriasis and cycloplegia, pupil size is a poor indicator of the cycloplegic effect[5]. Cycloplegic agents are indispensable in the diagnosis of latent hyperopia, pain relief from ciliary spasm, breaking or preventing irido-lenticular or irido-corneal adhesion, as well as penalization (or occlusion therapy) in eye care[6]. Hyperopic children generally have greater accommodative efforts in comparison to myopic children with relatively lower accommodation requirements[7]. Cycloplegic refraction is invaluable in the evaluation of patients with decreased vision or ocular deviation. The rationale for cycloplegic refraction is that patients have different levels of accommodation at different times[8]. Cycloplegic refraction helps determine full hyperopia in patients with accommodative esotropia and prevents overcorrection in myopic patients. It is also useful in prescribing correction in patients with limited cooperation during subjective refraction and amblyopic patients who have chaotic accommodation[8]. Cycloplegic refraction is considered as the gold standard for measuring refractive errors in epidemiologic studies in children and adolescents[9,10]. Recently, it was even proposed that cycloplegic refraction be performed not only in children and adolescents but also in adults aged less than 50 years[11]. However, several issues regarding cycloplegic refraction have not been completely addressed. First, although cycloplegic refraction in population-based studies could be done, under many circumstances, cycloplegic refraction is a great challenge in

population-based or school-based studies, especially in the studies of young children. Many parents and children do not agree to undertake cycloplegic refraction because of the blurred vision after cycloplegia.[12] In addition, feasibility and side effects of cycloplegia were also challenges. It has been well-established that generally myopia could be overestimated and hyperopia be underestimated if refraction was performed without cycloplegia, but to which extent the prevalence of refractive errors are overestimated or underestimated in different populations is different as the prevalence of refractive errors seems to be a major determinant for the difference between cycloplegic and non-cycloplegic refractive error. Cyclopentolate provides cycloplegia for 12 to 24 hours.

Side effects of cyclopentolate may be Ocular as well as systemic. Ocular side effects may include irritation, lacrimation, allergic blepharoconjunctivitis, conjunctival hyperemia, and increase in intraocular pressure. Systemic side effects include drowsiness, ataxia, disorientation, incoherent speech, restlessness, and visual hallucinations[13.] This study was focused on the side effects of cyclopentolate in cycloplegic patients.

MATERIALS AND METHODS

This study was carried out in Mardan Medical Complex Mardan. The duration of this study was three months from May 2017 to July 2017. A total of 96 patients were examined. Criteria for inclusion were children aged between 1 and 8 years. Children outside this range, those with other eye diseases and history of cardiovascular disease were excluded from the study. Subjects with a history suggestive of hypersensitivity to cyclopentolate were also excluded from the study.

96 patients were examined with instillation of one drop of 1% cyclopentolate at the interval of 10-15 minutes and three times before refraction was performed.

After 10-15 min of instilling drop of cyclopentolate the patients was observed for any possible side effect and continue till and after few hours of refraction. Refraction was done 45 min after instillation of the last drop of cyclopentolate. Side effects were observed till 3-4 hours after the last drop of cyclopentolate was instilled. Parents of the subjects were informed about possible post instillation side effects of the drugs and were told to present to the hospital immediately should any of these be observed.

RESULTS

A total of 96 patients, 58 male and 38 female were examined to determine the side effects of cyclopentolate.. Among 96 patients this was studied that blurred vision was found among 93 patients, out of which 57 were male while 36 were female, similarly redness was also found higher in number and was 72 out of 96 patients in which 39 were male and 33 were female patients.

Cyclopentolate cause watering from the eyes among 69 patients out of 96, in these 69 patients 36 were male and 33 were female. Fever was noted in 48 patients (27 male and 21 female) while asking from patients 45 have burning sensation to eyes in which 24 were male and 21 were female.

Table No.1: Frequencies of side effects in both genders for cyclopentolate

Side effects	No of patients n=96	Male N=58	Female N=38
Fever	48	27	21
Redness	72	39	33
Watering	69	36	33
Itching	33	21	12
Allergy	36	18	18
Blurred vision	93	57	36
Tachycardia	3	1	2
Hallucination	9	4	5
Headache	30	15	15
Difficulty in breathing	3	1	2
Burning sensation to eye	45	24	21
Dryness of mouth	24	15	9
Laziness	24	13	11
Bilateral swelling of lower lid	18	10	8
Others	12	6	6

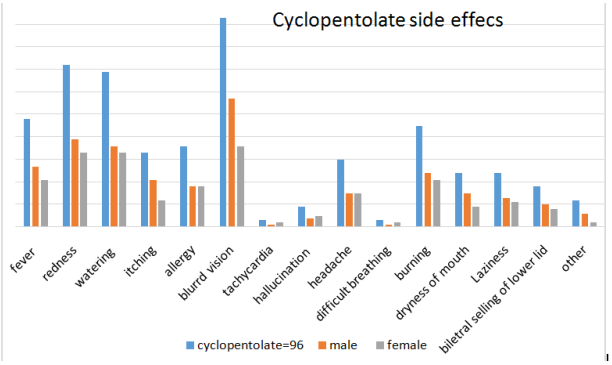

Figure No. 1: Side effects of cyclopentolate

36 patients have allergy in which 18 were male and 18 were female, similarly 33,30,24,18,12,9and 3 patients presented with itching, Headache, tachycardia, dryness of mouth, bilateral swelling of lower lids, laziness and difficulty in breathing respectively, as shown in the given Table.1.

Among the 96 patients 12 patients presented with Nausea and Drowsiness, which was listed as others in the Table 1.

The data were also analyzed through statistical graphs and the number of patients (both sexes) presented with the side effects. As shown from the given Figure 1, the number of patients were at Y axis while side effects were given at X axis.

DISCUSSION

Anticholinergic drugs (atropine, cyclopentolate, tropicamide, homatropine, scopolamine, etc) produce mydriasis and cycloplegia by relaxing the ciliary body and iris[14]. However, they also manifest cardiovascular, respiratory, cerebral and gastrointestinal effects when absorbed in the systemic circulation such as tachycardia, atrial dysrhythmias, fever and flush, bronchodilatation, prolonged gastric emptying time and alterations in mental status ranging from sedation or excitation and restlessness to acute psychotic reaction[15]. Myasthenia gravis-like syndrome has also been reported after topical administration of these drugs.[16]

This study was focused over the side effects of two mostly used cycloplegic drug,cyclopentolate.96 patients were examined with instillation of one drop of 1%cyclopentolate at the interval of 10-15 minutes and three times. All the 96 patients of the group age from 1-8 years for both male and female were carefully studied to examine the side effects of the drug. It was observed that Blurred vision was most commonly found among the patients. Many of the patients suffers from mild to moderate allergy to the eye drop which may be due to the active ingredients or may be due to the preservatives in the eye drop. The symptoms of allergy were redness of the eye lids and itching. Along with allergy some children were observed with watering from the eyes due to action of the drugs on the lacrimal glands.

Some of the systemic side effects like increase heart rate, flushing of the face, fever which was noted from mild to moderate in both male and female patients. As this drug is parasympatholytics, so it acts on blood vessels and causes an increase in blood pressure and also cardiac rhythm.

Drowsiness was noted in a single patient for cyclopentolate. Bilateral swelling and laziness which were not reported in previous literatures have also been observed.

CONCLUSION

In this study 96 pediatric patients from 1-8 years age group were examined for the side effects of the drug. Multiple side effects like Blurred vision, Allergy, Fever, redness, etc are commonly were observed among the patients and because of these side effects patients compliance was very poor specially with the installation of second and third drops. Bilateral swelling and laziness which were not reported in previous literatures have also been observed.

So to improve the patient compliance and to minimize the side effects of cycloplegic drugs we need to have drugs with fewer side effects and also the half-life of the drug may be reduced so that its effects will last for shorter amount of time after its instillation.

Author's Contribution:

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Final Approval of version:	Muhammad Tariq

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

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Original Article

Cervical Cancer Screening

Comparative Study of Visual Inspection of Cervix Through Acetic acid (VIA) and Papanicolaou (Pap) Smears for Cervical Cancer Screening

Shahzadi Neelam[1], Zartaj Hayat[2] and Arifa Bari[2]

ABSTRACT

Objective: To compare the accuracy of visual inspection of cervix through acetic acid with Pap smear using colposcopic guided biopsy as gold standard.

Study Design: Cross sectional study.

Place and Duration of Study: This study was conducted at the Department of Obstet & Gynae, Fauji Foundation Hospital, Rawalpindi from May 2013 to December 2014.

Materials and Methods: Total of 145 patients were included in the study. Demographic characteristics and VIA findings as positive, negative or unsure were recorded on a proforma. VIA positive and patients with unsure findings were asked to follow up in colposcopy clinic on a later date for colposcopic guided biopsy. Colposcopic directed biopsy was taken as the gold standard to assess visual inspection findings. SPSS version 17 was used for statistical analysis.

Results: A total of 130 patients were finally recruited for our study.VIA was positive in 11%, negative in 77%, and unsure in 11%.Pap smear report was normal in 117 (90%) patients and abnormal in 13(10%) patients. Pap smear abnormality was CIN 1in 11, CIN 3 in1 and cervical cancer in one patient. Histopathology was normal in 121(93%) patients and abnormal (CIN and carcinoma) in 9(7%) patients. Histopathology showed cervicitis in 13%(out of normal histopathology report), CIN in eight(6%),cervical cancer in one patient(0.7%) and benign endometrial polyp in one patient(0.7%). The results were statistically significant with p value of <0.05. Sensitivity, specificity, PPV, NPV calculated for VIA were 100%, 96%, 53% &100% respectively vs 100%, 97%,75% and 100% for Pap smear, taking histopathology as gold standard.

Conclusion: Visual inspection of the cervix after acetic acid application is an effective method of detecting pre-invasive phase of cervical cancer and a good alternative to Pap smear screening for cervical cancer in low resource settings.

Key Words: VIA, Pap Smear, Cervical Cancer Screening

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INTRODUCTION

Cancer of the cervix is the second commonest cancer among the women worldwide. About 500,000 new cases are diagnosed each year and more than 90% of these new cases are in developing countries.[1] In 2012, about 270,000 women died of cervical cancer, and again out of these deaths 86% were in less developed countries.[2]

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Unfortunately, most women with cervical cancer in developing countries are diagnosed at late stages of the disease and have no access to lifesaving treatment or prevention options.[3] The main reason for these high figures in under developed countries is lack of effective screening programs. According to an estimate only about 5% of women in developing countries have been screened for cervical cancer in the past five years, as compared to about 85% in developed countries.[4, 5, and 6]

Cervical cancer is one of the most preventable forms of cancer and effective screening programs can lead to a significant reduction in the morbidity and mortality associated with this cancer.[7]Conventional cervical cytology (Pap smear) is the most widely used cervical cancer screening test in the world,[8,9] and effectively lowered the incidence of cervical cancer in developed countries but this method is not easy to implement in developing countries due to lack of trained and skilled personnel and healthcare resources.[10,11]

Screening is considered optimal when the smallest amounts of resources are used to achieve the greatest

benefit. Visual inspection of the cervix after application of 3-5% acetic acid (VIA) is an alternative sensitive screening method in many developing countries.[12,14] It is simple, cheap and non- invasive and the results are available instantly. Nurses, midwives, and other non-physician health care providers can be easily trained in VIA, and it can be done in a low level health facility like community, which can greatly improve access to cervical cancer prevention services.[15,16]

Cervical cancer accounts for about 3.6% of all cancers in Pakistani women .[17]Incidence of cervical cancer in Pakistan is 13.6/100,000 population and currently cervical cancer screening coverage is only 1.9%.[17] Screening through VIA is an attractive alternate in Pakistan also as there is no well-developed Pap smear screening program. This can help to increase this very low rate of screening for cervical cancer.

This study was done to determine agreement between Pap smear and VIA, as screening methods for cervical cancer in low resource-settings. The non-invasive nature and immediate results make VIA a useful screening test in developing countries like Pakistan. It would reduce the burden of work on the already burdened cytopathology units by screening subjects in outpatient departments who are VIA-negative and disease-free. Thus, only patients who are VIA-positive would need to undergo further diagnostic tests.

MATERIALS AND METHODS

After taking permission from hospital ethical committee we conducted this cross sectional study in OBGYN department UNIT II Fauji Foundation Hospital Rawalpindi from May 2013 to Dec 2014. VIA was performed by the doctors who were trained through workshops and have experience in colposcopy clinics. A total of 145 patients fulfilling inclusion criteria were included in the study after taking informed consent. These patients presented to Gynae OPD with various gynecological complaints. Patients with vaginal bleeding, history of cervical procedure and obvious carcinoma cervix were excluded from the study. Procedure was performed in dorsal position. After visualizing the cervix with sterile speculum, 5% acetic acid was applied with the help of cotton swabs on sponge holding forceps for one minute. Cervix was examined after few seconds of application for any aceto-white areas. Demographic characteristics and VIA findings as positive, negative or unsure were recorded on a proforma. VIA positive and unsure patients were asked to follow up in colposcopy clinic for colposcopic guided biopsy that was taken as the gold standard to assess visual inspection findings. Colposcopic guided SPSS 17 was used for statistical analysis.

RESULTS

A total of 145 patients were examined after fulfilling the inclusion criteria. Ten patients were lost to follow up for colposcopy and histopathology of 5 patients was missing. These patients were excluded from study. So our study population was composed of 130 patients. Descriptive statistics were calculated for demographic variables like age, parity, education, contraception history, risk factors for cervical carcinoma and socioeconomic status. Age range of our patients was between 25-79 years with average age of 46±9 years. Sixty seven percent of patients were illiterate, 18% were educated up to primary and 13% were educated up to secondary school and above. Sixty three percent patients were from satisfactory background. One hundred and twenty five (96%) patients were multiparous and 4% were primiparous. Eighty four percent of patients were using some form of contraception. Ninety eight percent of patients have no risk factor for cervical carcinoma.VIA was positive in 11%, negative in 78%, and unsure in 11%. PAP smear report was normal in 117 (90%) patients and abnormal in 13(10%) patients. Pap smear abnormality was CIN 1 in 11, CIN 3 in one and cervical cancer in one patient. Histopathology was normal in 121(93%) patients and abnormal (CIN and carcinoma) in 9(7%) patients. Histopathology showed cervicitis in 13%(out of normal histopathology report), CIN in eight(6%), cervical cancer in one patient(0.7%) and benign endometrial polyp in one patient(0.7%).The results are statistically significant with p value of <.05. Sensitivity, Specificity, PPV, NPV calculated for VIA are 100%, 92%, 46%, 100% respectively vs 100%, 96%, 69% and 100% for pap smear, taking histopathology as gold standard (table 1,2).

Table No.1: Efficacy of VIA

	Abnormal histo-pathology	Normal histo-pathology	Total(unsure via patient excluded)
Via positive	7	8	15
Via negative	0	101	101
	7	109	116

Sensitivity =100%, specificity=92%, PPV=46%, NPV=100%

Table No.2: Efficacy of Pap smear

	Abnormal histopathology	Normal histopathology	Total
Abnormal pap smear	9	4	13
Normal pap smear	0	117	117
	9	121	130

Sensitivity =100%, specificity=96%, PPV=69%, NPV=100%

DISCUSSION

VIA has emerged as a good alternative to Pap smear in developing countries due to the fact that 80% of cervical cancer occur in these countries and logistics for Pap smear are difficult to meet. Visual inspection of cervix through acetic acid is a noninvasive, rapid, cost effective and easy to perform test in detection of cervical intraepithelial neoplasia in low resource countries. Our study has confirmed the results of previous national and international studies. Our study showed that the sensitivity, specificity, PPV, and negative predictive value of VIA and Pap smear are comparable and VIA can replace Pap smear as a tool of cervical screening in low resource countries. A study conducted in Civil Hospital Karachi, Pakistan in 2012 showed similar results for VIA and concluded that visual inspection of the cervix after acetic acid application is an effective method of detecting pre-invasive phase of cervical cancer and a good alternative to cytological screening for cervical cancer in resource-poor setting like Pakistan.[19]Another study conducted in Sir Ganga Ram Hospital in 2012 revealed that there was a fair agreement between VIA and Pap smear.[20] A comparative study between Pap smear and VIA using histopathology as gold standard was conducted at Guwahati showed sensitivity of VIA even more than pap smear making VIA a more reliable test.[21]Another local comparative study conducted in PIMS(Pakistan institute of medical sciences) Hospital Islamabad also revealed similar results. According to that study visual inspection with acetic acid has significantly higher sensitivity than Pap smear and may replace pap smear as a primary screening tool for universal screening.[22] The higher sensitivity of VIA in these studies was attributed to the experience of the VIA provider which is also true for our study. All the providers in our study have done the VIA workshop and have experience in colposcopy clinic, so it is very important for the VIA provider to be trained and experienced .This issue should be kept in mind before implementing VIA as national screening program. All health care providers should be trained before reporting independently. According to our study VIA is 100% sensitive, 92% specific with a positive predictive value of 46% and negative predictive value of 100%, hence proved a very reliable test. The 100% NPV means that the women can be reassured if the test is negative. The low positive predictive value of VIA in our study is due to false positive report of eight patients. Seven of these patients had cervicitis on histopathology revealing that cervicitis could lead to false positive report. This can be reduced by more training of the health care providers in VIA reporting. Cervicitis and experience of the VIA provider has also been coated as reasons of false positive results in other studies.[22] A study conducted at Egyptian teaching hospital also showed low PPV for VIA of 26%. Sensitivity, Specificity, NPV of VIA are comparable to our study. According to this study VIA performance is comparable to Pap smear performance.[23] Another study conducted by Albert O at Zaria has 56% PPV and NPV of 96% which is comparable to our study. In14 (11%) patients the reporter was not sure about the VIA findings in our study. Out of these 3 patients have normal histopathology, eight has cervicitis, two CIN, and one benign endocervical polyp on histopathology report. We can conclude from this finding that in cervicitis the VIA will be either positive or unsure, and it is good to label the VIA as unsure for the beginners in VIA reporting if they are not confident enough to label as negative. Two patients of unsure VIA were labeled as CIN II after colposcopic guided biopsy. Our study limitations are that it is an opportunistic study and population was low risk for cervical cancer. Community based study is required before implementing VIA as national screening program.

CONCLUSION

Visual inspection of the cervix after acetic acid application is an effective method of detecting pre-invasive phase of cervical cancer and a good alternative to Pap smear. It can be used with confidence as a screening method for cervical cancer in resource-poor countries.

Recommendation: The lack of effective and implementable screening program lead to reporting of advanced cases of Ca Cervix. If detected at CIN or early stage Ca cervix, effective treatment can be provided with encouraging results. Therefore effective cervical cancer screening programme need to be implemented in our country.

Author's Contribution:

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Data Analysis:	Zartaj Hayat, Arifa Bari
Revisiting Critically:	Shahzadi Neelam, Zartaj Hayat, Arifa Bari
Final Approval of version:	Shahzadi Neelam, Zartaj Hayat

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

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Original Article

Oral Melanesia and Cigarette Smoking: A Cross Sectional Study

Muhammad Nadeem[1], Uzma Zareef[2] and Irum Munir Raja[3]

ABSTRACT

Objective: To measure the melanin pigmentation in oral cavity with its distribution and relation with cigarette smoke habit.

Study Design: Descriptive / cross-sectional study

Place and Duration of Study: This study was conducted at the Private Dental College named Liaquat College of Medicine and Dentistry (L.C.M.D), Karachi from October 2017 to November 2017.

Material and Methods: In this study we involved 378 adult aged between 18 to 35 years old those who attended free dental camp organized by L.C.M.D. The sum of 440 individual visited in O.P.D with out of these 378 means (86%) satisfied the selection criteria and contributed in this research. In sequence on socioeconomic status and proportions of cigarette habit was finding with the help of taken written interview. All participants undergo a dental intraoral assessment to examine presence of O.M on "buccal- lingual mucosa, gingival, palatal tissue, and floor of the mouth. As statically we did χ^2 statistics, the proportions check with 95% confidence intervals (C.I) for the different sets.

Results: The duration of smoking in years (χ^2 = 24.6; P<0.001); the severity of smoking (χ^2=68.6; P<0.001); and the type of cigarette (χ^2=25.6; P<0.001) were significantly associated with the occurrence of O.M". In the smokers, melanin pigmentation was further regularly established on the buccal mucosa with result of chi square=35.1 and pie values is less than 0.001; on the other hand with non cigarette smoke person the mucosa on lingual side was more regularly affected chi square =0.02 and pie values is equal to0.53.

Conclusion: There is a significant dose response relationship between oral melanises and cigarette smoking.

Key Words: Oral Melanises, Cigarette Smoke habit, White Lesion

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INTRODUCTION

Many studies' results show that having consistently suggested a strong relation between oral melanin and cigarette smoke habit.[1-5] with several cross sectional researches mentions that the prevalence calculate approximately for melanin is 21% in 90% cigarette smokers[1,6]. "The term smoker's melanosis was coined by Hedin back in 1977 [7] and it has been hypothesized that this condition may be due to the physical effect of tobacco smoke on the oral tissues by heat and/or the direct effect of nicotine stimulating melanocytes located along the basal cells of the epithelium to produce more melanosomes, thus resulting in increased deposition of melanin" [2, 8].

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Many studies have found that melanin pigments distribution [1 - 10] mostly spotlight has been advanced on the periodontal supporting tissues in cigarette smoking[2,6] and it is not clear that the oral tissue can be affected in a same patter as compare to different among healthy individual who is not doing cigarette smoking. With this, as the conclusions of several researches propose "the existence of a dose response in the relationship between melanin pigmentations and smoking, with heavy cigarette smokers presenting more frequently with pigmentations than mild smokers [1,4] and with subjects who have smoked cigarettes for longer periods of time presenting more frequently with melanin pigmentations than subjects who have been exposed for shorter periods of time" [1,4,10,14,] as per our data, the potentially powerful role of the type of cigarette smoking has not been examined.

The purpose of the research were to "investigate the association between selected dimensions of exposure to cigarette smoking and O.M.P and to explore the intra-oral distribution of melanin pigmentations according to smoking status in a young adult population of volunteers attending a free dental camp for intra oral check ups".

MATERIALS AND METHODS

On behalf of L.C.M.D we arranged a free dental examination of individuals could check for routine

dental examinations in Darul Sehat hospital during October and November 2017. The hospital covers the Gulshan Town, Karachi and counts with clinical facilities that offered the opening for arranged following cross-sectional research. We did not offer any painful consultation or swelling. We did only oral cavity assessment and counsel of individuals on maintaining oral health status. Individuals were also discussed their current carious status with need of scaling and polishing.

Study population: There were 440 individuals age between 18 to 35 years old came for free dental consultations were invited in the cross section study. In participants having "current diabetic status, current hypertensive status, inflamed and bleeding gingiva, who history of radiation, signs of oral carcinoma, and habit of betel nut or pan use not include in this study. 2 were excluded because of alcohol use, 10 having diabetes, 10 having hypertension, 27 were not included due to pan user, and 5 were not included because of related to oral cancer. 8 participants didn't want to contribute in this research thus leaving 378 (86%) individuals. In this study we included different the cigarettes smoked (for example with filter or without), the smoking duration / years (less than 5, 5 to 9, 10 to 14 and more than 14 years), and the quantity of cigarettes smoked per day.

Sample Size: The sample approximate (n=323) was calculated with 95% level of the C.I, and 50% prevalence in target population.

Ethical Considerations: The study was approved L.C.M.D in "Department of Research and Ethics" and consent in writing was given by each individual.

Variables: "All participants filled a self-administered questionnaire containing information on age, gender, smoking status (current smoker/no smoker); the duration of smoking in years (less than 5, 5 to 9, 10 to 14 and more than 14 years); and the type of cigarettes smoked (with filter or without)".

Clinical outcome: An experienced pathologist with trained dentist who standardized against the pathologist carried out all the assessments. It's a double blind study so no one know about hypothesis. Each contributor was assist for the O.M in particular selected side of the oral cavity: "1) the buccal mucosa; 2) the lingual gingiva; 3) the buccal gingiva; 4) the hard and soft palate; and 5) the floor of the mouth". "The term 'oral pigmentation' is regularly used to a wide range of lesion or conditions featuring a change of colour of oral tissue. Lesions not associated with an accumulation of melanin pigment (e.g., Fordyce spots) were not classified as pigmented lesions" [11]. "The O.M pigmentation was dichotomized (Yes/No). For the purpose of the present analysis, the site with most prominent melanin pigmentation was considered at the individual level".

Statistical Analysis: χ^2 used to evaluate between clusters differences, proportions differences and the corresponding 95% C.I for the participants.

RESULTS

The 103 cigarette smokers (C.S) and 275 healthy (N.S) were in this study and 1,890 selected areas were inspected for the presence of Oral Melanin pigmentation (O.M.P). There were 40 (38.8%) pigmented sites between C.S and 26 (9.5%) sites affected with N.S.

"Intraoral distribution of melanin pigmentation according to smoking status": In cigarette smoking person, O.M.P was regularly started in the buccal site (17.5%), as with N.S the O.M.P was further common in lingual site (5.5%). The second number of O.M.P area in cigarette smokers was establish in the gingival site (7.8%) (Table 1).

Table No.1: Intraoral distribution of melanin pigmented sites according to smoking status

Sites	Smokers (n=103)		Non-Smokers (n=275)		Diff	95% CI	χ^2 statistic
	N	%	n	%			
Buccal	18	17.5	4	1.5	16	[9.5;24.5]	P<0.001, χ^2=35.10
Lingual	6	5.8	15	5.5	0.4	[-4.2;7.0]	P=0.53, χ^2= 0.02
Gingival	8	7.8	3	1.1	6.7	[2.4;13.5]	P=0.002, χ^2= 11.82
Palatal	6	5.8	2	0.7	5.1	[1.4;11.4]	P=0.006, χ^2= 9.4
Floor of the Mouth	2	1.9	2	0.7	1.2	[-1.1;6.1]	P=0.300, χ^2= 1.06
Total	40	38.8	26	9.5	29.4	[19.7;39.5]	

Diff= Differences between proportions 95% CI= 95% confidence intervals for the differences between groups
χ^2= Chi square statistics

'Oral melanin pigmentation distributions as per smoking duration': The maximum O.M.P sites were established in persons who cigarette smoking 14 years or more (67.5%). The rate of O.M.P was same as for individuals who had cigarette smoking between 5 to 9 years and those who is smoking 10 - 14 years. The occurrence of pigmented sites was significantly associated with the duration of smoking in years (χ^2=24.56, p<0.001). (Table 2).

'Oral melanin pigmentation distribution as per number of cigarettes smoked each day': Individuals exposure to do smoking minimum ten cigarettes or less a day was

considered to be "mild smokers". The subjects' exposure smoke more than 10 a day were considered to be "heavy smokers" [4]. The rate of O.M.P sites was considerably higher among heavy smokers (χ^2=68.63, p<0.001) (Table 3).

'Oral melanin pigmentation distribution as per type of cigarettes smoked each day': Individuals who used cigarettes without filter were considerably more present with O.M.P (χ^2=25.56, p<0.001) than did individuals smoking filtered cigarettes.

Table No.2: Distribution of melanin pigmentation among smokers according to the duration of smoking in years

Duration of Smoking	Pigmented Smoker (n=40)		Non Pigmented Smokers (n=63)	
	n	%	n	%
<5 years	3	7.5	11	17.5
5-9 years	5	12.5	9	14.3
10-14 years	5	12.5	30	47.6
>14 years	27	67.5	13	20.6
(χ^2= 24.56, df= 3, p<0.001)				

df=degrees of freedom χ^2= Chi square statistics

Table No.3: Distribution of melanin pigmentation among smokers according to the number of cigarettes smoked daily

Severity of Smoking	Pigmented Smoker (n=40)		Non Pigmented Smokers (n=63)		Diff	95% CI for the difference
	N	%	n	%		
Mild Smokers (< 10 cigarettes)	7	17.5	61	96.8	-79.3	[-88.4;-63.0]
Heavy Smokers (10 or more)	33	82.5	2	3.2	79.3	[63.0;88.4]
(χ^2= 68.63, df= 1, p<0.001)						

Diff= Differences between proportions
95% CI= 95% confidence intervals for the differences between groups
χ^2= Chi square statistics

DISCUSSION

To the best of our data, this is the first study investigative the relation between cigarette smoking with O.M.P in target population. The results of this study corroborate with previous studies suggesting "the existence of a dose-response relationship between exposure to cigarette smoking and the occurrence of oral melanin pigmentations both when exposure is measured as the number of cigarettes smoked.[1,2,4,10] and the duration of cigarette smoking in years" [1,4,10-16].

The pattern of O.M.P changed for C.S and N.S, with cigarette smokers showing most regularly with O.M.P on the buccal site as compare to N.S showed most regularly with O.M.P on the lingual site. This results is in agreement with previous findings "reported for a Nigerian population [17], but deviate from the results of other studies in which the attached gingiva has been found to be the most common location for pigmentations among Swedish[1], Thai and Malaysian[1,6,20], and Turkish smokers".

Our results show that on the statistically significant relationship between the cigarette smoked type (non-filtered) and higher frequency of O.M.P is novel for the oral sites investigated but is in agreement with "the results of a previous study concerning 'reverse smoking' suggesting that palatal mucosal changes are more frequent among users of non-filtered cigarettes" [12,16]. Our results showed that on cigarette type smoked may reflect an extra measurement of the severity of exposure to cigarette smoke. On the other hand, this should be interpreted with caution because the habit of smoking cigarettes without filter may also be related to unknown determinants of melanin pigmentation e.g., socio-economic position, which can therefore confound the reported association.

"It can also be seen as a limitation that no attempts were made to indentify ex-smokers. However, the disappearance of O.M.P after reducing or quitting smoking has been reported in the literature [8,21] and we do not expect that earlier exposure to smoking among ex-smokers affects the results of this cross-sectional investigation".

CONCLUSION

Cigarette Smokers showed more regularly with O.M.P (oral melanin pigmentations) than non cigarette smokers and the association suggested a effect depend on dose. O.M.P in cigarette smokers was most common on the buccal area and individuals smoking cigarettes without filter were more commonly affected.

Author's Contribution:

Concept & Design of Study:	Muhammad Nadeem
Drafting:	Muhammad Nadeem, Uzma Zareef,
Data Analysis:	Uzma Zareef, Irum Munir Raja
Revisiting Critically:	Muhammad Nadeem, Uzma Zareef, Irum Munir Raja
Final Approval of version:	Muhammad Nadeem

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

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Original Article

Pattern of Dental Plaque Distribution and Cigarette Smoking: A Cross sectional Study

Dental Plaque and Cigarette Smoking

Irum Munir Raja[1], Muhammad Nadeem[2] and Uzma Zareef[3]

ABSTRACT

Objective: To measure the incidence rate with distribution of dental plaque intraorally and its relationship with cigarette smoking habits in Pakistan population.

Study Design: Descriptive / cross-sectional study

Place and Duration of Study: This study was conducted at the Liaquat College of Medicine and Dentistry (L.C.M.D), Karachi from March 2017 to June 2017.

Material and Methods: The study population involved 388 adult individuals check up for free dental examination in a medical and dental camp arranged by Liaquat College of Medicine and Dentistry (L.C.M.D). Individuals who came to the Out Patient Department (OPD) were 425. In those 388 people (91%) were contributed in this study. A total of eight different sites of dentition were examined for the presence of dental plaque accumulation in each individual (3104 sites). Demographic and behavioural information including several dimensions of smoking habits was collected by questionnaire.

Main outcome measures: we did consecutive sampling for collecting data and individuals were allocated into groups on the basis of their smoking status (103 cigarette smokers and 285 non cigarette smokers), the dental plaque accumulated sites were examined by risk factors for example smoking habit, cigarette smoking /years, number and cigarettes' type/day.

Results: Smoking was considerably related with accumulation of dental plaque, predominantly significant in cigarette smokers on the lower anterior lingual tooth surface and in non cigarette smokers on upper buccal surface was highly affected.

Conclusion: More number of dental plaque accumulated sites was found in relation to the degree, duration of smoking and type of cigarettes.

Key Words: Dental Plaque Accumulation, Smoking Habit, Intra-Oral Distribution

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INTRODUCTION

"Dental plaque is considered to be a complex, metabolically interconnected, highly organized bacterial system consisting of dense masses of microorganisms, streptococci similar to strepto-coccusmutans, fixed in an inter-microbial matrix. A thin layer of fenestrated pellicle, which is an organic bacteria free film, deposits on the tooth surfaces within two hours after the teeth are brushed" [1-2]. The outcome of several researches have without fail recommended "a strong relationship between soft plaque and dental caries, gingivitis and periodontitis" [1,3,10].

The outcomes of previous researches "suggest that apart from genetic and constitutional factors, tobacco plays a pivotal rate in the occurrence of dental plaque accumulation association with periodontal diseases in different population". [4,6,18]

several researcher has explored "the distribution of dental plaque in human associated with smoking" [6, 15]. Although some have come across keen on the association among the cigarettes numbers and plaque buildup [7,8,13]. To the best of our facts, "the potentially influential role of the type of cigarettes smoked has not been investigated. Furthermore, the association is the above mentioned factors with distribution of plaque pattern are still a question mark for researchers" [9, 10].

The endeavor of this research were to look up the relationship between selected scale of contact to cigarette smoking and dental plaque build up and to examine the intra oral sharing of dental plaque pattern according to smoking status in a young adult population of subjects attending a free dental camp in Gulshan e Iqbal for free dental examination.

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MATERIALS AND METHODS

Participant Selection: Gulshan e Iqbal is one of the towns in Karachi. Community Dentistry department from L.C.M.D arranged a free dental camp in LCMD hospital. Darul Sehat hospital covers the huge residents of Gulshan e Iqbal. Chosen individuals were healthy. They tooth brush two times in a day. All applicants had full arch teeth present. Individual's age was between 18 - 35 years old. A consecutive sampling method was accepted out to.

Consent: The department of research and ethics of Liaquat College of Medicine & Dentistry Karachi, Pakistan approved this study. Written Consent forms were obtained by each participant before included in the study. All participants were informed about the purpose and extent of the study. Written concern forms were filled with signature of the selected participants before collecting

Data Collection: After satisfying with signing consent forms, data was together by questionnaire from each participant. Questionnaire included age, gender, cigarette smoking habit, duration, type, reason and past history and methods how they maintaining of oral health. Cigarette Smoking was there in the C.S while N.S did not smoking cigarette [11, 22, 27].

An experienced dental surgeon who standardized carried out all the assessments. It's a double blind study so no one know about hypothesis. Dentition was alienated into eight divisions lower labial, buccal, lingual anterior and lingual posterior, similarly in upper too. There were only 388 persons including 103 C.S and 285 N.C.S who were inspected in this research. There were 3104 area were inspected in cigarette smokers. We inspected each selected area to recognize dental plaque deposition. Our criteria that dental plaque should be present more than two third of the crown we nominated present. On the other hand we nominated No [19, 24, 26].

Statistical Analysis: With the help of SPSS ver. 21.0 we did statistical analysis. Quantitative variable for example age, quantity of cigarette were showed in mean. For analyzing between C.S with N.C.S we were used Chi Square. P-values =/<0.5 were noticeably important.

Inclusion & Exclusion Criteria: Health adult will be considered in inclusive criteria those have no clinical sign and symptom of any systemic disease with no history of betel nut and pan etc. A standardised methods of choice of individuals in importance of maintenance of oral health was having habit of tooth brushing two times in a day [17, 23-25].

Individuals having history and sign of systemic disease for example diabetic etc and history of Periodontitis were not including in this research. Individuals had history of radiation or had clinical signs of Oral Cancer were not include in this research.

Out of 425 only 388 full fill the criteria and include in this research.

Ethical Considerations: Written informed consent was given by each individual with research was accepted by the Department of Research and Ethics.

RESULTS

In this study total 103 C.Ss and 285 N.C.Ss were used. In those participant we analysed 3,104 areas were inspected for dental plaque. There were 53 areas in C.S and 48 areas affected in N.C.S.

Dental plaque distribution in oral cavity as per cigarette smoking habit: In C.S, dental plaque deposition were mostly establish in the lower lingual anterior site, although in N.C.S dental plaque was more common in the upper buccal area. (Table 1).

Dental plaque distribution in oral cavity as per cigarette smoking duration: The highest numbers area in which we observed dental plaque build up in C.S more than fourteen years habit of smoking. The occurrence of dental plaque growth was secondly for persons who had cigarette smoked 10 - 14 years. The occurrence of dental plaque accretion was similar for individuals who had smoked between 5 to 9 years and for those who had smoked less than 5 years. We conclude that duration and plaque deposition is directly proportion to each other (χ^2=17.64, p<0.001). (Table 2).

Dental plaque distribution in oral cavity as per number of cigarettes smoked each day: Individuals exposure to smoke minimum 10 cigarettes or less in each day were as a mild smokers. Individual's mentioned 10 cigarette or more per day were measured to be heavy smokers[23]. Our results showed that more cigarettes may affect dental plaque deposition. (Table 3).

Dental plaque distribution in oral cavity as per type of cigarettes smoked per day: Our research showed that those Individuals who using without filter cigarettes have more plaque accumulation on the other hand those using filter has less deposition.

Table No.1: Prevalence of sites of Dental Plaque Accumulation by Smoking Status

Different Sites	Smokers (103)		Non-Smokers (285)	
	n	%	n	%
Lower Labial	3	2.9	5	1.8
Lower Buccal	10	9.7	12	4.2
Lower Lingual Anterior	16	15.5	6	2.1
Lower Lingual Posterior	9	8.7	5	1.8
Upper Labial	3	2.9	3	1.1
Upper Buccal	12	11.7	15	5.3
Upper Palatal Anterior	0	0	1	0.4
Upper Palatal Posterior	0	0	1	0.4
Total sites	**53**	**51.5**	**48**	**17.1**

Table No.2: Prevalence of sites of Dental Plaque Accumulation in Smokers associated with duration of smoking in years

Duration of Smoking	Plaque Sites		Non Plaque Sites	Total Sites
	n	%	n	N
<5	4	3.5	107	112
5-9	4	3.5	106	112
10-14	10	3.6	271	280
>14	35	10.9	285	320
Total	**53**		**771**	**824**

(x2= 17.64, df= 3, p<0.001)

Table No.3: Prevalence of sites of Dental Plaque Accumulation in Smokers associated with Number of Cigarettes per Day

Number of Cigarettes	Plaque Sites		Non Plaque Sites	Total Sites
	n	%	n	N
Mild Smokers (less than 10 Cigarettes)	21	3.4	603	624
Heavy Smokers (10 or more Cigarettes)	32	16	168	200
Total	**53**		**771**	**824**

(x2= 40.17, df= 1, p<0.001)

DISCUSSION

According to our finding this is primary research examining relationship between smoking and dental plaque distribution in oral cavity in target residents. The result of this study confirms previous reports "suggesting the existence of a dose-response relationship between exposure to cigarette smoking and the occurrence of deposition of dental plaque in oral cavity both when exposure is measured in relevance to the frequency and duration of cigarette smoking[4,5,9, 19].

Our study mentioned that "the pattern of dental plaque differed between cigarette smokers and non cigarette smokers, with smokers presenting most regularly with dental plaque on the lower anterior lingual tooth surface, on the other hand, non cigarette smokers presented most frequently with dental plaque on the upper buccal tooth surface". This results is in agreement with previous findings "reported for a Swedish population and US population but deviates from the results of other studies in which there was no association between smoking and distribution of dental plaque accumulation".

Furthermore, a statistically significant association ($p < 0.001$) was noted between cigarette smoking with period & number of oral cavity areas involved by plaque accumulation. "The highest number of plaque accumulation oral tooth surface was observed in subjects smoking for maximum like more than 14 years (about 11%). On the other hand, the least number of accumulations of dental plaque tooth surfaces were noticed in individual cigarette smoking between 5 to 9 years and less than 5 years (3.5%)". This emphasizes the fact that increases in the duration of cigarette smoking adversely affects the oral hygiene status of an individual [5, 9, 25.]

"Cigarettes with filter were introduced to reduce the adverse effects of conventional cigarette smoking. To the best of our knowledge none of the previous studies have investigated the association between type of cigarette (filtered / non-filtered) smoked and accumulation of plaque in oral cavity. Our study showed a statistically significant difference between the level of plaque accumulated by filtered and non-filtered cigarettes".

Various factors have been suggested "to play a role in the increase in plaque accumulation in relevance to cigarette smoking. Although most of the studies emphasize that lower oxygen tension in the periodontal pocket of smokers favor the growth of anaerobic bacteria, thus, the quality of microbial flora [10, 12]. In addition to that, various studies have shown alteration of host immune response by cigarette smoking" [19,23,27]. Thus, the cumulative effect of these two factors may indirectly enhance plaque accumulated in cigarette smokers.

CONCLUSION

Cigarette Smokers showed more regularly with accumulation of dental plaque than non cigarette smokers and the association mentioned it's a dose-response effect. Dental plaque accumulation among cigarette smokers was most frequently found on the lower anterior lingual site on the other hand individuals who smoking cigarette without filtered and heavy smoker were more commonly affected.

Author's Contribution:

Concept & Design of Study:	Irum Munir Raja
Drafting:	Irum Munir Raja, Muhammad Nadeem
Data Analysis:	Muhammad Nadeem, Uzma Zareef
Revisiting Critically:	Irum Munir Raja, Muhammad Nadeem, Uzma Zareef
Final Approval of version:	Irum Munir Raja

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

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Original Article

Titanium Elastic Nailing in Adult Humerus Diaphyseal Fracture

Nailing in Humerus Diaphyseal Fracture

Abdul Karim[1], Malik Asrar Ahmed[2] and Ahsan ul Haq[1]

ABSTRACT

Objective: To study the union,joint stifness,deformity and incidence of infection after humerus diaphyseal fracture.
Study Design: Quasi experimental prospective study.
Place and Duration of Study: This study was conducted at the Sheikh Khalifa Bin Zayed Al-Nahyan Hospital Rawlakot Azad Kashmir from 01.08.2016 to 01.08.2017.
Materials and Methods: Thirty patients of either gender with age range between 18 years to 65 years with closed diaphyseal humerus fracture were included in study. Titanium elastic nailing was used to treat these patients. Outcome was measured in terms of union, infection rate, angulation and range of motion at shoulder and elbow joints.
Results: 30 patients were operated including 21 male and 9 female. We observed union in 23 patients. 07 patients had superficial infection around the margins of protuberant nail while 2 patients developed deep infection. Among the united fractures all patient had angulation in acceptable range. Seven patients who had delayed union or non-union showed limitation of range of movement at shoulder and elbow joints.
Conclusion: Adult humrus fracture fixed percutaneously takes less time,losses less blood,disrupts minimum tissue and the healing is natural. Selection criteria and procedure expertise make the best results outcome for this method and should be strictly observed**.**

Key Words: Titanium elastic nails, diaphyseal fracture adult humerus, trauma.

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INTRODUCTION

The fracture of humerus is relatively uncommon but recently the incidence of thisfracture in adults has increased,mainly due to the ageing of the population and increase in number of automobile accidents. [1]
The humerus fractures account for 3% to 5% of the skeletal injuries. The method of treatment of humerus fractures depends on many factors includingthe patient's general health,age of the patient, severity of trauma, the time from fractures to treatment and concurrent medical treatment.[2]
Conservative management is still considered the ideal method for the treatment of humerus shaft fractures.[3,4,5] Numerous authors apply short period of skeletal traction and then fracture bracing in ambulatory patients. Most surgeons believe that surgery intervention carries risk of infection.[6]
There is still controversy over implant selection when surgical intervention is considered in the management of diaphyseal fractures of thehumerus.

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Methods for Surgical treatment of the fracture humerus include close manipulation and fixation with intramedullary nail, open reduction and internal fixation with dynamic compression plate, external fixator and elastic intramedullay nails.
In our study, titanium elastic nails were used for adults having humerus diaphyseal fractures and the patients were followed up for one year. Percutaneous fixation of adult humerus with titanium elastic nails is time saving procedure with minimal soft tissue damage and infection.

MATERIALS AND METHODS

This study was carried out at department of orthopedic surgery, Sheikh Khalifa Bin Zayed Al-Nahyna Hospital Rawlakot Azad Kashmir from 01.08.2016 to 01.08.2017. Adult patient of 18 to 65 years of either gender with diaphyseal fracture of humerus were selected for the study. Only patients with closed or Gustilo type I open fracture were included in this study.
On admission, information regarding patient biodata, mechanism of injury, pattern of fracture and associated injury were recorded on a Performa.
After patient counselling and consent, pre-op preparation carried out. Operation was performed under general anesthesia on a fracture table under fluoroscopy guidance.
After short hospital stay, during which patient was educated about the care of operated limb, patient was discharged**.** Each patient was followed up at every two weeks interval for three months and then four weekly there after until completion of one year.

RESULTS

Thirty patients, complying with the inclusion criteria were included in the study. The mean age of patients in the study was 33.50 + 11.08 years and age rangewas 18 –65 years with 70% male and 30% female patients. There were 4 (13.3%) patients who had fracture with butterfly segment, 7 (23.3%) patients had short oblique fractures and 16 (53.3%) patients had transverse fracture. The1l union was seen in 76.7% patients and non-union in 23.3%.It was slightly higher in female patients.

Table No.1: Distribution of patients by union.

	Yes		No	
	No.	%	No.	%
Clinical Union	23	76.7	7	23.3
Radiological Union	23	76.7	7	23.3

Nonunion (total seven patients) was seen among 02 (6.66%) patients in age group of 18 – 30 years, 3 (10.0%) patients in age group of 31 – 40 years, 1 (3.33%) patients in 41 – 50 years age group and 1 (3.33%) patients in 51 – 65 years.

Table No.2: Age group distribution of Nonunion (n=7)

Age (Years)	Nonunion	
	No.	Percentage
18-30	2	6.66
31-40	3	10.0
41-50	1	3.33
51-65	1	3.33

The surgical site infection was observed in 9 (30%) patients. Among these patients, Deep infection was observed in only two patients while superficial infection was observed in seven patients.

Two patients with deep infection were treated with intra venous antibiotics according to culture and sensitivity test of discharge, removal of nails and temporary external fixator followed by fracture brace. Superficial infection was treated successfully in all seven patients with short course of oral antibiotics after culture and sensitivity test of discharge.

There were 23 (76.7%) patients in whom 0 º Angulation was observed after surgery, 5 (16.7%) patients with 5º Angulation and 2 (6.6%) patients with 10 º Angulation and none of the patients had > 10º Angulation. So, all the patients in our study had acceptable angulation.

Table No.3: Distribution of patients by Angulation at fracture site

Angulation	No.	Percentage
0 º Angulation *	23	76.7
5 º Angulation *	5	16.7
10 º Angulation *	2	6.6
> 10 º Angulation **	0	0

Shoulder stiffness was observed in 7 (23.3%) patients, while in other 23 (76.6%) patients, range of movements were in normal range.

At elbow joint, there were 23 (76.6%) patients in whom the flexion was in normal and in rest of 7 (23.3%) patients were labeled to have flexion lag. Elbow extension was normal in 23 (76.6%) patients, while in rest of 7 (23.3%) patients were labeled as extension lag.

Table No.4: Distribution of patients by the range of motion at the end of follow up

			No.	%age
Shoulder Joint	Flexion	145 º – 165 º	23	76.66
		< 145 º	7	23.33
	Extension	> 40 º	23	76.66
		< 40 º	7	23.33
	Abduction	> 140 º - 170 º	23	76.66
		< 40 º	7	23.33
Elbow Joint	Flexion	> 125 º – 145 º	23	76.66
		< 125 º	7	23.33
	Extension	0 º - 10 º	23	76.66
		> 10 º	7	23.33

DISCUSSION

The humerus fractures account for 3% to 5% of the skeletal injuries.[1,2] The method of treatment of humerus fractures depends on many factors including the patient's general health, age of the patient, severity of trauma, the time from fractures to treatment and concurrent medical treatment.[1]

Incidence of polytrauma is on rise due the high speed of transportation and mechanization. The treatment of humerus shaft fractures includes various methods from conservative to operative.[3]These fractures are more common in adults and middle aged group. Road traffic accidents are the predominant mode of injury.

A thorough knowledge of anatomy is important for the successful treatment of humeral shaft fractures.[4]

Union with shortening of the shaft less than 1 cm, angulation in antero-posterior view and lateral view of less than 20 degree and rotation of less than 30 degree are considered as acceptable criteria as it does not cause any functional and cosmetic deficiency.[5]

Conservative management is still considered the ideal method for the treatment of humerus shaft fractures.[6]

Historically, methods of conservative treatment included U plaster slab, skeletal traction, abduction casting, Velpeau dressing and hanging arm cast. Each with its own advantages and disadvantages.[6-8]

Non-operative treatment of these fractures requires longer period of immobilization, resulting in stiffness of shoulder and elbow joints.[9-10] Furthermore, non-union may result in about 10% of cases which may become difficult to treat without surgical intervention.[11-13]

There is recent trend to treat even simple humeral fracture with surgical stabilization to avoid these

problems of conservative treatment and to allow early mobilization and rapid return to work.[14,15]

Operative stabilization is required in patients with open fracture, multiple injuries, segmental humeral fractures, fracture with vascular injury, radial nerve palsy after fracture manipulation, fractures with ipsilateral forearm fractures and inability to maintain fracture alignment with non-operative treatment either due to angulation or noncompliance in obese or elderly patients.[4]

Fixation of a fracture of the humerus shaft in the multiple-injury patient allow increase in the mobility of the patient, helps in the difficult nursing care in intensive care unit and permit full access to the patient for pulmonary physiotherapy. Fracture fixation also controls the angulation and length of the fracture in a supine, unconscious patient and allows early mobilization of the upper extremity.[16]

Plate osteosynthesis is a familiar technique with advantages[17] of anatomical reduction, rigid fixation allowing early mobilization and more patient satisfaction but at the cost of larger incision, more periosteal stripping, loss of fracture hematoma and risk of radial nerve injury, infection and non-union.[18]

Rush nails were introduced by rush brothers for intramedullary fixation of long bones fractures. Later on Enders nails were designed and used in place of the Rush nails successfully, but usually multiple Enders nails were required to achieve fracture stability.[19]

Locked IM nails have been associated with postoperative shoulder pain and stiffness, the possibility of impingement from proximally prominent hardware and risk of further fracture comminution during reaming or nail insertion are complications of the rigid nailing.[20]

Reports in which plate fixation is directly compared with intramedullary fixation, the rate of complications associated with locked intramedullary nails has appeared to be higher than that associated with plate fixation.[21-23]

In the 1980s, JP Metaizeau and Jean Prevot in France designed Titanium Elastic Nails (TEN) based on the idea of the Rush nail. This nail was also designed on the principles of three point fixation to control rotation of the bone.[24]Two pre-tensioned nails are inserted from opposite sides of the bone. With this design, surgeons were able to create an elastic and stable fixation device.

Three point support and inner bracing Titanium elastic nails reduce chances of angulation in both anteroposterior and Varus/valgus by achieving axial and rotatory stability.[24]

It offers

- Stable fracture fixation
- Rapid, biological healing with external callus
- Easy implant removal with reduced risk of re-fracture
- Respect for the growth plate and blood supply of bone
- Early discharge from hospital and mobilization.[25]

Numerous studies are available on the use of titanium elastic nail in the femoral fractures of children with excellent results.[25-26]

The study on femoral fractures of children with excellent results encourages the use of titanium elastic nails in other long bone fractures.

This technique shows very good functional and cosmetic results. It allows an early functional and cast-free follow-up with a quick pain reduction. The elastic nailing of humeral shaft fractures is a minimally invasive, simple and well reproducible technique.[27]It preserves fracture hematoma that promotes early callus formation with less chances of infection. Removal of implant is quick, easy and less time consuming.[28]

Insertion site of the elastic nails remains controversial. Anti-grade or retro grade insertion was studied in 2008. This study showed that the insertion site morbidity is always due to the technique used by the surgeon. If proper attention is paid at the time of insertion of nail, the complication can be avoided altogether.[29]

There are limited studies available on the elastic nailing in adults.[24]

In this study we used titanium elastic nailing for adult humeral diaphyseal fracture with retrograde entry and evaluated the outcome in terms of union and complications rate.

CONCLUSION

Titanium elastic nailing is a very good alternative treatment option for adult humeral diaphyseal fractures with good clinical and functional outcome and minimal complications.

Author's Contribution:

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Data Analysis:	Malik Asrar Ahmed, Ahsan ul Haq
Revisiting Critically:	Abdul Karim, Malik Asrar Ahmed
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Original Article

Frequency of H. Pylori Infection in Children Presenting with Recurrent Abdominal Pain

H. Pylori Infection in Children

Jahanzeb Khan Afridi[1], Rahida Karim[1], Ahmad Khizar[2] and Muhammad Batoor Zaman[3]

ABSTRACT

Objective: To determine the frequency of helicobacter pylori among children presenting with recurrent abdominal pain.

Study Design: Descriptive / Cross-sectional study.

Study and Duration of Study: This study was conducted in the in the Department of Pediatrics Hayatabad Medical Complex, Peshawar from 1st April 2016 to 30th November 2016.

Materials and Methods: Sample size was 177 using 8% proportion of H.pylori among children with Recurrent Abdominal Pain (RAP), with 95% confidence interval and 4% margin of error using WHO formula for sample size estimation.

Results: The mean age group of our sample was 11.29 ± 2.74 years of which 75.1% were male and 24.9% were female children. Most of the sampled children were in the age group between 8-16 years. The mean duration of abdominal pain was 4.86 ± 1.14 months. On ELISA, H. Pylori was detected in 24.9% of patients.

Conclusion: H. Pylori is quite common in our pediatric population presenting with recurrent abdominal pain. It is a serious calamity in children and we recommend more research to find out risk factors related to this high burden of H. Pylori.

Key Words: ELISA, Helicobacter Pylori, Recurrent abdominal pain

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INTRODUCTION

Many children seek medical advice for Recurrent Abdominal Pain (RAP). Recurrent Abdominal Pain hinders the daily activities of 4% to 25% of school going children . It seems to be a benign problem, but morbidities associated with RAP include poor school attendance, hospital admission and laprotomies, symptoms sometimes continue to adulthood[1,2].

Social withdrawal, poor physical abilities, school absentees occur in 10% to 15% of school children due to recurrent abdominal pain on regular basis that result in increased health care visits and has poor effect on child's well being[3] [4]. The burden of disease is under scored as 1 out of 3 experience chronic abdominal pain for minimum of 5 years[5].Irritable bowel syndrome, a functional gastro-intestinal disorder is one of adulthood complication of childhood RAP[6].

Acidic environment of stomach is site for growth of H.pylori, a pathogenic Gram-negative spiral bacillus.

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It is a leading cause of chronic gastritis, peptic ulcers, non-ulcer dyspepsia, gastric adenocarcinoma and mucosa-associated lymphoid tissue (MALT) lymphoma. 50% of the total world population is infected with H. pylori according one estimate. Developing World currently is on hit list of H.pylori[7].

Longstanding exposure to H. pylori is usually asymptomatic but can lead to chronic gastritis in children and sometimes peptic ulcer disease is linked to it[8]. Epigastric pain was considered as red flag symptom in one study, H pylori and abdominal pain were found to have significant associations in pediatric patients[9]. No causal relationships between abdominal pain and H. pylori infection have been found in other studies[10].

In 65% of Turkish children presenting with recurrent abdominal pain and dyspepsia H. Pylori infection was the cause[11]. The prevalence of H. pylori children infectionwith recurrent pain abdomen was 8.0% (70/873) as observed in another study[8].

The present study is designed to determine the frequency of H. Pylori among children presenting with recurrent abdominal pain. H. Pylori is not uncommon in our population and as mentioned above, the literature suggested variations in its prevalence rates from region to region. Moreover, few studies suggested an association between H pylori and RAP among children while other studies failed to do so. In this study, we will determine its frequency among local children presenting with RAP. The results of this study will give us local magnitude of the problem and will be shared

with other local pediatricians and gastroenterologists to develop future research strategies.

MATERIALS AND METHODS

This descriptive cross sectional study was conducted in Pediatric Department Hayatabad Medical Complex, Peshawar. The study was conducted over the period of 8 months. Sample size was 177 using 8% proportion of H. Pylori among children with Recurrent Abdominal Pain (RAP), with 95% confidence interval and 4% margin of error using WHO formula for sample size estimation.

Children of both genders, age 5 – 16 years, who presented with RAP for at least 3 months were enrolled. Children with previous diagnosis or who received treatment for H. Pylori and those with history of intake of PPI in last 2 week were not enrolled in the study.

Date Collection Procedure: Hospitals research and ethical board approved the study to be conducted. All the subjects fulfilling inclusion criteria (recurrent abdominal pain according to Rome II criteria) were enrolled in the study through OPD department.

The aims and importance of the study was explained to the parents and a written informed consent was obtained. History and examination were carried out in all the children.

Five milliliter of blood was drawn under strict aseptic technique and was sent to hospital laboratory for detection of H pylori using ELISA method. All the investigations were done from hospital laboratory by single expert pathologist.

Data Analysis Procedure: All the data was stored and analyzed on SPPS version 14. Mean ± SD was calculated for quantitative variables like age and duration of abdominal pain. Frequencies and percentages were calculated for categorical variables like sex and H pylori. H pylori were stratified with age and gender to observe the effect modifications. Post-stratification was performed using chi-square test keeping a p-value ≤ 0.05.

RESULTS

A total of 177 children presenting with recurrent abdominal pain were enrolled in the study.The mean age of the sample was 11.29 ± 2.74 years. The range of age in our study was 9.5 years with minimum age of 6.5 years and maximum age of 16.00 years. On grouping the sample in different age groups, we observed that 15.3% of patients were in the age group between 5.00 to 8.00 years, 39% were in the age group 8.01 to 12.00 years and 45.8% of patients were in the age group 12.01 to 16.00 years.

While distributing the patients with regards to gender, we observed that in our study 75.1% of the samples were male and 24.9% were female gender. (Table 1)

The mean duration of abdominal pain in our sample was 4.86 ± 1.14 months.

From all the children, a 5cc of blood was drawn under strict aseptic technique and sent to hospital laboratory for detection of H pylori using ELISA method.

Table No.1: Gender-wise distribution of sample (n=177)

Gender		Frequency	Percent
	Male	133	75.1
	Female	44	24.9
	Total	177	100.0

Table No.2: Frequency of helicobacter pylori (n=177)

H. Pylori		Frequency	Percent
	Yes	44	24.9
	No	133	75.1
	Total	177	100.0

Table No.3: Age group wise stratification of H. Pylori (n=177)

			H. Pylori		Total
			Yes	No	
Age Groups	5.00 to 8.00 years	Count	9	18	27
		% within Age Groups	33.3%	66.7%	100.0%
	8.01 to 12.00 years	Count	17	52	69
		% within Age Groups	24.6%	75.4%	100.0%
	12.01 to 16.00 years	Count	18	63	81
		% within Age Groups	22.2%	77.8%	100.0%
Total		Count	44	133	177
		% within Age Groups	24.9%	75.1%	100.0%

P Value: 0.511

Table No.4: Gender group wise stratification of H. Pylori (n=177)

			H. Pylori		Total
			Yes	No	
Gender of the Children	Male	Count	27	106	133
		% within Gender of the Children	20.3%	79.7%	100.0%
	Female	Count	17	27	44
		% within Gender of the Children	38.6%	61.4%	100.0%
Total		Count	44	133	177
		% within Gender of the Children	24.9%	75.1%	100.0%

P Value: 0.015

On report, H. Pylori was detected in 24.9% of children (Table 2)

While we stratified H. Pylori with regards to age groups, we obtained a statistically insignificant difference using chi square test with and a p-value of 0.511 (Table 3).

While we stratified H. Pylori with regards to gender, we observed that the difference was statistically significant when we applied chi square test and p value of 0.015 (Table 4).

DISCUSSION

In general practice at Netherlands, 5% of childhood consultations were for abdomen pain[12], while 2% to 4% consultation occurred in studies performed in Austria and the United States[13]. Label of Functional abdominal pain is given to undiagnosed medical cases. Poor physical and mental activity, as well as disturbed social life and school failure due to repeated return of abdomen pain found in 10% to 15% of school subjects, resulted in frequent health care visits[3,4]. This problem is underestimated as one out of three children suffer from tummy pain for at least 5 years5. Irritable Bowel Syndrome in adults is considered to be continuation of functional gastrointestinal disorders in childhood[6,14].

Few factors have been identified to predict weather childhood functional abdominal pain, interferes with wellbeing of victims, as it persists for years. Recently, functional gastrointestinal disorders in young adulthood have been associated with higher level of non-gastrointestinal symptoms[4,14]. Children with Functional abdominal pain having somatic symptoms in addition to abdominal pain can be used as clinical marker for prediction of poor outcome. Subjects with long term persistence of abdominal pain can be correlated to parents, if they also have gastrointestinal symptoms. In the light of these facts family physician can identify those subjects who are at risk for long term abdomen pain. They can plan more appropriate management strategies before any sequel, such as strict fallow up or consulting other health care colleagues if required.

H. Pylori is the most common pathogen in children worldwide[16], it is gram negative bacterium present in more than 50% of the world population, most of the infected children remain asymptomatic, although chronic gastritis and peptic ulcer occurred due to prolong exposure to H. Pylori infection.

H. Pylori prevalence varies with age, region and race. Increase in age in associated with increase prevalence of H. Pylori infection. Socioeconomic status modifies its prevalence as its frequency is variable in developed and developing countries.

In addition to socioeconomic factor personal hygiene and other member in the family being infected are consider to be important factors in determining the frequency of H. Pylori infection in childhood[17].

Transmission of H. Pylori infection occurs from person to person and even within families[18].

A study was conducted in 2005 on 15,916 healthy people who had age above 16years. Those who were in 20s prevalence of H. Pylori was 29.3%, those in their 30s, their prevalence was 49.1%, 57.8% in those who were in 40s, 61.5% for those in their 50s this shows increase prevalence with increase in age[19].

Our data is comparable to other developing countries, studies performed in Republic of Benin[20], Egypt[21], India[22], and reported from other Pakistani23 studies, had similar results as ours. 7% to 15% prevalence of H.Pylori infection among pediatric age group has been reported in New Zealand24, Germany[25], and the United States[26]. The major reasons for difference in prevalence of H. Pylori infection among children in developed and developing countries are due to low socioeconomic status, poor environmental and living condition[20,21]. Literature has reported low socioeconomic class to be at high risk for H. Pylori infection[27]. Children belonging to low income group have poor living condition and sanitary habits thus predisposing them to H. Pylori infection; but this is not always true as other sources of infection that are independent of social class also exists.

Controversial reports have been generated regarding association between H. Pylori infection and recurrent abdominal pain. No links between H. Pylori infection and recurrent abdominal pain have been proven from India[28] and Sweden[29]. Similarly no association between H. Pylori and recurrent abdomen pain has been shown in many reviews and Meta analysis[30]. In our study we found that children with recurrent abdominal pain had prevalence of H.Pylori infection. Studies from Saudi Arabia[31] and the United States[32] are comparable to our studies. Helminthiasis is common cause of recurrent abdomen pain in children in our society especially in low socio-economic class. It is common practice for General Physician and parents to administering antihelminthics to children with recurrent abdominal pain. Our study suggested additional role of H. Pylori in recurrent abdominal pain. These finding require additional interventional study in large population of children to document role of H. Pylori in recurrent abdomen pain.

Subjects included in the study were recruited from hospital which was major limitation which was difficult to generalize our result as subject from general pediatric population were excluded. It is very difficult to find subject from general pediatric population for research purpose as they do not give assent or consent for blood sampling. Community base study on H. Pylori in our population has limitation because of this reason. In developing countries research test such is urea breath test or fecal antigen test as they are acceptable to the community are recommended..

CONCLUSION

Recurrent abdominal pain due to H. Pylori is common in our pediatric population. Therefore further research to explore risk factors for H. Pylori infection is recommended. This will reduce the burden of H. Pylori and associated morbidities.

Author's Contribution:

Concept & Design of Study:	Jahanzeb Khan Afridi, Rahida Karim
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Original Article

Pattern of Substance Abuse in Patients; A Cross Sectional Study at Khawaja Muhammad Safdar Medical College Sialkot, Pakistan

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ABSTRACT

Objective: The objective of the current study was to assess the pattern of substance abuse in patients coming to our hospital.

Study Design: Cross sectional study.

Place and Duration of Study: This study was conducted at the Department of Psychiatry & Behavioral Sciences, AIMTH affiliated to KMSMC Sialkot, Pakistan from October to November 2017.

Materials and Methods: Adult patients coming in contact through OPD, indoor and emergency were approached. Non-probability convenience sampling technique was used to get a sample size of 200 patients. Inclusion criteria were patients who were actively using and dependant on any type of substance of abuse according to the ICD-10 Criteria. Written informed consent was taken. Patients suffering from severe physical illness needing urgent and emergency care, unconscious or in delirium were excluded from the study. The data was collected on a sheet and analyzed by SPSS v 21.

Results: There were 188 males and only 12 females. 53.5% belonged to low economic status. 21.5% of the patients from rural areas while 58.5% from urban areas and 20% were homeless. 89.5% were jobless. 21% of the patients had family history of drug abuse. 40% were poly substances abusers. 27.5% abused opium and heroin, 18% cannabis, 7% injections, 6.5% benzodiazepines and 1% others.

Conclusion: Most of the patients coming to our hospital were urban jobless males from lower economic status. One fifth of the patients had family history of drug abuse. 40% were poly substances abusers. 27.5% abused opium and heroin, 18% cannabis, 7% injections, 6.5% benzodiazepines and 1% others.

Key Words: Drug abuse, Pattern of substance abuse, Teaching Hospital, Health Services,

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INTRODUCTION

Substance abuse is a major health problem. One of the definitions proposed that it is the pattern of substance being used which is maladaptive which leads to clinical and significant impairment and/or distress. The subject also experiences tolerance as well as withdrawal.[1]

Common drug used in west is alcohol. Other drugs are like MDMA, benzodiazepines and opioids. They may result in harm to health. Depression in students of medical can be due to stress [2] and they might start ruminating.[3]

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People who are abusing drugs are at increased risk of suffering from various medical problems and might be referred inappropriately in hospitals.[4] They may get anxious and depressed during or after surgery.[5] They get complications in surgery for example keloids and hypertrophic scars.[6] There is also chance that they are not satisfied with the treatments provided in hospital.[7] Female may be subject of battering and abuse as a consequence of substance abuse.[8] Psychotic illnesses eg schizophrenia may a consequence of substance abuse and a cause of major burden on the family and caregivers.[9]

As can be seen substance abuse is major problem to health, both physical and psychological. It can cause enormous burden which may be economic, social and at country level can become a problem which can be considered in the realms of public health needing urgent and prompt action. The physical illnesses can be damage to lungs, heart, liver, HCV infections,[10] HIV, GIT, kidneys and lack of nutrition. The psychological problems can be psychosis, schizophrenia, depression, mania, anxiety and delirium.[11] It is imperative to address this issues on urgent basis as it is already

becoming a public health issue. To address the issue we need to know what kind of substances are being used in our area to make plan for betterment. To our knowledge no research has been carried out in our hospital up till now on this issue. The objective of the current study was to assess pattern of substance abuse in patients coming to our hospital.

MATERIALS AND METHODS

It was a cross sectional study carried out in the form of a survey at AIMTH, Sialkot from October to November 2017. The study was carried out at the department of Psychiatry and Behavioral Sciences. Guidelines in the declaration of Helsinki were followed. Ethics review committee approved the study. Adult patients coming in contact through OPD, indoor and emergency were approached. Non-probability convenience sampling technique was used get a sample size of 200 patients. Inclusion criteria were patients who were actively using and dependant on any type of substance of abuse according to the ICD-10 Criteria. Written informed consent was taken. For patients who were illiterate, data collectors made sure that they understand all the aspects of the study by reading or telling them in their native language all the details. Title along with purpose of the study was explained to the patients and they were assured of the complete confidentiality of their data. Patients suffering from severe physical illness needing urgent and emergency care, unconscious or in delirium were excluded from the study.

A data sheet was designed to collect information about demographics and other details of the patients. Data about the substance being abused was collected from patients ensuring privacy and confidentiality. They were provided with the available treatments in our hospital. As it is a large public sector hospital, all treatment is provided by the state free of cost. They were also encouraged to keep follow up with the treatment provided. The data was collected on the sheet and analyzed by SPSS v 21.

RESULTS

The results show that there were 188 males and only 12 female patients. There was preponderance of male patients. It may be because of stigma that many female patients suffering from drug abuse could not or were not able to reach the hospital to get treatment. Most of the patients 53.5% belonged to the low economic status. Patients from middle class were 26% and from upper class 21.5%. The large number of patients from poor economic background may be due to their downward drift because of drug abuse. The other hypothesis is that may be our hospital is a large public sector hospital and all the treatment is provided free to all patients by the state so patients from poor back ground resorted to getting treatment from here. 21.5% of the patients resided in rural areas while 58.5% in urban areas. 20% were homeless. The largest percentage from urban area may be because it was easy to reach hospital from city than a far flung rural area or it could be because of awareness in urban patients of the availability of treatment in hospital. The 20% patients, who described themselves homeless, usually lived on streets or roads and slept whatever place they could find. They mostly lived in urban rather than rural areas but it was difficult to classify them to one category as they kept on moving from place to place. Most of the patients 89.5% were jobless. Only 10.5% had regular or permanent jobs. Joblessness may be due to their drug abuse or they may have started the drug abuse due to joblessness. It was not the objective of this study, so it was not further probed. 21% of the patients had family history of drug abuse. Many theories have been postulated from genetics to environment and debate of nature verses nurture is still going on. The impact of observational learning may be a factor. Table 1.

Table No.1. Characteristic of patients N=200

Gender	**Frequency**	**Percentage**
Male	**188**	**94%**
Female	**12**	**6%**
Economic status		
Low	**107**	**53.5%**
Middle	**52**	**26%**
Upper	**41**	**20.5%**
Residence		
Rural	**43**	**21.5%**
Urban	**117**	**58.5%**
Homeless	**40**	**20%**
Having job		
Yes	**21**	**10.5%**
No	**179**	**89.5%**
Family history of drug abuse		
Yes	**42**	**21%**
No	**158**	**79%**

Table No.2: Pattern of substance abuse

Type	**Frequncy= n**	**Percentage %**
Opium	12	6 %
Heroin	43	21.5 %
Poly substance	80	40 %
Cannabis	36	18 %
Injections	14	7 %
Benzodiazepines	13	6.5 %
Others	2	1 %

The most common were patients with poly substance abuse. They abused more than one substance at a time and kept on shifting from one drug to other. In our study we classified poly substance abuse patients as those patients who were doing it at the time of interview. Some patients had used only one type of drug in the past but now were using two or more than two drugs at the time of interview. This group was the

largest about 40% of the whole sample. Although it was not the objective of the study but they were suffering from most medical, surgical and psychological problems than the other type of patients with drug abuse. 21.5% of the patients exclusively used heroin and 6% used opium. These are similar substances and belong to opioid group of drugs. Heroin in many forms is used mostly now. There are many street names of it like crystal and button. These differ in potency and price. 18% of the patients used cannabis. They used it in different local forms like bhang, booti or garda etc.7% of the patients used injections. They used i/v injections mostly tramadol and other pain killers with effects like euphoria. Use of benzodiazepines was seen in 6.5% of patients and mostly these were pills. Table 2

DISCUSSION

The results of our study show that most of the patients coming to our hospital were urban jobless males from lower economic status. One fifth of the patients had family history of drug abuse. 40% were poly substances abusers. 27.5% abused opium and heroin, 18% cannabis, 7% injections, 6.5% benzodiazepines and 1% others. Another study has reported similar findings that males, being unmarried and belonging to age group 18-44 and poor economic conditions were risk factors for indulging in drug abuse. Genetic and family factors also play a role.[12]

The pattern of substances being abused differs in different societies. Culture and attitudes are different across societies and may determine what kind of substances people will use. In our study poly substance abuse was the most common followed by opioids and cannabis. There is easy availability of these drugs as our country lies in the infamous route of drug transport from Afghanistan.[13]

In our study 20% patients were homeless. A study reports that people who belong to a family which is supportive have lower chances of getting into the problem of drug abuse. On the other hand parents who are strict may increase the chances of drug abuse in children.[14] Our patients did not report alcohol abuse. This has also been reported by another study. Alcohol is banned strictly and carries social taboo so patients might not report it.[15]

Our study has some strengths and limitation. The strength of the study was its easy methodology. Data was collected easily from patients coming to hospital. It did not require any psychometric scale of English language to be translated in Urdu Or Punjabi. Simple survey sheet was used to collect data during interview. Data collectors had the ease of data collection in hospital during treatment process and separate time or resources were not needed to be allocated. The limitations of the study are that it is a hospital based study and results may not be generalized to community. In future community based studies using robust methodology are needed to resolve the issue further.

CONCLUSION

Most of the patients coming to our hospital were urban jobless males from lower economic status. One fifth of the patients had family history of drug abuse. 40% were poly substances abusers. 27.5% abused opium and heroin, 18% cannabis, 7% injections, 6.5% benzodiazepines and 1% others.

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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

Surgical Site Infection

Surgical Site Infection Rate at Tertiary Care Hospital Sialkot

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ABSTRACT

Objective: The purpose of study was to observe surgical site infection rate at Department of Surgery, Allama Iqbal Memorial Teaching Hospital Sialkot.

Study Design: Observational / prospective study.

Place and Duration of Study: This study was conducted at the General Surgery Unit 2 at Allama Iqbal Memorial Teaching Hospital Sialkot an allied institute of Khawaja Muhammad Safdar Medical College from January 2017 to November 2017.

Materials and Methods: Total of 1400 patients were included. Before conduction of study Ethical review committee permission was sought and access to patient data for follow up was obtained. Only those patients who completed follow up for 30 days were included, patient lost to follow up or deceased were excluded. All admitted patients undergoing elective surgery were included and categorized broadly into Abdominal Surgery, Surgery on Thyroid and Parathyroid, Breast Surgery and Perineal Surgery. Demographic data, wound type, comorbid factors, type of surgery, duration of hospital stay were noted on structured questionnaire. All Patient who underwent surgery were managed according to CDC recommendation for prevention of Surgical Site Infections [5]. Wound condition was recorded daily using ASEPSIS score during hospital stay. All patients were given pre-operative prophylactic and postoperative antibiotics. Patients were followed up after discharge weekly for 30 days. In event of Surgical Site Infection wound swab or pus for culture and sensitivity was obtained and appropriate antibiotics according to sensitivity were given. Data was analyzed on SPSS version 22. Continuous variables like age and length of stay were displayed as mean and standard deviation. Percentages were calculated for categorical variable such as gender, type of procedure and co morbid factors.

Results: A total of 1400 patients were enrolled in study out of which 195 patients were excluded due to loss of follow up or death, the remaining 1205 patients were studied among them 14.1% (n171) developed Surgical Site Infection (SSI). Rate of infection related to clean, clean contaminated, contaminated and dirty wounds was 1.5%, 3%, 8% and 25% respectively in studies conducted in developed world[1]. Rate of surgical site infection in our study in clean, clean contaminated, contaminated and dirty wounds was 3.3%, 10.4%, 17.2% and 26.9% respectively.

Conclusion: Frequency of surgical site infection in our study was comparable to developing countries but higher than developed countries.

Key Words: Surgical Site, Infection Rate, Tertiary Care Hospital.

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INTRODUCTION

Loss of protective barrier in form of skin makes patients undergoing surgery prone to infections. Surgical site wound infection is one of the most common nosocomial infection encountered in hospitals[1]. To name a few problems associated with surgical site infections increasing health costs, prolonged hospital stay, re-admission, loss of patient confidence in physician[2,3].

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As prevention is better than cure a number of predictive risk factor scoring systems have been developed, among them one is of particular interest National Nosocomial Infections Surveillance [NNIS] Basic SSI Risk Index and American College of Surgery National Surgical Quality Improvement Program[4]. Surgical site infection according to CDC definitions is classified as Superficial Incisional: involving skin and subcutaneous tissue under incision; Deep incisional primary: surgical site infection in primary incision involving muscle and fascia in a patient who has surgery performed by more than one incisions; Deep Incisional secondary: surgical site infection involving muscle and fascia in a secondary incision in a patient who had surgery performed by more than one incisions; Organ/ space related surgical site infection: involving any part of the body opened or manipulated during operation[5].

Surveillance of Surgical site infection is needed to determine the burden of disease and to correct any significant deterrent to achieve lowest rates of SSI

possible keeping view of ground realities. The purpose of our study is to assess frequency of Surgical Site infections in General Surgery ward and identify its risk factors.

MATERIALS AND METHODS

This study was conducted in General Surgery Unit 2 at Allama Iqbal Memorial Teaching Hospital Sialkot an allied institute of Khawaja Muhammad Safdar Medical College over a period of one year, a total of 1400 patients were included. Before conduction of study Ethical review committee permission was sought and access to patient data for follow up was obtained. Only those patients who completed follow up for 30 days were included, patient lost to follow up or deceased were excluded. All admitted patients undergoing elective surgery were included and categorized broadly into Abdominal Surgery, Surgery on Thyroid and Parathyroid, Breast Surgery and Perineal Surgery. Demographic data, wound type, comorbid factors, type of surgery, duration of hospital stay were noted on structured questionnaire. All Patient who underwent surgery were managed according to CDC recommendation for prevention of Surgical Site Infections[5]. Wound condition was recorded daily using ASEPSIS score during hospital stay. All patients were given pre-operative prophylactic and postoperative antibiotics. Patients were followed up after discharge weekly for 30 days. In event of Surgical Site Infection wound swab or pus for culture and sensitivity was obtained and appropriate antibiotics according to sensitivity were given. Data was analyzed on SPSS version 22. Continuous variables like age and length of stay were displayed as mean and standard deviation. Percentages were calculated for categorical variable such as gender, type of procedure and co morbid factors.

RESULTS

Total of 1205 patients who were studied gender distribution 492(40.82%) patients were male and 713(59.17%) patients were female according to procedure is shown in Table1. Overall infection rate in our study across all procedure was 14.1%. Mean age of patients was 38.9 years ± 14.3 years. Distribution of wound types in Abdominal Surgery 497(41.2%), Breast surgery 53(4.3%), Thyroid and Parathyroid 65(5.3%) and Perineal Surgery 575(47.6%) were given in Table 2. Rate of surgical site infection in different types of surgical patients was highest in perineal surgery 17.2%, followed by abdominal surgery 12.9%, breast surgery 3.9% and lowest in thyroid parathyroid surgery 3% as shown in Table 3. This shows perineal surgery with highest number of contaminated and dirty wounds had highest rate of surgical infection and breast, thyroid parathyroid surgery has lowest rate as these surgeries have mostly clean wounds. Rate of surgical site infection in clean, clean contaminated, contaminated and dirty wounds was 3.3%, 10.4%, 17.2% and 26.9% respectively as shown in table 4. All patients were receiving prophylactic antibiotics ceftriaxone and ciprofloxacin; but no statistical difference was observed in surgical site infection rate.

Mean length of hospital stay for all patients was 4.7 day±2.04 days. Mean Length of hospital stay for Clean 3.948 days, Clean Contaminated 5.714 days, Contaminated 4.000 days and Dirty wound 5.875 days as shown in table 5.

Table No. 1 Gender Distribution in Surgical Site Infection

S#	Gender	Abdominal Surgery	Breast Surgery	Thyroid and Parathroid	Perineal Surgery	Total
1	Male	214(17.7%)	0	4(0.33%)	274(22.7%)	492(40.82%)
2	Female	283(23.4%)	53(4.3%)	61(5.0%)	316(26.2%)	713(59.1%)

Table No. 2 Wound Distribution in Surgical Site Infection

S#	Wound	Procedure				
		Abdominal Surgery N(%	Breast Surgery N(%)	Thyroid and Parathroid N(%)	Perineal Surgery N(%)	Total N
1	Clean	0	53(4.3%)	65(5.3%)	0	118
2	Clean Contaminated	497(41.2%)	0	0	0	497
3	Contaminated	0	0	0	575(47.6%)	575
4	Dirty	0	0	0	16(1.3%)	16
Total		497(41.2%)	53(4.3%)	65(5.3%)	591 (48.9)	1205

Table No. 3 Distribution of Sites in Surgical Site Infection

Surgical Sites Infection	Abdominal Surgery N(%)	Breast Surgery N(%)	Thyroid and Parathyroid N(%)	Perineal Surgery N(%)
None	436(87%)	51(96.2%)	63(96.9%)	488(82.7%)
Present	65(12.9%)	2(3.9%)	2(3%)	102(17.2%)

Table No. 4 Distribution of Wounds in Surgical Site Infection

	Type of Wound			
Surgical Site Infection	**Clean**	**Clean Contaminated**	**Contaminated**	**Dirty**
None	114(96.6%)	436(89.5%)	475(82.7%)	19(73%)
Present	4(3.3%)	51(10.4%)	99(17.2%)	7(26.9%)
Total	118	487	574	26

Table No. 5 Mean Duration of hospital stay (days) in different wounds

Wound	Mean Duration (days)	No. of cases	Std. Deviation
Clean	3.948	116	1.0701
Clean Contaminated	5.714	497	2.7575
Contaminated	4.000	574	.0000
Dirty	5.875	18	4.0311
Total	4.728	1205	2.0449

DISCUSSION

Surgical site infection is one of the biggest problems in healthcare industry effecting surgical and it costs 1.47-19 billion Euros[6]. Rate of Surgical site infection has been progressively decreasing in developed world with rates reported as low as 2.6%[7]. Rates of infection in laparoscopic procedures Cholecystectomy, colonic surgery appendectomy and gastric surgery are even lower 0.69%, 4.32%, 1.37%, 2.71%[8,9]. Rates of infection in Pakistani tertiary care hospital at Karachi has been reported to be 7.32%[10]. Comparative analysis of studies reporting surgical site infections in Brazil 5.1% Philippines 7.8% and Nepal 7.3% are lower than any hospital in Pakistan this proves that more is to be done in prevention, risks assessment and management[11]. When compared to other hospitals in our country reported rates of Surgical site infection in our study is higher (14.1%)[10]. Causative factors identified in studies conducted in our country are indiscriminate use of antibiotics leading to growth of resistant organisms, poor nutritional status of patient leading to poor wound healing, absence of barrier nursing and inadequate sterilization. Patient overcrowding in public sector hospitals leads to cross infection[12]. Another trend noticeable in our study has been increasing rate of infection from clean wounds toward dirty wounds apparent in other studies with as high as 23% surgical site infection, this has been noticeable in units conducting laparoscopic and open colorectal surgery[13,14]. No statistical difference was noted when surgical site infection rate was compared with age and co morbid factors[14]. Cohen et al identified risk factors for surgical site infections as estimated blood loss over 1 litre (P=0.017), previous Surgical site infection (P=.012) and diabetes (P=0.050)[15] and similar trend has been noted in our study. Duration of procedure and BMI has also been established as independent risk factors[16]. Surgical site infection risk score calculation by Walraven et al have included patient factors like smoking BMI , operative factors like surgical urgency; increased ASA class; longer operation duration; infected wounds; general anaesthesia; performance of more than one procedure; CPT score, and co morbidities like peripheral vascular disease, metastatic cancer, chronic steroid use, recent sepsis in their predictive score.[17]

No association between use of antibiotics, surgical site infection and hospital stay could be identified.

CONCLUSION

Frequency of Surgical site infections is similar to developing countries but very much higher than developed countries with poor compliance to sterilization protocols, unabated use of antibiotics, and poor socioeconomic status of patients. No apparent surveillance protocols of SSI like American College of Surgery National Surgical Quality Improvement Program and absence of infectious disease specialists at most tertiary care public sector hospitals, result in higher Surgical site infection. Areas in need of attention are establishment of surveillance protocols and reporting system. Establishment of Clinical audit and review, judicious use of antibiotics.

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Original Article

Evaluation Dyslipidemia and Resistin in Diabetic Obese Patients in Mirpur AJK

Dyslipidemia and Resistin in Diabetic

Sohail Iqbal[1], Kinza Alam[4], Anwar ul Isam[2] and Asnad[3]

ABSTRACT

Objective: .This study was planned to compare and correlate the potential role of resistin in obese patients with T2DM

Study Design: Comparative study

Place and Duration of Study: This study was conducted in Pharmacology and Biochemistry Department of Mohtarma Benazir Bhutto Shaheed Medical College Mirpur-AJK from April 2016 to November 2017.

Materials and Methods: In this study we also collaborate with Medicine department of DHQ Hospital of Mirpur AJK. In this study we had taken 120 (Eighty) male and female obese patients. Pregnant women were not considered in study. We also ensured that patients had taken any medicine. In our study, we select the range of patient from thirty six to fifty nine year (36 to 59).

Results: In type 2 diabetic patients we found high level of Serum resistin i.e. (38±8 ng/ml) as compare to controls. Serum cholesterol (206.2 ± 69 mg/dl), serum triglycerides (184.3 ± 73mg/dl), serum LDL(165.4 ± 36mg/dl) was significantly higher in diabetic obese Patients. Serum HDL (39.1 ± 14) mg/dl) was significantly low in diabetic subjects. Our study showed that cholesterol, triglyceride (TG) and low density lipoprotein (LDL) are found higher in obese diabetic patients as compared to obese controls. Resistin, total cholesterol and LDL-cholesterol were not exist significantly in obese diabetic patients when we compared the result with obese controls. But on other side we observed the results of TG (triglycerides) is significant higher in obese diabetic patients as compare obese controls. it means that there is positive correlation present between TG (triglycerides) and obese diabetic patient.

Conclusion: Lipid profile is disturbed with resistin which ultimately caused to insulin resistance in diabetes mellitus in obese subjects. We should try to control hormone such as resistin will be helpful to control diabetic obese patients with dyslipidemia

Key Words: Diabetes mellitus, Dyslipidemia, Resistin, Obesity

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INTRODUCTION

Lipid metabolism is the process in which lipid is synthesized and utilized by body in normal process but any defects in metabolism this lipid is accumulate in different organ cell of body such as in liver cells, muscle and pancreas cells which ultimately caused Lipotoxicity. It means that anabolism of lipid increased.[1]

In specific organs cells, fatty acids, metabolites of fatty acids such as acyl-CoA, Ceramide and diacylglycerols are accumulate due to abnormal metabolism process in body, uptake of fatty acids are increased and oxidation of fatty acids are disturbed.[2]

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The metabolites inhibit different process in body such as phosphorylation process major process Receptors (insulin receptor substrates) phosphorylation and IRS-1 and IRS-2 tyrosine receptor. By phosphorylation inhibition, ultimately inhibiting insulin-mediated glucose uptake .[3] Free fatty acids are produced in large quantities due to abnormal lipid abnormal metabolism and the reason is Type 2 diabetes mellitus.[4] Dyslipidemia is main problem in obese patients. The reason for dyslipidemia is high lipid profile. In this disease, high density lipoprotein cholesterol (HDL) is high in blood serum. And also low density lipoproteins (LDL) are high in combination. So due this free fatty acids (FFA) and triglycerides (TG) ultimately caused Dyslipidemia.[5]Hormonal also effects the lipid metabolism due to abnormal metabolism the triacylglycerol are accumulated in different organ cell specially liver cells and muscles cells which is the main reason of insulin resistance and abnormal hormone also increase free fatty acids in blood circulation.[6] Decreased High density lipoprotein (HDL-C) have link with decreased level of Apo-A. we know very well that abnormal Lipoprotein such as (HDL) caused decreased High density Lipoprotein –C (HDL-C).[7] In abnormal metabolism the high concentration of triacylglycerol (TG) and High density lipoprotein (HDL) particles are

produced in liver cells which caused decreased Apo protein A (Apo-A) and it is due to high breakdown of HDL particles.[8,9] Resistin is hormone which is protein in nature with high no of cysteine amino acids (polypeptide cysteine-rich). This hormone is present in rodents and also in human beings which is found in specific tissue that is adipose tissue.[10] Due to the protein in nature this hormone effects free fatty acid concentration by different enhancement mechanism. Free fatty acids are decreased in muscles cells by this hormone. It is also effects free fatty acid concentration by disturbance of re-esterification process of free fatty acids in adipose tissue.[11,12]

Lipogenesis is decreased by ephosphorylation reduction reaction which is the main reason (AMPK) which is ultimately increased free fatty acids.[13]

MATERIALS AND METHODS

This study was conducted in Pharmacology and Biochemistry Department of Mohtarma Benazir Bhutto *Shaheed* Medical College Mirpur-AJK. In this study we also collaborate with Medicine department of DHQ Hospital of Mirpur AJK. In this study we had taken 120 (Eighty) male and female obese patients. Pregnant women were not considered in study. We also ensured that patients had taken not any medicine. In our study, we select the range of patient from thirty six to fifty nine year (36 to 59).

We take 3ml blood sample in test tube and centrifuge for 15 minutes. Test was performed Micro lab 300. Serum Cholesterol, Total Cholesterol, serum triglycerides, HDL and LDL were estimated.

RESULTS

In type 2 diabetic patients we found high level of Serum resistin i.e (38±8 ng/ml) as compare to controls. Serum cholesterol (206.2 ± 69 mg/dl), serum triglycerides (184.3 ± 73mg/dl), serum LDL(165.4 ± 36mg/dl) was significantly higher in diabetic obese Patients. Serum HDL (39.1 ± 14) mg/dl) was significantly low in diabetic subjects. Our study showed that cholesterol, triglyceride (TG) and low density lipoprotein (LDL) are found higher in obese diabetic patients as compared to obese controls. Resistin, total cholesterol and LDL-cholesterol were not exist significantly in obese diabetic patients when we compared the result with obese controls. But on other side we observed the results of TG (triglycerides) is significant higher in obese diabetic patients as compare obese controls. It means that there is positive correlation present between TG (triglycerides) and obese diabetic patient.

Table No.1: Lipid profile in the diabetic and non diabetic groups

Variables	Diabetics n= 60 Mean ±SD	Non Diabetics n=60 Mean±SD	p value
Cholesterol mg/dl	206.2 ± 69	152.1 ± 36	**0.000
Triglycerides mg/dl	184.3 ± 73	123.2 ± 35	**0.0001
LDL mg/dl	165.4 ± 36	140.3 ± 36	*0.0229
HDL mg/dl	39.1 ± 14	53.1 ± 14	**0.000

n = number of subjects

* = significant ** = highly significant

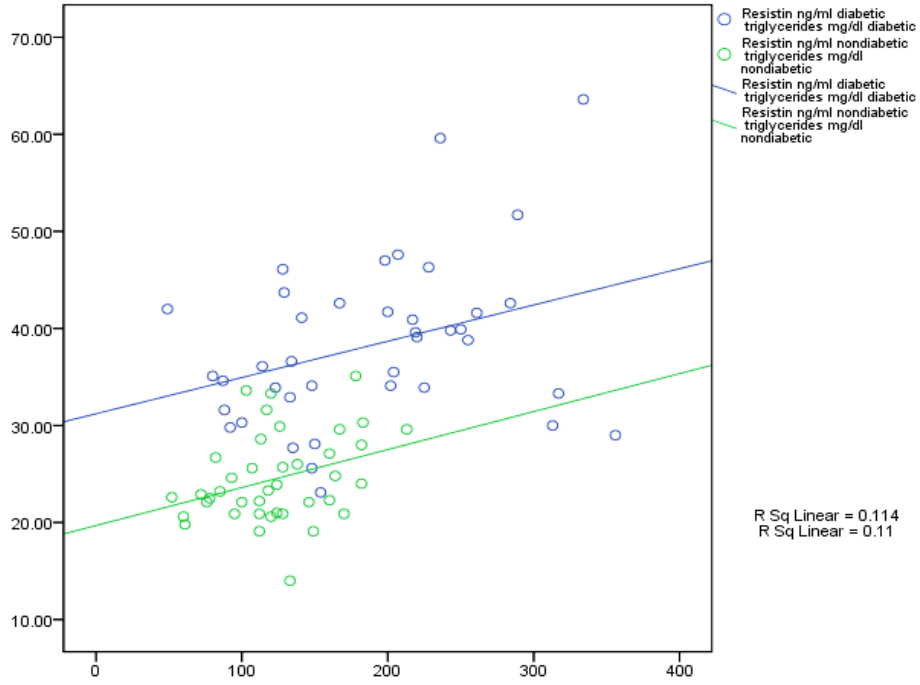

Figure No.1: Triglycerides(mg/dL)

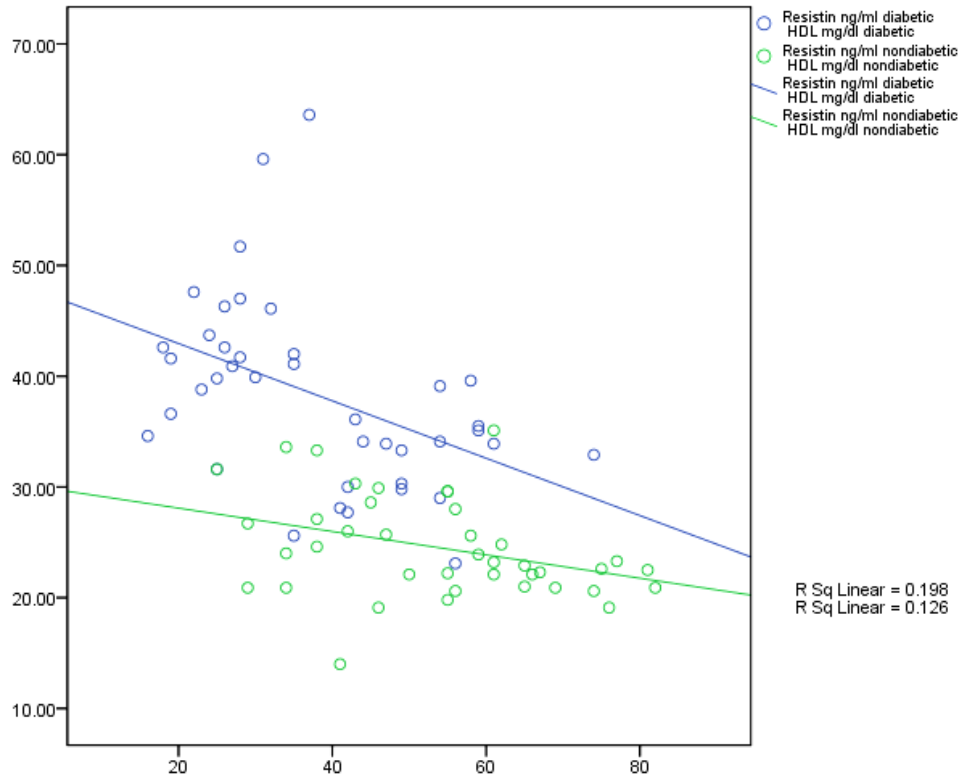

Figure No.2: HDL(mg/dL)

DISCUSSION

Obesity and type 2 diabetes are major problems of Dyslipidemia and it is also found that it is worldwide as an epidemic due to insulin resistance metabolic abnormality.[14] Lipid is major biomolecule and its metabolism effect whole body system. The main reason of type 2 diabetes and obesity is abnormal lipid metabolism and Insulin resistance.[1]Our study showed that cholesterol, triglyceride (TG) and low density lipoprotein (LDL) are found higher in obese diabetic patients as compared to obese controls. Resistin, total cholesterol and LDL-cholesterol were not existed significantly in obese diabetic patients when we compared the result with obese controls. But on other side we observed the results of TG (triglycerides) is significant higher in obese diabetic patients as compare obese controls. It means that there is positive correlation present between TG (triglycerides) and obese diabetic patient.

But on other side we observed the results of resistin is significant higher in obese diabetic patients as compare obese controls. it means that there is positive correlation present between resistin and obese diabetic patient. We observed the results of HDL- cholesterol is lower in obese diabetic patients as compare obese controls. it means that there is negative correlation present between HDL- cholesterol and obese diabetic patient. The result of Asano et al. (2010) is also supported our studies. According his study that there is positive correlation present between resistin and obese diabetic patients and also positive correlation present between TG(triglycerides) and obese diabetic patients. However this in correlation present between LDL-cholesterol and total cholesterol and obese diabetic patients. The result of Hoseen et al. (2010) is also supported our studies. He study in rodent According his study that there is positive correlation present between resistin and obese diabetic patients and also positive correlation present between TG(triglycerides) and obese diabetic patients. However, this in correlation present between LDL-cholesterol and total cholesterol and obese diabetic patients

The result of Contrary to this Qi et al. (2008) is also supported our studies. According his study that there is no significant correlation present between resistin and lipid in Metabolic syndrome .The result of Mohammad zadeh et al. (2008 is also supported our study. He study in metabolic syndrome according his study that there is link exist between obesity, dyslipidemia and insulin resistance with insulin resistance.

CONCLUSION

Triglycerides is significant higher in obese diabetic patients as compare obese controls.it means that there is positive correlation present between TG (triglycerides) and obese diabetic patient

But on other side we observed the results of resistin is significant higher in obese diabetic patients as compare obese controls. It means that there is positive correlation present between resistin and obese diabetic patient. HDL- cholesterol is lower in obese diabetic patients as compare obese controls. it means that there is negative correlation present between HDL-cholesterol and obese diabetic patient.

Lipid profile is disturbed with resistin which ultimately caused to insulin resistance in diabetes mellitus in obese subjects. We should try to control hormone such as resistin it will be helpful to control diabetic obese patients with dyslipidemia.

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

Hepatotoxicity in Anti TB Drugs

Drug Induced Hepatotoxicity and the Risk Factors for Liver Injury During Treatment of Pulmonary Tuberculosis

Jeando Khan Daidano, Mujahid Chandio, Mukhtiar Abro and Rafique Ahmed Memon

ABSTRACT

Objective: To determine the frequency of drug induced hepatitis due to ATT the presentation of the patient during treatment of pulmonary tuberculosis and the risk factors.

Study Design: Retrospective / Descriptive study.

Place and Duration of Study: This study was conducted at the Department of Medicine at PMCH Nawabshah from August 2015 to August 2017.

Materials and Methods: 100 patients were selected after inclusion criteria on a preformed Performa. Patients selected for this study were from all age groups and gender, diagnosis was made by history, clinical examination of the patient and investigations. All patients were on ATT in pulmonary tuberculosis.

Results: 100 patients participated for this study. 61 were males and 39 were females. Jaundice was present in all the patients, hepatomegaly was noted in 68 patients, Serum Bilirubin ranged 4.90 to 16 mean10.18 , SGPT ranged 279 to 432 mean 329.31, PT ranged 17-26 mean 21.16. Pyrazinamide was found more hepatotoxic than isoniazid and rifampicin after weekly trial after normalization of SGPT and Bilirubin. Statical analysis was done using software SPSS 15 version.

Conclusion: Due to drug induced hepatitis treatment failure or drug resistant in pulmonary tuberculosis is a big problem. Liver function test during treatment is essential especially in risk factors. Awareness of the patients and their relatives about treatment of pulmonary tuberculosis and drug induced hepatitis is necessary to reduce complications and mortality.

Key Words: Hepatoxicity ATT Pulmonary Tuberculosis

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INTRODUCTION

Incidence of tuberculosis was at increased level in 2003, now there is a slow decline. 9 millions new cases are reported every year and death ratio estimated to be 1.5 million per year.[1] Pulmonary tuberculosis is major problem worldwide.[1] First line anti tuberculosis drugs are Rifampicin, Isoniazid, Ethambutol and Pyrazinamide initially two months followed by four months of Rifampicin, Isoniazid or Ethambutol.[2] Three drugs Isoniazid, Pyrazinamide and Rifampicin are metabolized by liver. Incidence of drug induced liver injury by ATT is reported in 2-28%. Pathogenesis and biochemical mechanism of these ATT drugs to cause liver injury is not clear. During treatment of tuberculosis therapeutic drug monitoring is helpful to check drug resonse to treatment, drug drug interaction and drug resistance TB.

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There are chances of treatment failure if one of the drug is terminated. Risk factors for anti-TB drug induced hepatitis can be due to acetylators of of isoniazid metabolites, may be a cause of hepatotoxicity.[3] Pyrazinamide is more hepatotoxic than other first line anti TB drugs. Pyrazinamide induced hepatotoxicity is decreased due to changing in standard dose. Pyrazinamide is thought to be the most common drug causing anti TB drug induced hepatitis.[4] Complication include co infection with HCV, HBV, HIV and CLD. Advanced age, malnutrition, female sex and slow acetylators increase risk of hepatotoxicity.[5] Roussel Uclaf Causality Assessment Methos (RUCAM) score is used in cases of suspected drug induced liver injury. Patients who are on isoniazid monotherapy for latent TB transaminitis with ATT may represent hepatic adaptation and occurs in 20% of patients. Criteria based on ALT, ALP and Bilirubin to guide cessation of ATT were used by drug induced liver injury expert working group and DILIGEN study.[6] ALT >5 x ULN or if the patient is icteric than recommendation for treatment cessation or if ALT is 3-5 x ULN and the patient has nausea, vomiting, anorexia, jaundice and abdominal pain than cessation of treatment recommended by ATS.[7] Patients with drug induced liver injury were managed according to local guidelines. If ALT was 3-5 xULN with symptoms or >5 x ULN without symptoms.

ATT was changed and non-hepatotoxic regimen Ethambutol plus Amikacin is prescribed stopping Pyrazinamide, Rifampicin and Isoniazid.[7]

MATERIALS AND METHODS

This retrospective descriptive study was conducted in the department of medicine PMCH Nawabshah. 100 patients were enrolled for this study on a preformed proforma with questionnaire, informed consent was taken from all the patients who participated for the study, all patents were on ATT due to pulmonary tuberculosis. History was taken from all the patients along with general physical examination and systemic examination. All patients were investigated for SGPT, serum BILIRUBIN,PT, HBsAg, anti HCV, HIV, Urea, RBS and Ultrasound of abdomen.

Inclusion criteria:

Jaundice positive
History of ATT
Increased Bilirubin
Raised SGPT

Exclusion criteria:

Jaundice negative
No history of ATT
Normal Bilirubin
Normal SGPT

RESULTS

All patients presented with jaundice, all were on ATT due to pulmonary tuberculosis. Males were 59 and females were 41. Age ranged from 43 to 69 years mean 58.28. 32 patients presented with vomiting, 49 patients presented with pain in right hypochondrium and epigastrium. Itching was noted in 23 patients, loss of appetite in all patients, dark colour urine noticed by 84 patients. On examination jaundice was positive in all the patients, hepatomegaly was present in 68 patients.

Table No.1: Descriptive Statistics

Variables	N	Min.	Max.	Mean	Std. Deviat.
Age	100	43.00	69.00	58.2800	5.19922
Sex	100	1.00	2.00	1.3900	0.49021
Education	100	1.00	3.00	1.3500	0.57516
Occupation	100	1.00	3.00	1.6100	0.68009
Bilirubin	100	4.90	16	10.1822	2.78840
SGPT	100	279.00	432.00	329.3100	28.56101
PT	100	17.00	26.00	21.1600	2.25953
RBS	100	92.00	197.00	151.0100	22.92918
Urea	100	23.00	41.00	33.2100	4.40912
Valid N(listwise)	100				

Table No.2: Paired Correlations

Variables in Pairs	N	Correlation	Significant
Pair 1 Age & Sex	100	-0.297	0.003
Pair 2 Bilirubin & SGPT	100	0.352	0.000
Pair3 Education & Occupation	100	-0.087	0.392
Pair 4 PT & SGPT	100	0.349	0.000

Table No.3: ANOVA

Variables	Sum of Squares	df	Mean Square	F	Significant
Age Between Groups	112.329	2	56.164	2.125	0.125
Within Groups	2563.831	97	26.431		
Total	2676.160	99			
Sex Between Groups	4.507	2	2.254	11.336	0.000
Within Groups	19.283	97	0.199		
Total	23.790	99			
Occupation Between Groups	12.907	2	6.454	19.037	0.000
Within Groups	32.883	97	0.339		
Total	45.790	99			
Bilirubin Between Groups	17.770	2	8.885	1.146	0.322
Within Groups	751.975	97	7.752		
Total	769.545	99			
SGPT Between Groups	84.259	2	42.129	0.51	0.951
Within Groups	80673.131	97	831.682		
Total	80757.390	99			
PT Between Groups	71.414	2	35.707	7.980	0.001
Within Groups	434.026	97	4.474		
Total	505.440	99			
RBS Between Groups	8309.859	2	4154.929	9.214	0.000
Within Groups	43739.131	97	450.919		
Total	52048.990	99			
Urea Between Groups	97.687	2	48.844	2.593	0.080
Within Groups	1826.903	97	18.834		
Total	1924.590	99			

Serum Biirubin ranged 4.9 to 16, SGPT ranged 279 to 432, PT ranged 17 to 26. ATT was stopped and liver non toxic drugs ethambutol and amikicin were continued. Instructions to patients were given about treatment of jaundice and tuberculosis, investigated weekly for LFT.After normalization of SGPT and Bilirubin, and patient become symptom free, trial of isoniazid and later rifampicin were given, it was observed that out of 100 patients only in 3 patients hepatitis reoccur due to isoniazid, 7 patients with rifampicin and trial of pyrazinamide was not given due to its toxic effect more than isoniazid and rifampicin. Rifampicin and isoniazid reintroduced in the regimen in all the patients who were not affected by rifampicin and isoniazid. In statical analysis male denoted by 1 and female by 2, education uneducated by 1, primary by 2, middle by 3, occupation farmer by 1, housewife 2, self employed by 3. Statical analysis analysed using software 15 version.

DISCUSSION

Tuberculosis is a major disease worldwide. First line ATT are rifampicin, isoniazid, pyrazinamide and ethambutol, hepatitis due to rifampicin, isoniazid and pyrazinamide is big problem of treatment failure. Risk factors for ATT induced hepatitis are female gender, old age, alcoholism, HIV infection and underlying liver disease studies done previously.[8] Few patients presented with drug induced hepatitis in first 2 weeks of drug intake,87% patients presented in first 2 months after ATT.[9] Drug induced hepatitis vary in different countries ranging 1-10% in developing countries ratio is 8-10% , in western countries ratio is 1% to 3.3%.[10] In developing countries risk factors noted are old age, past history of jaundice, CLD, indiscriminate use of drugs, viral hepatitis B, viral hepatitis C intestinal parasite infestation, alcoholism, female gender, low body mass index, HIV,[11] acetylator status, hypoalbuminemia and malnutrition. It was observed in one study that malnutrition and disseminated TB were independent predictors in the development of drug induced hepatitis in the TB patients with HIV infection.[11] Rifampicin and isoniazid are the main drugs in TB, mechanism of action is separate, direct toxicity from isoniazid metabolites cause hepatocyte death and elevation of tranaminase, histopathological was similar to viral hepatitis.[12] Metabolism of rifampicin is through liver and excretion is through bile duct, rifampicin cause drug interaction with other drugs like warfarin through enterohepatic circulation.[13] Rifampicin in combination with other anti tuberculosis drugs increase hepatotoxicity 1.6-2.55 % in adults.[13] Pyrazinamide associated with increased in incidence of hepatotoxicity. Ederly patients are at increased risk of hepatitis due to comorbid disease and additional drugs compared with young population.[14] There was increased risk of hepatitis in age >40 years in a study.[14] Female gender was at increased risk of hepatitis due to ATT. The pathogenesis and biochemical mechanism of ATT to cause hepatitis is not clear. Hepatitis associated with pyrazinamide in high dose >40 mg/kg,[15] in pharmacodynamic and phrmakokinetic studies pyrazinamide in high doses is effective than the current recommended doses.[15] In studies rifampicin in high doses is effective. Low serum level of isoniazid and rifampicin associated with low therapeutic efficacy and high treatment failure.[16] Limited data are available if physician increase the dose of ATT, may lead to hepatitis in tuberculosis patients. Tuberculosis in the USA has increased due to many reasons, none of those are more important than HIV. HIV may predispose to the development of drug induced liver injury with ATT. HCV and HIV are independent additive risk for the drug induced liver injury. Alcohol and antiretroviral drugs with ATT increase hepatotoxicity. Chronic alcohol abuse is important risk for the hepatotoxicity with ATT.[17] Rifabutin a rfamycin derivative is more effective in the TB treatment and less hepatotoxic than rifampicin. An immune related mechanism of drug induced hepatitis exist for isoniazid and rifampicin.[18] ALT elevated 3 times ULN with symptoms or ALT level elevated of 5 times ULN, stop the ATT, give non hepatotoxic ethambutol, flouroquinolone or cycloserine could be considered. When liver enzyme normalize, than give first line ATT and discard the toxic agent drug by trial.[19] Re exposure to the same drugs leads to recurrence of drug induced hepatitis.[20] According to ATS and BTS restart ATT one at a time. Restart ATT all the drugs simultaneously advice by WHO and IUAT. If there is second bout of hepatotoxicity then the ATT drugs are to be re introduced consequently.[20] Reintroduction without pyrazinamide showed safety of regimen.[21] Regimen without pyrazinamide was suitable to those individuals who were at risk of drug induced hepatitis; malnutrision HIV, low albumin and alcoholics.[20] NICE guidelines 2016 do not have clear guidance about liver function test in patients with active TB to detect drug induced hepatitis. They recommend full dose reintroduction of ATT in those patients who were interrupted due to drug induced hepatitis.

CONCLUSION

There is increased incidence of treatment failure of pulmonary tuberculosis after drug induced hepatitis. Liver function should be monitored during treatment. Patient and their relatives counseled for the treatment of pulmonary tuberculosis. Monitor risk factors old age, malnutrition, female gender, alcohol, concomitant infection with HCV, HBV and HIV. Regular monitoring of the treatment is helpful enhances its effectiveness. Early weeks to months are essential to monitor the hepatotoxicity. Recognition of more toxic drug is important and continue with remaining drugs, complications and mortality can be reduced.

Author's Contribution:

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Original Article

Association of Total Red Blood Cell Count with Hemoglobin A2 Level in Beta Thalassemia Trait

RBC with HbA2 in Thalassemia

Shahtaj Khan[1], Awal Mir[2], Baber Rehman Khattak[1] and Tahir Jamal[2]

ABSTRACT

Objective: To evaluate the association of Red blood cells count with Hemoglobin A2 level in Thalassemia trait individuals.

Study Design: Descriptive / Observational / cross sectional study.

Place and Duration of Study: This study was conducted at the Diagnostic Laboratory, Rehman Medical Institute, Peshawar from April 2017 to October 2017.

Materials and Methods: A total of 200 beta Thalassemia trait and 100 normal healthy individuals as a control group were taken in the study. 2ml of blood was collected in EDTA tube and performed CBC and HbA2 from all subjects. All the data collected was recorded and analyzed in SPSS-22. Person correlation was used to find out association between the variables.

Results: We analyzed a total number of 200 thalassemia trait individuals and among them 116 (58%) were male and 84 (42%) were female participants. The study population age ranges from 1 year to 81 years with median age of 16 years. Highly significant correlation was found between RBC count and HbA2 level with P- value of 0.001. These finding reveals that increase RBC count is directly proportional to the Hb A2 level.

Conclusion: From the present study it is concluded that hemoglobin A2 level in Thalassemia trait individuals is highly associated with Red blood cell count. Moreover this study confirms that raised RBC count in contrast to Hb with low MCV, MCH and normal MCHC is indication for proceeding with Hb study for diagnosis and counseling them to prevent the birth of beta Thalassemia major children.

Key Words: Beta Thalassemia Trait, Hemoglobin A2 level, RBC count

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INTRODUCTION

Beta Thalassemia trait is a heterozygous form of genetic mutation of beta gene leading to compensatory hemolytic disease. Most of beta Thalassemia traits (BTT) are asymptomatic and some present with mild anemia[1].Approximately 5-7% of the globe populations carry a defected beta gene that responsible for propagation of Beta Thalassemia across the world as well as in Pakistan.[2] Although patient with BTT do not usually have increased morbidity and mortality but when both parents are beta Thalassemia trait (heterozygous) there is a 25% risk to give birth a child with beta Thalassemia major (homozygous) at each pregnancy.[3]

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Laboratory feature of BTT often present with normal to mild lower hemoglobin level, decrease MCV, MCH, normal MCHC and RDW.[4] Total RBC count is usually high (>5.0 million/µl)in contrast to hemoglobin concentration. Peripheral blood film reveals microcytic hypochromic red blood cells, occasional target cells and basophilic stippling. Raised Hemoglobin A2 level (>3.5%) on hemoglobin electrophoresis is diagnostic finding.[5]

In normal circumstances heme concentration regulates hemoglobin chain syntheses.[6] Decrease in heme concentration that activates the heme regulated inhibitor (HRI) that responsible for inhibition of globin chain synthesis and lead to depletion of hemoglobin A2 synthesis in iron deficiency anemia. When β-thalassemia trait individual present with iron deficiency anemia may shows normal or borderline A2 level and due to this impact of iron deficiency anemia on A2 level is cause of Beta gene propagation.[7, 8]

The association of total red blood cell count with hemoglobin A2 level is not fully understood. For stable hemoglobin molecules it is necessary that alpha chain, beta chain and heme must be in balanced with ratio of 2:2:4 respectively. Imbalance between these ratios lead to instability in hemoglobin quantity and quality.[9] Two beta genes (HBB) is responsible for beta chain synthesis, one gene is inherited from each

parents. In beta Thalassemia trait one gene is defected and one is normal.[10] In heterozygous state both beta genes are capable to synthesize up to 70-80% of beta globin chain. There is 20 to 30 % of beta chain deficiency in β-thalassemia trait.[11] Almost 70-80% of beta globine chain binds with alpha chain and heme molecules to formed a stable hemoglobin tetramer. The remaining 20-30 % free alpha chains have capability to form alpha and alpha chain tetramer.[12] Alpha chain tetramer is unstable and have tendency to precipitate with in a cell, which is cytotoxic for red blood cell and lead to ineffective erythropoiesis and peripheral erythrocytosis.[13] In Beta Thalassemia syndrome human body try to neutralize the free alpha chain by combing with alpha chain stabilizing protein, delta chain and gamma chain. Therefore it is observe that raised levels of hemoglobin F in beta Thalassemia major and Hemoglobin A2 in beta Thalassemia trait.[14]
Small amount of free alpha chain in beta Thalassemia trait individual become precipitate with in red blood cells that lead to premature destruction of erythrocytes. Premature red cell destruction causes the ineffective erythropoiesis with in compensation phenomena.[14] Compensatory ineffective erythropoiesis is leading cause of peripheral erythrocytosis in beta Thalassemia trait.[16] The present study is design to evaluate the association of total red blood cell count with hemoglobin A2.

MATERIALS AND METHODS

It was a descriptive comparative cross sectional study carried out at diagnostic laboratory Rehman Medical Institute, Peshawar Pakistan. Duration of this study was sixth months i.e. from April 2017 to October 2017.
A total of 200 beta Thalassemia trait and 100 normal healthy individual as a control for comparison were taken in the present study. Those beta thalassemia trait individuals were excluded who also iron deficiency anemia. A 2 ml of venous blood was collected from all diagnosed beta Thalassemia trait and normal healthy individuals in EDTA (Purple top, BD) vacutainer tube for CBC and Hemoglobin studies. Complete blood count (CBC) was performed by automated hematology analyzer (XN-1000, Sysmex, Japan) to determine red blood cell count and red cell indices. HbA2 level were evaluated by HPLC analyzer (D-10, Bio-Rad, USA),
All collected data was recorded and analyzed in SPSS-22. Chi-square and odd ratio were used for measurement of comparison between variables. Results were presented in tables and graphs. P value is less than 0.05 it was consider as statistical significant.

RESULTS

The total number of known thalassemia trait individual was 200. Out of total individuals116 (58%) were male and 84 (42%) were female individuals. The patients age ranges from 01 year to 81 years with median age were 16 years. All patient hemoglobin level (Hb), RBC count, MCV, MCH, MCHC, RDW and HbA^2 level were analyzed and show in table 1.
All beta thalassemia trait individual red cell indices and HbA2 mean level and standard deviation were compared .No statistical significant differences were found between HB, MCV, MCH, MCHC and RWD. Highly significant correlation was found between RBC count and HbA2 level with P- value is 0.001. Study result revealed that higher the RBC count is directly proportion to the Hb A2 level.

Table No.1: Red cells indices and Hb A2 level median, minimum and maximum levels.

S/No	Parameter	Median	Min.	Max.
1	Hemoglobin(Hb)	10.5000	4.36	18.70
2	RBC count	5.6350	2.26	8.31
3	MCV	59.850	45.8	86.2
4	MCH	18.300	12.6	29.8
5	MCHC	31.650	13.7	37.7
6	RDW	17.0000	00	36.80
7	HbA2 level	5.800	3.5	8.1

DISCUSSION

Present study result reveals that Thalassemia trait individual hemoglobin A2 level is highly interlinked with the total red cell count. In present study hemoglobin A2 is always higher than 3.5 percent in thalassemia trait. The mean value of MCV and MCH in the studied population is 59.850 fl and 18.300 pg that are lower than normal limit. The mean value of MCHC and RDW in included patients is 31.650 g/dl and 17 percent (CV) respectively that is within normal range. So it is also important that to measure the value of MCHC and RDW in diagnosing the thalassemia patient.
Elevated HbA2 level is due to βTT in almost all cases, and an elevated HbA2 level in the presence of microcytosis are indicative for ultimate diagnosis of βTT. Although elevated, the HbA2 level varies but rarely reaches 6%. It has been also suggested that the HbA2 levels in βTT may correlate with particular classes of β-globin chain gene mutations.[4,17] Zhanhui Ou et al study revealed that a large number of pregnant women with a mild increase in HbA2 levels without βTT. Elevated HbA2 level other then BTT also observed hyperthyroidism and HbS (sickle cell trait/disease).[18] In our studied population no symptoms of hyperthyroidism were documented and no TFTs (thyroid function tests) were advised and the possibility of hyperthyroidism cannot be definitely excluded.
Estrogen induces the expression of TBG (thyroxin-binding globulin). Total thyroid hormones are mostly increased during pregnancy. It is necessary to find that whether there is a relationship between the levels of TBG and HbA2.

Rarely βTT cases with certain β-globin gene mutations (CAP+1) may have normal HbA2 level with normal or abnormal RBC indices. In addition, HbA2 elevation is not a feature of the α-Thalassemia trait, and coexistence with an α-thalassemia mutation may give a normal level of HbA2. When HbA2 is used as the screening test, these cases will be missed. With doubtful result genetic studies must be done to actual result.[4]

Assessment of red blood cell parameters in the Complete blood count (CBC) is an important laboratory investigation and diagnostic workup for thalassaemias.[19,20] The red cell parameters good way for these mutations, lower hemoglobin concentration, low MCV and MCH, normal MCHC, RDW and increased TRBC.

CONCLUSION

From the present study it is concluded that hemoglobin A2 level in thalassemia trait patient is deeply associated with Red blood cell counts. This study further confirms that raised RBC count with low hemoglobin, MCV, MCH are indication for proceeding further with hemoglobin electrophoresis to screen for beta Thalassemia trait and further counseling them to prevent the birth of beta Thalassemia major children in Khyber Pakhtunkhwa.

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Original Article

Hypertensive Retinopathy in Pregnancy

Prevalence of Hypertensive Retinopathy in Patients with Pregnancy Induced Hypertension

Nasrullah Khan[1], Raza Farrukh[2] and Muhammad Zubair[3]

ABSTRACT

Objective: To investigate prevalence of hypertensive retinopathy in patients with pregnanacy induced hypertension and association between retinal changes and severity of PIH

Study Design: Cross sectional study

Place and Duration of Study: This study was conducted at the Mola Baksh Hospital, Sargodha which is a maternity wing of DHQ Teaching Hospital Sargodha from July 2017 to December 2017.

Materials and Methods: After taking the informed consent from the patients their blood pressure were recorded, urine examination reports were taken to document protein uria. Name, age, date of admission and gravidity were recorded on a proforma. Tropicamide 1% eye drops were instilled into the patient's eyes to dilate the pupils. Once dilated direct ophthalmoscopy was done to visualize the fundus and the signs of hypertensive retinopathy. All findings were noted on a data sheet.

Results: 100 pregnant women with diagnosed pregnancy induced hypertension were included in the study. 36 were primigravida while 64 were multigravida. Out of 100 patients 88 (88.00%) were diagnosed with pre-eclampsia while 12 (12.00%) with eclampsia. Amongst pre-eclampsia patients 58(65.91%) had signs of hypertensive retinopathy on fundoscopic examination while amongst eclampsia patients 5(41.67%) had these signs present. In total 63(63.00%) patients out of 100 had signs of hypertensive retinopathy while in 37(37.00%) patients these were absent. .

Conclusion: Signs of hypertensive retinopathy are commonly found in pregnancy induced hypertensive patients and are important indicator of severity of disease.

Key Words: Pre-eclampsia, eclampsia, Prenancy induced hypertension, hypertensive retinopathy

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INTRODUCTION

Hypertensive retinopathy is retinal vascular damage caused by hypertension. Acute blood pressure elevation typically causes reversible vasoconstriction in retinal blood vessels and hypertensive crisis may cause optic disk edema .Fundoscopic examination shows arteriolar constriction, arteriovenous nicking, vascular wall changes, flame-shaped hemorrhages, cotton-wool spots, yellow hard exudates, and optic disk edema. Acute hypertension is associated with pregnancy include Pre-eclampsia & Eclampsia.

Pregnancy induced hypertension(PIH) is a hypertensive disorder in pregnancy that occurs in absence of other causes of hypertension.PIH consists of pre –eclampsia and eclampsia.

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Pre-eclampsia is defined as presence of hypertension (BP≥140/90 mmHg) and proteinuria (300 mg or more in 24 hour urine) after 20 weeks of gestation[1]. Eclampsia is defined as onset of convulsions in a woman with pre-eclampsia that cannot be attributed to other causes[2].

Pre-eclampsia and eclampsia are the disorders solely associated with pregnancy. Pre-eclampsia is a multi-system disorder that arises from placenta. According to Roberts et al main reason of it is maternal endothelial dysfunction which ultimately leads to diverse clinical manifestations[3]. Ophthalmoscopic changes occur mostly in severe disease. Amongest these changes most common is vasoconstriction of the retinal arterioles[4,5]. These changes however resolve immediately after delivery[6]. Statistically, about 5-11% of all the pregnant women develop hypertensive disorders(pre-eclampsia & eclampsia) and amongst these 40-100% have retinal changes in them[7,8]. Worldwide PIH results in nearly 10-15% maternal deaths[9] while in Pakistan it is among the leading cause of maternal death[10].

Opthalmoscopic changes mainly occur due to loss of autoregulation phenomenon in retinal vessels that occur at diastolic blood pressure of 100mmhg or above. Aim of this study was to determine the presence of these changes among pregnant women,

difference of their prevalence among primigravida and multigravida.

MATERIALS AND METHODS

This cross-sectional study was carried out at MolaBaksh Hospital Sargodha which is a maternity wing of DHQ Teaching Hospital Sargodha. In this study only those patients were included who were pre-diagnosed with PIH as per the standard definition.

Patients with pre-existing hypertension, diabetes, renal disease and cataract were not included in this study. After taking informed consent from patients, tropicamide 1% eye drops were instilled into patients eyes at rate of one drops per 15 min until pupils were dilated, patients' name, age, weeks of gestation, date of admission, blood pressure, proteinuria, gravidity, funduscopic findings and pregnancy outcome were noted on a performa.

Fundoscopic examination was carried out in dark room using direct ophthalmoscope and both eyes were examined to find the funduscopic changes due to PIH. Once the data was collected, data was compiled and analyzed. Results were statistically confirmed using Minitab 17.1.0 in two different tests.

RESULTS

All this data after being input into Minitab 17.1.0 gave following statistical results. Former is the Chi-Square test applied to find the prevalence of hypertensive retinopathy in patients with pre-eclampsia and eclampsia in our target population .P value less than 0.05 was considered significant.

Total of 100 patients were examined, out of these 36 (36.00%) were primigravida while 64 (64.00%) were multigravida. Their average age was 24.6 years, average blood pressure noted was 170/100mmHg, average age of gestation was 38 weeks+ 5 days. Total number of patients with pre-eclampsia were 88 (88.00%) and 12 (12.00%) had eclampsia. Out of 88 patients of pre-eclampsia; 58(65.91%) patients had positive fundoscopic findings while 30(34.09%) patients had normal fundus (Table 1). Amongst 12 patients with eclampsia; 5(41.67%) patients had positive fundoscopic findings while 7(58.33%) patients had normal fundus.

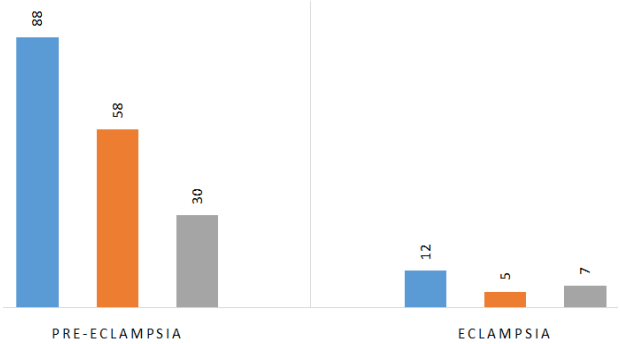
Narrowing of arterioles and dot blot hemorrhages were consistently found in all the patients with positive fundoscopic findings. Outcomes of the ongoing pregnancies was also noted.

In total; 63(63.00%) patients had positive signs of hypertensive retinopathy while 37 (37.00%) patients had normal fundus.

Table No.1: Details of Patients having positive or normal fundus with percentage.

	Total=100	Patients with positive findings	Patients with normal fundus
Pre-eclampsia	88(88.00%)	58(65.91%)	30(34.09%)
Eclampsia	12(12.00%)	5(41.67%)	7(58.33%)

Following bar chart 1.1 exhibits prevalence of hypertensive retinopathy among target population of 100.



Bar Chart No.1: Prevalence of Pre-eclampsia and eclampsia among target population of 100.

DISCUSSION

Pregnancy induced hypertension(PIH) is a leading cause of maternal mortality and morbidity in developing countries.[11]PIH affects all blood vessels in the body including placental blood vessels.[12]It can lead to fetal and maternal complications if not treated properly.[13]

Hypertensive retinopathy is a disease of retinal and choroidal vasculature that can occur in acute as well as chronic hypertension. Retinal vasculature is auto-regulated but whenever diastolic blood pressure exceeds 110-115mmHg this auto-regulation is lost. This results in damage to retinal vasculature leading to subsequent ischemic necrosis which manifests as cotton wool spots(Ischemia to nerve fibers), uniform narrowing of arterioles, flame & dot-blot hemorrhages and sometimes papilledema. The potential complications of hypertensive retinopathy in pregnancy are development of central serous chorio-retinopathy (CSCR) and serous retinal detachment[14].

Ophthalmoscopic changes are common in hypertensive disorders of pregnancy. These hypertensive disorders have a much less incidence in developed countries like US where it is merely 4%[13].While in Pakistan it is much higher. In our study we examined 100 patients who already had been diagnosed with pre-eclampsia/eclampsia. We found a significantly high incidence of hypertensive retinopathy in these patients i.e; 63%. The results of our study show significant association between level of

PIH and hypertensive retinopathy. But this is in contrary to study of Tadin et al as they showed a significant correlation between PIH and hypertensive retinopathy.[15] Therefore, fundoscopic examination should be carried out in patients having these acute hypertensive changes of pregnancy not only to assess the risks associated with the outcome of pregnancy but also to avoid the potential serious ophthalmic complication.

CONCLUSION

Routine fundoscopic examination should necessarily be done in patients with PIH(pre-eclampsia and eclampsia) so that measures should be taken before hand in managing the ophthalmic status of the patient and maternal well-being.

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Original Article

Role of Anti-Oxidant on Ciprofloxacin Induced Toxicity in Intact Bone Length of Juvinile Albino Rats

Haji Muhammad Aslam Channa[1], Naheed Baqir[2] and Bhojo Mal Tanwani[3]

ABSTRACT

Objective: To investigate whether ciprofloxacin induced chondrotoxicity with normal therapeutic dosage is preventable by zinc chloride if given simultaneously.

Study Design: Prospective / experimental study.

Place and Duration of Study: This study was conducted at the Department of Anatomy Basic Medical Science Institute Jinnah Postgraduate Medical centre Karachi from Jan 2014 Dec 2014.

Materials and Methods: Ciprofloxacin & ZnCl2 was administrated to juvenile albino rats. Ciprofloxacin with a dose of 20 mg/kg body weight & ZnCl2 120 µg/100 gm body weight two times therapeutic dose for 20 days. (From day -1 to day 20 after birth.) Each animal was measured their intact bone length and were compared with similar value of control animals. The results were statistically analyzed to find out the significance.

Results: Our study reveals that ciprofloxacin administered in juvenile albino rats decreased intact bone length , of Humerus right & left 9.91 ± 0.18 mm, Femur right & left 11.49 ± 0.12 mm respectively. That ciprofloxacin & ZnCl2 administration maintained the intact bone length of Humerus right & left 18.48 ± 1.25 mm, Femur right & left 14.54 ± 0.09 mm respectively. That ZnCl2 administration increased the intact bone length of Humerus right & left 14.60 ± 0.13 mm, Femur right & left 14.58 ± 0.10 mm respectively.

Conclusion: The ciprofloxacin & ZnCl2 post-natal administration in juvenile albino rats affected the mean intact bone length. ZnCl2 maintained intact bone length leading to growth of the juvenile albino rats.

Key Words: Ciprofloxacin, ZnCl2, Juvenile albino rats and Intact bone length

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INTRODUCTION

Quinolones are the fluorinated derivatives, these are ciprofloxacin, sparfloxacin, clanofloxacin, travo-floxacin, ofloxacin, and norfloxacin[1] .

Ciprofloxacin was introduced in 1987.It is on the World Health Organization's List of Essential Medicines it is an antibacterial substance with wide bacterial spectrum activity, which belongs to the chemical class 4-quinolones, and is entirely synthetic, therefore this substance is among the most commonly used antibiotics nowadays for different kinds of infections, it functions by inhibiting DNA gyrase, and a type II topoisomerase, topoisomerase IV, necessary to separate bacterial DNA, thereby inhibiting cell division [2]

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Along with its wide range of activity and common usage the drug has many side effects, i.e, degenerative changes in weight bearing joints and damage to the growing cartilage in young animals[3]. Therefore is not generally recommended for use in children, adolescents, and during pregnancy.. Some reports on hypersensitivity, chondrotoxicity and super-infection have been reported with ciprofloxacin[4] .

Zinc is the trace elements and essential for the synthesis of DNA, RNA and proteins, and physiological functions of several enzymes and fetal organ development. In addition to its role in catalysis and gene expression, zinc stabilizes the structure of proteins and nucleic acids and preserves the integrity of sub cellular organelles such as mitochondria [5]

The large number of factors are involved in skeletogenesis i.e., harmones, growth factors, receptors, signaling mediators, transcription factors, extracellular matrix components and enzymes. Factors determining the identity of skeletal cells are called differentiation factors and factors specifying the number, size and shape of skeletal elements are called patterning factors [6]

MATERIALS AND METHODS

Forty spontaneously ovulating female & 20 fertile male wistar albino rats of 16-18 weeks age were taken from animal house of basic medical science institute, Jinnah Postgraduate Medical Centre Karachi. The female rats

were mated with of same strain according to the method described by Rough[7]. Thus one male rat was mated with two female rats in a separate cage. On next day each female rats were examined for signs of mating. Such a blood strained vagina or vaginal plugh of mucoid greenish white material. Presence of both or any of these signs were considered a day zero of pregnancy, the mean gestation period of albino rat is 21 to 23 days.

Randomly selected 40 juvenile albino rats were divided into four groups, A, B,C and D. each group comprising 10 animals, group A juvenile albino rats act as control and were given normal saline in equal volume (0.1 ml) intra-peritoneally twice daily for 20 days (from day, 1 today, 20 after birth), group B were given injection ciprofloxacin at a dose of 20 mg/kg weight (0.12 mg in 1.1 ml) intra-peritoneally twice daily for 20 days (from day -1 to day -20 after birth), group C were given injection ciprofloxacin plus zinc chloride 120 µg/100 G body weight prepared in distilled water (7.4 µg in 0.1 ml) intra-peritoneally 30 minutes before administration of ciprofloxacin twice daily for 20 days (from day ,1 to day ,20 after birth), group D were given injection zinc chloride at a dose of 120 µg/ 100 G body weight prepared in distilled water (7.4 µg in 0.1 ml) twice daily for 20 days (from day ,1 to day ,20 after birth), and on day-21, the juvenile albino rats were sacrificed by giving deep anesthesia, and were operated to obtain their long bones. Skeletal specimen processed through 96% ethanol and acetone and bulk tissue stained with alizarin red "S" and alcian blue. Than material was cleared in 1% potassium hydroxide and stored in glycrine[8] . This technique demonstrate the ossified bone with Alizarin Red "S" and cartilage with Alcian blue as shown in Figs. 1 and 2. The double stained cleared specimen was observed under spenser stereomicroscope. The fore and hind limbs were disarticulated and total length of cartilaginous models of long bones of extremities were measured under stero microscope. The values from control and experimental groups were compared for statistical analysis.

RESULTS

Post-natal changes in tintact bone length (mm) of juvinile albino rats treated for 20 days: The mean value of intact bone length as determined by measuring the length of long bones of right and left fore limb (Humerus) and hind limb (Femur) respectively with the help of electronic digital vernier caliper of groups A, B, C and D is presented in Table . .

Humerus: The mean value of postnatal treated humerus (right and left) length measured in group A animals was 13.67 ± 0.93 mm. A highly significant increase in length was observed when compared with animals group B ($P < 0.001$) as shown in Table .

The mean value of postnatal humerus (right and left) measured in group B was 9.91 ± 0.18 mm. A highly significant decrease in length was observed when compared with group A, C and D ($P < 0.001$) as shown in Table.

The mean value of postnatal treated humerus (right and left) length measured in group C animals was 12.48 ± 1.25 mm. A highly significant increase in length was observed when compared with group B ($P < 0.001$) as shown in Table .

The mean value postnatal treated humerus (right and left) length measured in group D animals was 14.60 ± 0.13 mm. A highly significant increase in length was observed when compared with animals in group A and B ($P < 0.001$) as shown in Table .

Table No.1: Comparison of intact bones length (mm) of juvinile albino rats between postnatal control and treated groups

Intact Bones Length (mm)	Group A Control (n=10)	Group B Ciprofloxacin (n=10)	Group C Ciprofloxacin + Zinc Chloride (n=10)	Group D Zinc Chloride (n=10)
	Mean ± SEM	Mean ± SEM	Mean ± SEM	Mean ± SEM
Humerus				
4X - Right	13.67 ± 0.93$^{øø,◊◊}$	9.91 ± 0.18	12.48 ± 1.25^{øø}	14.60 ± 0.13 $^{**,øø,◊◊}$
4X - Left	13.67 ± 0.93 $^{øø,◊◊}$	9.91 ± 0.18	12.48 ± 1.25^{øø}	14.60±0.13 $^{**,øø,◊◊}$
Femur				
4X - Right	14.88 ± 0.04 $^{øø,◊◊,ΔΔ}$	11.49± 0.12	14.54 ± 0.09^{øø}	17.58± 0.10 ^{øø}
4X - Left	14.88 ± 0.04 $^{øø,◊◊,ΔΔ}$	11.49 ± 0.12	14.54 ± 0.09^{øø}	17.58± 0.10 ^{øø}

** p<0.01 highly significant as compared to Control (A), ^{øø} p<0.01highly significant as compared to Ciprofloxacin (B),
$^{◊◊}$**p**<0.01 highly significant as compared to Ciprofloxacin + Zinc Chloride (C)
^{ΔΔ}p<0.01 highly significant as compared to Zinc Chloride (D)

Femur: The mean value of postnatal treated femur (right and left) measured in group A was 14.88 ± 0.04 mm. A highly significant increase in length was observed when compared with animals in group B ($P < 0.001$) as shown in Table .

The mean value of postnatal treated femur (right and left) length measured in group B was 11.49 ± 0.12 mm.

A highly significant decrease in length was observed when compared with group A, C and D ($P < 0.001$) as shown Table .

The mean value postnatal treated femur (right and left) measured in group C animals was 14.54 ± 0.09 mm. A highly significant increase in length was observed when compared with group B ($P < 0.001$) as shown in Table.

The mean value of postnatal treated femur (right and left) length measured in group D animals was 17.58 ± 0.10 mm. a highly significant increase in length was observed when compared with animals in groups A and B ($P < 0.001$) as shown in Table.

Figure No.1: Photograph of fore limb right humerus bone of juvenile albino rats on 20th post natal day showing comparison of double staining technique i.e. Alizarin Red-S staining bone & Alcian blue staining cartilage, between control and treated groups-A,B,C & D used in this study.

Figure No.2: Photograph of hind limb left femur bone of juvenile albino rats on 20th post- natal day showing comparison of double staining technique i.e. Alizarin Red-S staining bone & Alcian blue staining cartilage, between control and groups-A,B,C & D used in this study

DISCUSSION

Present study was designed to observe the morphological effect of ciprofloxacin and zinc chloride separately and when administered simultaneously in post-natal juvenile albino rats.

Ciprofloxacin administered in a dose of 20 mg/kg body weight to juvenile albino rats, morphology showed

highly significant decrease intact bone length, (Humerus and femur) were observed in post-natal juvenile albino rats.

Regarding juvenile albino rats A highly significant decrease in intact bone length in post-natal group B may be attributed to less food intake and degenerative changes in growing cartilage occurred following administration of ciprofloxacin. These observations are in accordance with the findings of Berkovitch[9], and Cukerski[10] . Who found that only constant findings of ciprofloxacin was decrease in weight and length post-nataly.

The post-natal groups C showed increase in their length which may be attributed to the partial protection by zinc against the unwanted effect of ciprofloxacin on bone length. These findings are in agreements with the results of MacDonald[11] . Who found that the supplementary zinc has beneficial effect on growth by increasing protein synthesis. Zinc participates in regulation of cell proliferation in several ways, it is essential to enzyme systems that influence cell division and proliferation.

Similarly, the intact bone length in post-natal group D. A highly significant increase was observed in comparison with other groups, which may be attributed to increased protein synthesis by zinc chloride. These results are in agreement with Salgueiro[12] and Jou[13] . Who found that after supplementation of zinc, the mean bone length increase was significantly greater

Our observations are in consistence with Adikwu[14] who reported the condrotoxicity of quinolones as observed in immature animals, can effect articular cartilage and the epiphyseal growth plate, depending on the development stage. Stahlmann[15] noted the juveniles are especially sensitive and in animal at an early developmental phase the epiphyseal growth is also damaged by the quinolones and these effects are associated with reversible bone damage and growth inhibition.

The non-significant change was obtained in intact bone length simultaneously given Zinc chloride animals in group C was found to be in humerous and in femur when compared with the age matched controls, these findings are attributed to protective role of zinc chloride. Our observations are in agreement with those by Hickory[16], who found that zinc help in access formation of collagen increase osteoblastic activity and increase rate of longitudinal growth and bone remodeling in experimental rats. Prassad[17] , stated that zinc directly stimulates DNA synthesize either by enzyme stimulation or by altering the binding of F1 & F3 histones to DNA, so as to effect RNA synthesize.

CONCLUSION

The ciprofloxacin & ZnCl2 post-natal administration in juvenile albino rats affected the mean intact bone length. ZnCl2 maintained intact bone length leading to growth of the juvenile albino rats. There is need for a greater focus on frequent use of antibiotics and more research should be done to help learn to affectively treat the negative side effects of ciprofloxacin with simultaneous use of anti-oxidant Zinc chloride,

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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

Anemia in Pregnancy

The Incidence of Anemia in Pregnant Population of Pakistan Belonging to Different Socioeconomic Groups

Ghazala Irshad[1], Farah Deeba Khan[1] and Saira Mushtaq[2]

ABSTRACT

Objective: To rule out anemia based on conventional method like CBC in pregnant population of Pakistan in three different socioeconomic groups.

Study Design: Prospective/ Comparative / cross sectional study.

Place and Duration of Study: This study was conducted at the Social Security Hospital Manga Raiwind Road, Lahore and Sharif Medical Trust hospital, Lahore for a period of one year during 2010-2011.

Materials and Methods: 60 pregnant females from different socioeconomic groups in late first trimester were included. All included women were followed through all three trimesters of pregnancy and their Hb, MCV, MCHC, HCT, RBC count was estimated. Hematology auto analyzer of social security hospital model XT-2000i was used for analysis.

Results: The incidence of anemia is still high in our pregnant population regardless of their socioeconomic status**.** The mean hemoglobin level, were found lowest in third trimester as compared to first and second trimester of pregnancy in spite of socioeconomic status of females. All the three socioeconomic groups have almost equal %prevalence of anemia.

Conclusion: The prevalence of iron deficiency anemia in all socioeconomic groups of pregnant population is still alarming in our country**.** Measures such as prophylaxis iron treatment and food fortification should be started after the diagnosis even by simple and conventional tests such as hemoglobin and red cell indices.

Key Words: Anemia, Iron deficiency anemia, Pregnant, socioeconomic groups

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INTRODUCTION`

Anemia is very common in developing countries[1,2].Iron deficiency anemia is most prevalent and neglected nutritional deficiency in theses countries.[3]About two third of pregnant population is affected by this disease[4]. Anemia is defined as reduction of hemoglobin from 14-16g% in males and 12-14 g% in females[5]. Low level of hemoglobin results in insufficient oxygenation of peripheral tissues measured by hematocrit, which is defined as proportion of blood sample that is occupied by red cells [6].Anemia is one of the common complications of pregnancy. Iron stores are already low in most of womenat the beginning of pregnancy whilst its requirements are greater although absorption rate of iron after first trimester increases and continues throughout pregnancy [7].

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According to food and nutrition board of national academy of sciences pregnancy increases iron requirement approximately 3.5 mg/day[8]. Iron deficiency anemia is not a disease but manifestation of many diseases so its diagnosis is very important [9]. For the diagnosis of iron deficiency anemia According to Royal College of obstetrician and Gynecologist especially the hemoglobin level should be less then 11gm/dl in first trimester and less than 10.5gm/dl in second and third trimester or MCV falls from 76 fL will be considered as anemic[10]. Diagnosis ofanemia during pregnancy is very important as it is associated with many complications like vasomotor disturbance [11] behavioral changes [12]and decrease immunity[13]. It also associated with increase mortality[14], rate of premature delivery[15], preeclampsia and eclampsia[16]. Iron stores of mother also effect the prevalence of anemia in new born babies.[17]Although very advance and reliable methods like serum ferritin are available for diagnosis of anemia but our most general practioners use red blood cell indices because it is conventional and inexpensive.[18]

MATERIALS AND METHODS

After approval from ethical review board 60 pregnant females of different age, parity and in late first trimester were included from social security hospital Manga

Raiwand Road Lahore and Sharif Medical Trust hospital Lahore. These women were divided in poor, middle and upper class according to monthly income and dietary habits of their family. All included women were followed through all three trimesters of pregnancy and their Hb, MCV,MCHC, HCT, RBC count was estimated. Diagnosis of anemia was made based on CDC (center for disease control and prevention criteria) according to which hemoglobin level was less than 11 gm/dl in first and third trimester and less than 10.5 gm/dl in second trimester [19].Hematology auto analyzer of social security hospital model XT-2000i was used for CBC analysis. History of patient, demographic information and biochemical results were included in Performa.

Exclusion criteria: Patients with diabetes, hypertension, renal failure malignancy or any other serious disease.

In this Cross sectional comparative study 60 pregnant females of different age, parity, socioeconomic groups and in late first trimester were included.

RESULTS

In this study 60 pregnant females of different age, parity, socioeconomic groups and in late first trimester were included. Out of 60 women 3 aborted, 2 went for preterm delivery and 10 women left the study uncompleted. Finally 45 females were followed from first to third trimester. Data was collected and assessed by using analysis of variance (ANOVA) for over all comparison least significant difference (LSD) for pair comparison[20].

Mean Hemoglobin level g/dl and analysis of ANOVA in different socioeconomic groups and in three trimesters were

Table No.1: Mean Hb levels g/dl in different socioeconomic groups and three trimesters of pregnancy

Group	1st Trimester	2nd Trimester	3rd Trimester
Poor	11.9±1.3	10.2±1.4	9.8±1.3
Middle	12.1±0.9	10.5±0.8	10.2±1.0
Upper	12.1±1.1	10.5±1.3	10.6±1.2
Total	12.1±1.1	10.4±1.2	10.1±1.1

Table No.2: Analysis of variance (ANOVA) of Hbg% in different socioeconomic groups and three trimesters of pregnancy

Source	Type III sum of squares	df	Mean square	F	Sig
Trimester	81.5	1	81.5	142.9	*0.0
Intercept	15804.7	1	15804.7	5.1	*0.0
Group	6.316	2	3.15	1.0	NS0.3
Error	130.1	42	3.1		

Table No.3: Mean corpuscular volume (MCV) level (fL)in different socioeconomic groups and three trimesters of pregnancy

Group	1st Trimester	2nd Trimester	3rd Trimester
Poor	81.0±5.5	76.3±5.4	76.4±8.6
Middle	80.2±9.7	79.7±9.4	76.2±8.2
Upper	78.7±4.7	75.7±2.7	75.3±11.5
Total	80.1±7.1	77.4±6.9	76.0±2.7

Table No.4: Analysis of variance(ANOVA) of Mean corpuscular volume (MCV) level (fL)in different socioeconomic groups and three trimesters of pregnancy

Source	Type III sum of squares	df	Mean square	F	Sig
Trimester	365.37	1	365.3	25.0	*0.0
Intercept	797368.6	1	797368.6	6.0	*0.0
Group	107.5	2	53.7	0.47	NS0.73
Error	5553.93	42	132.2		

DISCUSSION

The prevalence of IDA during pregnancy in developing countries like Pakistan make it serious problem due to its relation with child health and maternal mortality rate. The present study was aimed to detect the anemia by conventional method in pregnant population belonging to three different socioeconomic groups. Although many advance and reliable methods are available to screen anemia but they all are expensive .In countries like Pakistan many practioneers still using conventional methods like CBC to diagnose anemia as they are cheap and convenient. In this study total of 60 females of different socioeconomic groups were included and their Hb, MCV and HCT levels were analyzed by hematology auto analyzer through three trimesters of their pregnancy. Total prevalence of anemia was found 65% in total pregnant population. Total incidence of anemia and was 46%, 57% and 75% in first, second and third trimester respectively collectively in three socioeconomic groups. Poor class of pregnant population has highest incidence of anemia at the beginning of study i.e. 56% while the middle and upper class has this incidence 47% and 33% respectively. During second trimester the incidence of anemia almost remain same except for upper class i.e. 75%. During third trimester the incidence of anemia was raised dramatically and is 75% for each class. The mean Hb levels were lowest in poor class. The Hb levels were also found lowest in third trimester in all three socioeconomic groups (Table 1). There were significant changes ($p<0.05$) were observed between Hb levels of all three trimesters and non –significant changes ($p>0.05$) were observed in different socioeconomic groups. The MCV levels were also

towards lowest range in third trimester regardless of socioeconomic grouping.(Table 3 &four). The other red cell indices like MCH, MCHC, and RBC count shows linear positive correlation with hemoglobin.

CONCLUSION

From the present study it is concluded that incidence of anemia is still alarmingly high in our population even with use of in sensitive methods of detection. There is no significant difference between the Hb levels of different socioeconomic groups. The Low levels of Hb even in upper class may be due to lack of knowledge, Malnutrition, over cooking of food, genetic error or worm infestations that should be rule out.

Recommendations: Daily food items of our population like flour (maize or wheat), rice salt, beverage, milk, sugar, should be fortified with iron .This will boost Iron stores and improve hemoglobin level of our population. In developing countries like Pakistan prophylaxis iron supplementation should be given to every iron deficient patient even diagnosed by conventional method.

Author's Contribution:

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Original Article

Propranolol and Steroid for Infantile Hemangioma

Comparison of Efficacy between Propranolol and Steroid for Infantile Hemangioma

Muhammad Kashif[1], Abdus Sami[2] and Neelam Mumtaz[1]

ABSTRACT

Objective: To determine the efficacy and safety of propranolol compared with steroid as a first-line treatment for Infantile Hemangioma.

Study Design: A Randomized Control Trial study.

Place and Duration of Study: This study was conducted at the Department of Peads Surgery, Children Hospital, Multan and Department of Peads Surgery, NMU, Multan April 2014 to April 2017.

Materials and Methods: After obtaining ethical permission from hospital ethical committee and informed consent from parents of participants. A total of 84 patients were included in trial through non probability consecutive sampling technique, and divided into two equal groups. After completion of information and data collection, analyses was done by using SPSS software, for continuous variables mean ± SD like age, size of hemangioma, weight, BMI and surface area was calculated. Frequencies and percentages were calculated for categorical variables like gender, color of hemangioma. T test and chi square were used to check difference in both groups. P value less than or equal to 0.05 was considered as significant.

Results: Overall, 84 patients were included in this study, both genders. The study group was further divided into two equal groups, 50% (n=42) in each. Mean volume, surface area and height of lesion was smaller in steroid group but, the difference was statistically insignificant p=0.801, p=0.479 and p=0.402 respectively.

Conclusion: Results of our study revealed that therapeutically propranolol is not inferior to steroids in treatment of infantile hemangioma.

Key Words: Hemangioma, Propranolol, Steroids, Infants.

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INTRODUCTION

In infants and young adults infantile hemangioma is the leading type of tumor which is not problematic if in small size[1]. Place of hemangioma and its associated complications like bowel obstruction, respiratory obstruction, and vision loss due to abnormal growth of eye require treatment modalities. In ancients infantile hemangioma (IH) treated with steroids and found to be antiangiogenic in vitro setting. Steroids also found effective clinically but their long term use can cause some serious complications like growth problems and gastroesophageal reflux[2,3].

At the point where steroids does not affect an immune modulator or anti-cancer drug interferon Alfa can be used in cases of severe hemangioma[4]. Interferon Alfa itself have some serious adverse effects like high fever, systemic myalgia, and muscle pain if it is more severe liver problems, thyroid disease and neurological side effects may occur[5]. Because of these lot of complications pediatric patients does not accept treatment they prefer to live without treatment[6].

Another new treatment was introduced in 2008 and improvement was observed when beta blocker propranolol was used. After this initial step many centers conducted studies and case reports on propranolol use for the treatment of IH[7,8]. Propranolol used worldwide in treatment of IH but data available on this topic and it's off label use is insufficient. Its efficacy and safety also compared with steroids[9]. Another trial was conducted in 2015 but results of this study do not suggested propranolol as drug of choice and 1st line treatment. Multiple studies and comparative trials required to label propranolol[10].In this study we compared steroids with propranolol to check the efficacy and safety of propranolol over steroid use in treatment of IH.

MATERIALS AND METHODS

This randomized control trial was conducted in Department of Peads Surgery, Children Hospital, Multan and Department of Peads Surgery, NMU, Multan April 2014 to April 2017. After obtaining ethical permission from hospital ethical committee and informed consent from parents of participants. Total

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number 60 patients included in the study and divided into two equal groups (group C and P) by lottery method in which every patient has equal chances to be included in the group. Children from birth to 9 months age who were diagnosed with IH, normal cardiac function and not treated for IH were included in the study. Children of preterm delivery, any congenital anomaly and co morbid disease were excluded from the study. Size of tumor was measured with magnetic resonance imaging (MRI).

In group P patients were given propranolol 3 mg/kg per dayorallythree times in a day and patients were admitted in hospital and dose reached to maximum doses on their fix timing. After one hour start of medication regular monitoring was started for heart rate, hypoglycemia, and blood pressure and breathing status. After three days patient was discharged and asked for follow up four hourly till 20 weeks from the day of initial treatment. Doses were adjusted; study protocol was not followed at the point where guardians requested for further treatment of remaining IH. Treatment was reevaluated if any complications were observed.

Group C treated by giving steroid prednisolon1 mg/ml syrup oral at dose of 2 mg per kg.Primary outcome of this study is clinical response of medicine after sixteen weeks; it was labeled as regression. About 25% decrease in volume, surface area and height in hemangioma labeled as regression. Secondary variables include surface area of hemangioma, volume and height of hemangioma. After completion of information and data collection material entered into SPSS software and analyzed for continuous variables (mean ± SD) like age, size of hemangioma, weight, BMI and surface area, categorical variables (number and percentages) like gender, color of hemangioma. Independent sample t-test and chi-square test was applied to see significance. P value less than or equal to 0.05 was considered as significant.

RESULTS

Overall, 100% (n=84) patients were included in this study, both genders. The study group was further divided into two equal groups, 50% (n=42) in each. Gender distribution, in propranolol group, was observed as 59.5% (n=25) males and 40.5% (n=17) females. While, in steroid group, there were 57.1% (n=24) males and 42.9% (n=18) females. The mean age, weight, height, systolic blood pressure, diastolic blood pressure, heart rate, respiration rate and body temperature of the propranolol group patients was 3.28±2.19 years, 5.64±2.63 kg, 61.47±1.71cm, 88.12±1.85 mm Hg, 49.76±1.80mm Hg,129.80±1.72beats/min, 36.97±2.86 beats/min and 38.74±1.98° Crespectively. While, the mean age, weight, height, systolic blood pressure, diastolic blood pressure, heart rate, respiration rate and body temperature of the propranolol group patients was 3.64±1.96 years, 6.04±2.34kg, 61.66±1.67 cm, 91.69±1.31 mm Hg, 51.92±1.77 mm Hg, 141.76±2.08 beats/min, 36.76±2.56beats/min and 38.24±2.11 °C respectively. For propranolol group, location of hemangiomas i.e. scalp, face, chest, abdomen, back, upper extremity and lower extremity noted as 7.1% (n=3), 59.5% (n=25), 16.7%(n=7), 4.8% (n=2), 7.1% (n=3), 14.3% (n=6) and 7.1% (n=3) respectively.

Table No. 1: Demographic characteristics of the study groups

Characteristics	Propranolol Group(n=42)	Steroid Group (n=42)	Test of Sig.
Gender	M=59.5% (n=25), F=40.5% (n=17)	M=57.1% (n=24), F=42.9% (n=18)	χ^2 =0.049, p=0.825
Age (years)	3.28±2.19	3.64±1.96	t=-0.78, p=0.433
Weight (kg)	5.64±2.63	6.04±2.34	t=-0.744, p=0.459
Height (cm)	61.47±1.71	61.66±1.67	t=-0.52, p=0.608
Blood pressure Systolic (mm Hg)	88.12±1.85	91.69±1.31	t=-10.11, p=0.000
Blood pressure Diastolic (mm Hg)	49.76±1.80	51.92±1.77	t=-5.55, p=0.000
Heart rate (beats/min)	129.80±1.72	141.76±2.08	t=-28.63, p=0.000
Respiration rate (beats/min)	36.97±2.86	36.76±2.56	t=0.361, p=0.719
Body temperature (°C)	38.74±1.98	38.24±2.11	t=1.12, p=0.265
Hemangiomas			
Location			
Scalp	7.1% (n=3)	11.9% (n=5)	χ^2 =0.55, p=0.457
Face	59.5% (n=25)	73.8% (n=31)	χ^2 =1.93, p=0.165
Chest	16.7% (n=7)	4.8% (n=2)	χ^2 =3.11, p=0.078
Abdomen	4.8% (n=2)	7.1% (n=3)	χ^2 =0.213, p=0.645
Back	7.1% (n=3)	11.9% (n=5)	χ^2 =0.553, p=0.457
Upper extremity	14.3% (n=6)	16.7% (n=7)	χ^2 =0.09, p=0.763
Lower extremity	7.1% (n=3)	11.9% (n=5)	χ^2 =0.553, p=0.457
Color			
Red	66.7% (n=28)	92.9% (n=39)	χ^2 =8.93, p=0.003
Purple	16.7% (n=7)	4.8% (n=2)	χ^2 =3.11, p=0.078

P<0.05 is considered as significant

While, location of hemangiomas of steroid group i.e. scalp, face, chest, abdomen, back, upper extremity and

lower extremity noted as 11.9% (n=5), 73.8% (n=31), 4.8% (n=2), 7.1% (n=3), 11.9% (n=5), 16.7% (n=7) and11.9% (n=5) respectively. Color, for propranolol group, red and purple observed as 66.7% (n=28) and 16.7% (n=7) respectively. Whereas; color, red and purple observed as 92.9% (n=39) and 4.8% (n=2) respectively, for steroid group. The differences between demographic characteristics were statistically insignificant except systolic blood pressure, diastolic blood pressure, heart rate and red color. (Table. 1).

Table No. 2: Outcome Variables

Characteristics	Propranolol Group (n=42)	Steroid Group (n=42)	Test of Sig.
Size			
Baseline Volume , mm^3 by MRI*	29672.70 ±25.17	29682.8± 24.31	t=0.25, p=0.801
Volume , mm^3 by MRI*	14129± 11.98	14345± 13.07	
Regression in Baseline Volume , mm^3 by MRI*	15543.7	15337.8	
Baseline Surface area, mm^2	4099.01± 49.72	4145.34± 44.19	t=0.71, p=0.479
Surface area, mm^2	1322.26± 16.03	1375.23± 14.25	
Regression in baseline Surface area, mm^2	2776.75	2770.11	
Baseline Height, mm	8.40±3.12	9.87± 2.55	t=0.84, p=0.402
Height, mm	4.66±1.74	5.65± 1.60	
Regression in base-line Height, mm	3.74	4.22	

*** MRI, magnetic resonance imaging, P<0.05 is considered as significant**

The main outcome variables of this study were volume, surface area and height. The MRI scans were conducted for all the patients, the IH baseline volume was 29672.70±25.17 mm^3 for the propranolol group and it was 29534.2±24.31 mm^3 for the steroid group. The MRI scans were conducted for all the patients, the IH volume was 14129±11.98mm^3 for the propranolol group and it was 14345±13.07 mm^3 for the steroid group. Regression in baseline volume, mm^3 by MRI**,** for propranolol and Steroid was 15543.7 and 15337.8 respectively. But, the difference was statistically insignificant (p=0.801). An image of the lesion was taken for all participants in each group, and the mean baseline surface area for the propranolol group was 4099.01±49.72 mm^2, while it was, for the steroid group, 4145.34±44.19 mm^2. The mean surface area for the propranolol group was 1322.26±16.03 mm^2, while it was, for the steroid group, 1375.23±14.25 mm^2. Regression in baseline surface area, mm^2 for propranolol and Steroid was 2776.75 and 2770.11 respectively. The difference was statistically insignificant (p=0.479).The baseline height, for the propranolol and steroid group, was 8.40±3.12 mm and 9.87±2.55 mm respectively. The height, for the propranolol and steroid group, was 4.66±1.74 mm and 5.65±1.60 mm respectively. Regression in baseline height, mm for propranolol and Steroid was 3.74 and 4.22 respectively. The difference was statistically insignificant (p=0.402).(Table. 2).

DISCUSSION

Since the day of propranolol introduced it was globally accepted for treatment of hemangioma in infants because it is found to be effective as steroids. But there was limited literature available on effectiveness and its efficacy over steroids. In our study we found more reduced volume, surface area and height with steroids as compare to propranolol but values are not significant (p=0.801, p=0.479, p=0.402).

A recent study was conducted by Malik MA et al [11] on comparison of prednisolone and propranolol and reported that propranolol have better therapeutic effects with safety and efficacy, combination of both prednisolone and propranolol is also effective but less than propranolol alone, steroid alone have some serious adverse effect due to which its non compliance is too much. This study is comparable with our study.

Another recent study was conducted by Bauman NM et al [12]in 2014 and concluded that both drugs are equally beneficial; steroids have rapid effect and treatment option. On other hand propranolol has safety better than steroids as it has little complication rate and better compliance rate as compare to steroids. This study is also comparable with our study. Another study conducted by Léauté-Labrèze C et al[13] and concluded that propranolol is an effective drug for the treatment of infantile hemangioma as other drugs like steroids.

Bennett ML et al [14]also conducted a similar study on use of propranolol and steroids in treatment of hemangioma and reported that systemic steroids are better and more effective in subcutaneous hemangioma. He use similar variables in his study as we use in our trial. Similar studies were conducted by Price CJ et al[15], Enjolras O et al[16], they used same variables and reported that propranolol is as effective as steroids in treatment of hemangioma.

In our study systolic blood pressure, diastolic blood pressure, heart rate and red color of hemangioma are statistically significant shows that propranolol is not bad for hemodynamic stability. In a study Izadpanah A et al [17]reported that propranolol is a favorite drugs as compared to corticosteroids when use in treatment of IH in infants. Its adverse effects profile is more safe and reliable as compared to drugs of corticosteroids group. This study is also comparable with our findings.

Propranolol have some major side effects like bradycardia, hypotension and hypoglycemia, to overcome these complications some studies suggested selective beta blocker (Atenolol) in place of propranolol

with more safety and superiority[18, 19]. In a study Chim H et al [20]recommended propranolol 3 mg/kg or 1 mg/kg is more effective in treatment of hemangioma of infancy

CONCLUSION

Results of our study revealed that therapeutically propranolol is not inferior to steroids in treatment of infantile hemangioma.

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Original Article

Comparison Between Efficacy of Methylprednisolone and Triamcinolone in Intra Articular Injection for Osteoarthritis Pain Relief

Hassan Jameel, Faiza Liaquat and Sabir Khan

ABSTRACT

Objective: To compare the effect of two different corticosteroid regimens methylprednisolone acetate and triamcenolone acetate in bilateral and symmetrical knee osteoarthritis (OA) pain relief.

Study Design: A Randomize Control Trial study.

Place and Duration of Study: This study was conducted at the Department of Anaesthesia, Intensive care and Pain Management, Hameed Latif Hospital, Lahore from 1st November 2016 to 30th October 2017.

Materials and Methods: After getting ethical approval from hospital ethical committee and informed consent from patients to be included in study. Total 100 patients were enrolled in study through non probability consecutive sampling technique, and all patients were divided in two equal groups randomly using lottery method. Data was collected on pre designed Performa. Statistical analysis was done by using SPSS version 24 for all variables, mean and SD presentation for continuous data like age and VAS score, WOMAC score and frequency percentage presentation was given for categorical data like gender. P value ≤ 0.05 was considered as significant.

Results: Total 100 patients were included, in this study. The mean age and BMI of the patients was 60.33±2.61 years and 27.06±2.42 kg/m^2 respectively. A significant decrease in VAS score for both knees (right and left) was observed after intra articular injection bilaterally. Measurements were done at 2, 4, 8, 12 and 24 weeks after injection administration ($p<0.005$).

Conclusion: Results of our study revealed that intra articular injection is an effective mode of treatment when used for the management of osteoarthritis knee pain ($p<0.005$). When we compared two steroid regimens Methylprednisolone and Triamcenolone it was observed that there is no significant difference among both groups, both are equally effective.

Key Words: Intra-aticular injection, Triamcenolone acetate, Methylprednisolone, Osteoarthritiss

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INTRODUCTION

Knee pain in adult age is more probably due to the osteoarthritis OA, it reduces the quality of life and a continuous disability is the fate of person[1,2]. Main goal of such patients is control of pain with conservative management, exercise, physical therapy, medication and weight loss[3]. Surgical management also indicated in such patients but when disease in advance stages. American collage of advance rheumatology indicated intra-articular injection for its treatment and consider as a part of conservative management of knee osteoarthritis[4]. Mechanism of action of thus injection is not yet clear but it is reported that corticosteroids inhibits the release of leukocytes in synovial fluid and prevent the release of prostaglandins and interleukins[5].

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Clinical effectiveness of this injection was reported in many studies. Main concern of this treatment is cartilage destruction which is reported as progression in some studies, few reports shows reduction in progression of cartilage destruction[6,7]. Results of this corticosteroid injection are not consistent, short term benefits also reported in literature (about four weeks). On other hand some studies on this topic reported 24 weeks effect[8]. Some clinical trials on comparison of different corticosteroids are also available for intra articular injection[9].

Along with these benefits some adverse effects and perceived efficacy are the main concern of osteoarthritis especially in knee osteoarthritis[10]. Among corticosteroids of intra articular injection triamcinolone hexacetonide and methylprednisolone acetate are common. Over more than of one third people of more than 65 years of age suffered from osteoarthritis who presents with pain which most common presenting complaint of patients[11,12]. Aim of our study is to compare two different types of drugs used in intra articular injections.

MATERIALS AND METHODS

This randomized control trial was completed in department Pain Management of Hameed Latif Hospital,Lahore under supervision of consultant anaesthesiologists of institution. Study duration was one year from 1stNovember 2016 to 30thOctober 2017. Study was started after ethical approval from ethical review board of hospital. Informed consent was obtained from patients as per hospital rules. Sampling technique used was non probability consecutive sampling and CI of 95, power of 80% with mean VAS score after treatment in both groups was 7.7 ± 1.3 vs 7.5 ± 1.5 right and left knee was used to calculate sample size.

Pain of patients was assessed by using visual analogue score scale (VAS). Patients presented in Pain clinic outdoor with bilateralknee pain and baseline pain score was noted. Radiological investigation for grade 3 OA was done as per Kellgren Lawrence classification and who were unsatisfied from previous conservative mode of treatment were included in the study. Patients with history of previous intra articular injection, unstable joint, secondary arthritis, diabetes, any malignant cancer, BMI more than 30 and who were contraindicated to injections like presence of infection, on anti coagulant therapy and allergic to drug used were excluded from the study.

In our study we used methylprednisolone acetate in right knee and triamcinolone hexacetonidein left knee of same patient. Lateral position for injection was used in sitting position with 90 degree knee flexion. Skin was cleaned with pyodine swab before injection, no anesthetic was given before procedure. Methyl prednisoloneacetate 40 mg 1 ml was mixed with 3 ml of lidocain 1% and triamcinolone hexacetonide40 mg 2ml mixed with lidocaine 1% with 22 G needle. A third person who is unaware of study was appointed to evaluate the study variables. Before injection patients were evaluated and than at 2nd week, 4th week, 8th week, 12th week and 24th week. Severity of pain was assessed by using VAS score and functionality of joint was assessed by using WOMAC scale. All possible complications and side effects were evaluated and recorded on pre designed Performa.

Statistical analysis was done by using SPSS version 24 for all possible variables, mean and SD presentation for continuous data like age and VAS score, WOMAC score and frequency percentage presentation was given for categorical datalike gender. P value less than or equal to 0.05 was considered as significant.

RESULTS

Overall 100 patients were included, in this study. The mean age and BMI of the patients was 60.33±2.61 years and 27.06±2.42 kg/m^2 respectively. (Table. 1). At first admission, the mean VAS score for the right knee, the left knee and WOMAC was 8.04±2.1, 7.37±1.5 and 68.64±3.0 respectively. At 2nd week, the mean VAS score for the right knee, the left knee and WOMAC was 2.34±1.3, 2.07±1.1and 30.90±2.1 respectively.

Table No. 1: Demographic Characteristics

Variables	Mean±S.D
Age (years)	60.33±2.61
BMI (kg/m^2)	27.06±2.42

Table No.2: Mean VAS scores of right and left knee and mean WOMAC scores of the patients

First Admission			2nd week			4th week		
VAS R	VAS L	WOMAC	VAS R	VAS L	WOMAC	VAS R	VAS L	WOMAC
8.04±2.1	7.37±1.5	68.64±3.0	2.34±1.3	2.07±1.1	30.90±2.1	2.23±1.3	2.22±1.1	33.78±3.8
8th week			12th week			24th week		
VAS R	VAS L	WOMAC	VAS R	VAS L	WOMAC	VAS R	VAS L	WOMAC
4.1±1.5	3.8±1.1	47.1±2.8	5.5±1.1	5.1±1.13	58.1±2.19	5.9±1.43	5.66±1.33	60.80±2.49

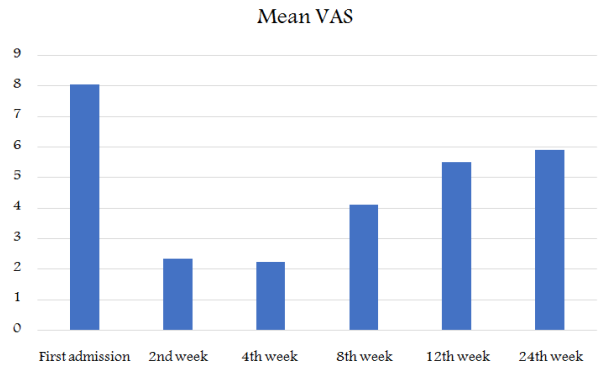

Figure No.1: Mean VAS score in methyl-prednisolone acetate after injection

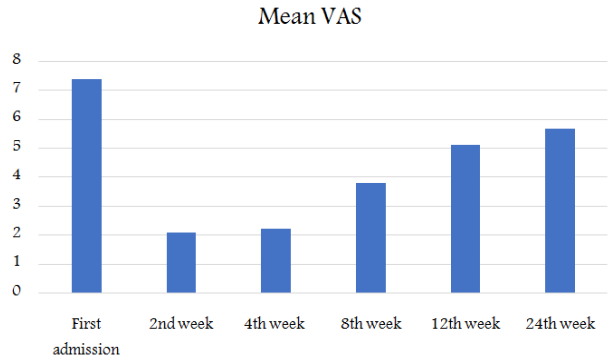

Figure No.2: Mean VAS score after injection in triamcinolone hexacetonide

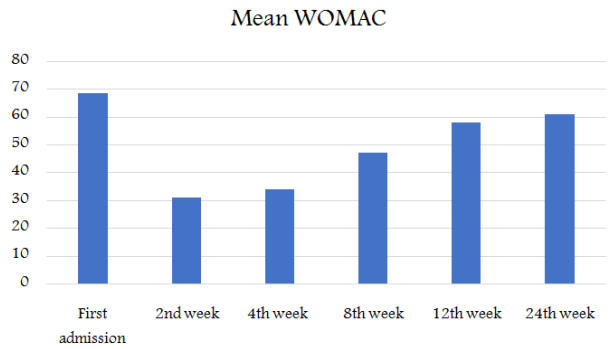

Figure No.3: Mean of WOMAC Score in both knees

At 4th week, the mean VAS score for the right knee, the left knee and WOMAC was 2.23±1.3, 2.22±1.1and 33.78±3.8 respectively. At 8th week, the mean VAS score for the right knee, the left knee and WOMAC was4.1±1.5, 3.8±1.1and 47.1±2.8 respectively. At 12th week, the mean VAS score for the right knee, the left knee and WOMAC was 5.5±1.1, 5.1±1.13 and 58.1±2.19 respectively. While, at 24th week, the mean VAS score for the right knee, the left knee and WOMAC was 5.9±1.43, 5.66±1.33 and 60.80±2.49 respectively. A significant decrease in VAS score for both knees (right and left) was observed after intra articular injection bilaterally. Measurements of was done at 2, 4, 8, 12 and 24 weeks after injection administration $p<0.005$ (Table. 2).

Graphical representation of mean VAS scores was after injection with methylprednisolone acetate, triamcinolone hexacetonide were given in Figure. 1 and 2. Similarly graphical representation of mean WOMAC scores for both knees was given in figure. 3).

DISCUSSION

Results of our study showed significant decrease in VAS score for both knees (right and left) was observed after intra articular injection bilaterally. Measurements of was done at 2, 4, 8, 12 and 24 weeks after injection administration $p<0.005$. In comparison between the groups there was not a remarkable difference, both regimens are almost equally effective.

In a study conducted by Arroll B et al[13] reported that intra articular injection in the treatment of knee pain after osteoarthritis is an effective mode of treatment and have reliable effects on quality of life. In another study conducted by Godwin M et al[14] reported similar findings that intra articular injection is an effective and useful technique for the relief of osteoarthritis knee pain. These two studies are comparable with our results.

In a double blind study of placebo control was conducted by Raynauld et al[15] and reported that not only a single use but repetitive use of intra articular injection is useful for the relief of osteoarthritis symptoms, it will never destroy the anatomical position and structure of knee. In a study Pyneet al[16] compared triamcenolone and methylprednisolone in intra articular injection and reported that triamcenilone is more effective than methylprednisolone in pain relief.

While in study Yavuz et al[17] reported that methylprednisolone is more effective as compared to triamcenolone when their efficacy was compared in intra articular injection for relief of osteoarthritis pain until 6 weeks of injection administration.In a study conducted by Buyuk AF etal[8] reported that there is no difference in effectiveness of both corticosteroids regimens in knee pain relief.

Recommended dose of methylprednisolone in intra articular injection is 20 to 80 mg and for triamcenolone 20-40 mg[18, 19]. In our study we use similar dose 40 mg for both regimens as used by Buyuk et al [8]in his study.Jain P et al[20] conducted a study on this topic and reported that intra articular injection for pain relief is an effective and use of corticosteroid especially methylprednisolone is more beneficial as compared other regimens.

In another study by Shikharet al[21] reported a significant improvement in WOMAC score in methylprednisolone group as compared to triamcinolone. VAS score is also showing good effects as compared to other regimens when compared to other corticosteroids. This study is comparable with our study.

Another study conducted by Smith et al[22] reported similar findings as methylprednisolone is more effective as compare to other regimens of corticosteroids when used in intra articular injection for relief of osteoarthritis pain. We can also compare this study with our study.

CONCLUSION

Results of our study revealed that intra articular injection is an effective mode of treatment when used for the management of osteoarthritis knee pain ($p<0.005$). When we compared two steroid regimens Methylprednisolone and Triamcenolone it was observed that there is not a significant difference among both groups, both are equally effective.

Author's Contribution:

Concept & Design of Study:	Hassan Jameel
Drafting:	Faiza Liaquat, Hassan Jameel
Data Analysis:	Faiza Liaquat, Sabir Khan
Revisiting Critically:	Hassan Jameel, Faiza Liaquat, Sabir Khan
Final Approval of version:	Hassan Jameel

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

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general practice: development and impact of training in a cluster randomised controlled trial. BMC Family Pract 2016;17:173.
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Original Article

Outcome of Manipulation under Anesthesia in Treatment of Frozen Shoulder with and without Steroid Injection in Terms of Range of Motion

Shujaat Hussain, Tayyab Mahmood, M. Iqbal Buzdar and M. Iqbal Mustafa

ABSTRACT

Objective: This study was conducted to compare the mean difference in the range of motion (ROM) between manipulation under anesthesia (MUA) with and without intra-articular injection of steroid in patients of Frozen Shoulder (FS).

Design: Randomized controlled trial study.

Duration and Place: This study was conducted at the Orthopedic Department, BV Hospital Bahawalpur from May 15th, 2016 to October 14th, 2017

Materials & Methods: A total of 156 patients of 30 to 75 years of age with FS were included in the study. Patients with metabolic bone disease and osteoporosis were excluded. Pre-operative measurements of the ROM (flexion, abduction, external rotation and internal rotation) of FS were taken in all patients. Selected patients were placed randomly into 2 groups i.e. Group A (MUA without steroid) & Group B (MUA with steroid), by using lottery method.

Results: The mean age of women in group A was 55.65 ± 8.13years and in group B was 55.23 ± 8.26years. Out of these 156 patients, 36.54% were male and 63.46% were females with ratio of 1:1.74. Post-manipulation, the results have shown that there was significant improvement (p-value<0.05) in ROM in group B (MUA with steroid injection) compared to group A (MUA without steroid injection).

Conclusion: In combined treatment (MUA with steroid injection) ROM is significantly improve as compared to in single treatment (MUA) in FS.

Key Words: Flexion, adhesive capsulitis, intra-articular injection, rehabilitation.

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INTRODUCTION

Shoulder joint is hyper mobile joint ofhuman body.[1] Due to this hypermobility, shoulder joint may become unstable but glenoid labrum, ligaments, tendon and rotator cuff muscles give the stability of joint [2,3]. If the capsule of shoulder joint islax, ROM becomes more and the joint in turn may dislocate. On the other hand if the capsule becomes tight the ROM decreases and the joint is very much held together and cannot dislocate.[5] The main component of FS is loss of motion and pain of shoulder joint for a specific period [4].

The incidence of FS in general population is about 2%.[4] Individuals between age of 40-70 years are most commonly affected. The Risk factors are female sex, age older than 49 years, diabetes mellitus[40], cervical disc disease, prolonged immobilization, hyperthyroid-dism, stroke, myocardial infarction, Dupuytren's disease, autoimmune disease and trauma [6,7]. Etiology of FS is unknown but one of predisposing factors is virus[8]. As the shoulder loses its motion, even normal activities like changing dress, phone calling, or other working become difficult.[9] Studies suggest that about 50% of people with frozen shoulder continue to experience symptoms up to seven years after the condition starts. However, with appropriate treatment it is possible to shorten the period of disability[10]. The aim of treatment is to get pain free joint with full range of motions. The treatment depends upon, how severe frozen shoulder is and how far it has progressed.[11]

Various modalities of treatment have been proposed and are in practice. These include non-steroidal anti-inflammatory drugs (NSAID), oral corticosteroids, physiotherapy, intra-articular steroid injection, distension arthrography, manipulation under anesthesia (MUA), open surgical release and arthroscopic capsular release.[4,5,11,12] Each modality can be determined by using different shoulder scoring system e.g. Constant Shoulder Score (CSS), University of Pensyvania Shoulder Scale and Functional Assessment

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Questionnaire.[10,13] Meta-analysis has been done to assess score.[14]

Most noninvasive therapeutic strategies are based onstretching or rupturing the tight capsule by manipulative physical therapy with success rate for achieving good to fair results nearing 100.0%.[15] The good result of physical therapy with intra-articular corticosteroid injections, with or without hydraulic distension, ranges from 44.0% to 80.0%.[16,17]. MUA and arthroscopic or open release, are a popular form of therapy especially for resistant frozen shoulder. The published success rate for this therapy varies 69% to 97.0%.[18,19]. MUA alone or with combination with intraarticular steroid injection is easy, effective, inexpensive and less time consuming treatment modality.[20] Role of physiotherapy is very important for success.[21] This study was conducted to compare the mean difference in the range of motion (ROM) between manipulation under anesthesia (MUA) with and without intra-articular injection of steroid in patients of Frozen Shoulder (FS).

MATERIALS AND METHODS

This was randomized controlled trial conducted at department of Orthopedic, Bahawal Victoria Hospital, Bahawalpur, from 15thMay 2016 to 14thOctober 2017. Total 156 patients of FS syndrome were considered using probability, consecutive sampling. Patients were of both genders, aged 30-75 years. Patients having metabolic bone disease and osteoporosis, unfit for general anesthesia or having recently healed fractures were excluded from the study.

After approval from local ethical committee, informed, written consents were taken after explaining the aims, methods, reasonably anticipated benefits, and potential hazards of the study from all the participants. Subjects were informed that their participation is voluntary. Pre-operative measurements of the ROM of FS (flexion, abduction and external rotation) were taken in all patients with standard goniometer by researcher himself and were recorded on a specific proforma. All cases were selected randomly by pick up slips,(half slips labelled letter 'A' and half slips labelled letter 'B')and patient were placed in 2 groups A and B.Base line investigations like complete blood count, random blood sugar, Urine Complete Examination, Renal functions tests and ECG (where needed) were done in every patient on admission for anesthesia purposes. Antero-posterior and lateral X-rays of the affected shoulder were done in all patients.

All patients in Group A (n=78) were given general anesthesia and the frozen shoulder was manipulated in its full range of motion keeping in view the recommendations to keep short lever arm and manipulated in order of flexion, extension, abduction, external rotation and internal rotation. While all patients in Group B (n=78) were undergone all above steps along with that an intra-articular steroid (40 mg methyl prednisolone) was given through anterior approach (sub-acromion). After this all patients of both groups were made to undergo a regular physiotherapy session of 20 minutes daily for two weeks.

The follow up examination of all patients of both groups was conducted after two weeks of the procedure and ROM of FS was calculated (flexion, abduction, external rotation and internal rotation) was calculated with standard goniometer and was documented on specified performa.

The data collected was entered in computer software SPSS version 10. Mean and standard deviation were calculated for age and ROM (flexion, abduction, external rotation and internal rotation) in both groups before and after manipulation. Frequency and percentage were calculated for the qualitative variable like gender. Diagrams and tables were made. The outcome variable i.e. ROM (flexion, abduction, external rotation and internal rotation) were compared for any difference between both groups. P-value ≤ 0.05 was considered as significant.

RESULTS

A total 156 patients were included in the study. Mean age was 55.41 ± 8.17 years (range 30-75 years).The mean age of patients in group A was 55.65 ± 8.13years and in group B was 55.23 ± 8.26years.Seventy two (46.15%) patients were between age46 to 60 years, as in Table 1.Fifty seven (36.54%) patients were male and 99 (63.46%) patients were females with ratio of 1:1.74in both groups (Fig 1). Eighty nine (57%) patients were diabetic and 67 (43%) patients were non diabetics in both groups (Fig 2).

Table No.1: Age distribution for both groups (n=156).

Age (years)	Group A (n=78)		Group B (n=78)		Total (n=156)	
	No. of patients	%age	No. of patients	%age	No. of patients	%age
30-45	19	24.36	20	25.64	39	25.0
46-60	37	47.44	35	44.87	72	46.15
61-75	22	28.20	23	24.49	45	28.85
Mean ± SD	55.65 ± 8.13		55.23 ± 8.26		55.41 ± 8.17	

Table No.2: Pre-manipulation Range of motion in both groups.

Range of Motion	Group A (n=78)		Group B (n=78)		P-value
	Mean	SD	Mean	SD	
Flexion	83.41	22.34	83.74	21.49	0.9252
Abduction	65.13	17.61	64.98	17.18	0.9571
External Rotation	28.33	22.19	28.02	21.79	0.93
Internal Rotation	1.24	0.53	1.29	0.47	0.534

Pre-manipulation ROM (flexion, abduction, external rotation and internal rotation) has shown no significant difference between two groups as shown in Table 2

while post-manipulation, the results have shown that there was significant improvement (p-value<0.05) in ROM in group B (MUA with steroid injection) compared to group A (MUA without steroid injection) as shown in Table 3.

Table No.3: Post-manipulation Range of motion in both groups.

Range of Motion (degree)	Group A (n=78)		Group B (n=78)		P-value
	Mean	SD	Mean	SD	
Flexion	153.41	18.20	163.85	23.25	0.0021
Abduction	137.32	15.19	161.27	18.11	<0.0001
External Rotation	45.67	7.28	53.53	8.62	<0.0001
Internal Rotation	3.18	0.79	3.97	1.09	<0.0001

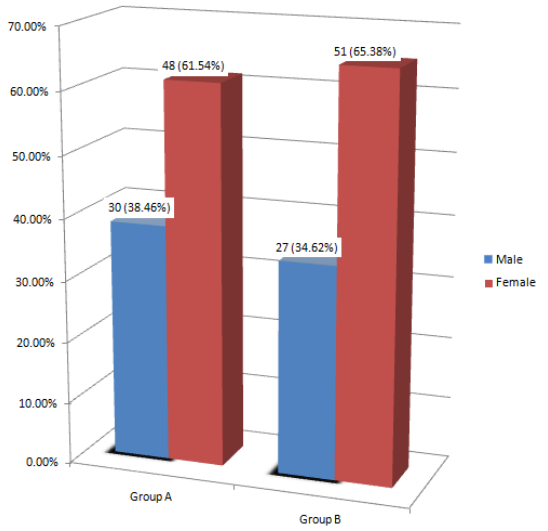

Figure No.1: %age of patients according to Gender in both groups

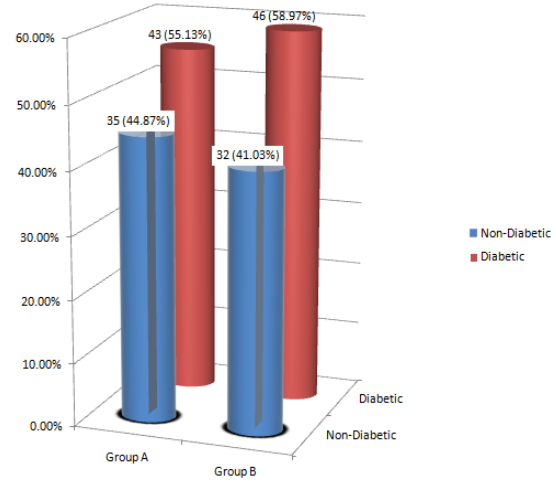

Figure No.2: %age of patients according to Diabetes Mellitus in both groups

DISCUSSION

Frozen shoulder is a self-limiting disease that improves over an 18 to 24month period. In 2004, Diercks and Stevens[23]describedabout increase in constant shoulder scores with time when it was treated with ‘‘supervised neglect.’ FS does notappear on X-rays. Occasionally on MRI can confirm findings of frozen shoulder, but is often not needed.[25]

Corticosteroid injection decreases inflammation and reduces in capsular fibrosis. This allows enhancement of joint motion and reduces the functional recovery time[26.]

In this study the mean age of patients was 55.41 ± 8.17 years which was very much comparable to studies of Saqlain HA et al[20] and Wang JP et al[27] who had found a mean age of 54 and 55 years respectively. In Khan JAet al[28]study mean age is 50 years in his study which is a little lower compared to this study. In FS above 40 years of age adhesive capsulitis is common and below 40 years of age it is needed to investigate for any medical problems. No racial predilection has been described in the literature.[29,30]In our study, majority of patients 63.46% were female and 36.54% were males with ratio of 1.74:1. These results coincide with results of many previous studies which have shown the incidence of FS two times greater amongst men than women[12, 19, 22]. A blinded, randomized trial with a 1 year follow-up, by Kivimaki J et al[31] evaluated 125 patients with a frozen shoulder to determine the effect of manipulation under anesthesia. Patients were randomly assigned to either a manipulation group or a control group. In manipulation group ROM was better with small difference then controlled group but in term of shoulder pain there was no difference in 2 groups in total follow-up. Small differences in the range of movement were detected in favor of the manipulation group. Ng CY et al[32] conducted a prospective trial to evaluate the efficacy of MUA followed by early physiotherapy in FS syndrome. For disability, pain and ROM,DASH (disability of arm shoulder hand) score and VAS (visual analogue score) score were also calculated and it was found that combined MUA and physiotherapy decreases pain and increases recovery and function of shoulder in FS disease[32].

In this study, the results shows that there was significant improvement (p-value<0.05) in range of motion in group B (MUA with steroid injection) compared to group A (MUA without steroid injection). These findings contradict with the results of Kivimaki J et al[33] who had found no extra advantage of intra-articular steroid injection alongwith MUA for FS. Hazelman B et al[34] in his review has demonstrated the use of intra-articular corticosteroids injection and reported that success of treatment is totally dependant

on the disease duration. The ideal time of MUA is about 6 to 9 months after start of the symptom [35]. Results of MUA and steroid injection are better in many studies [33, 36] as described in this study. Repeated MUA with steroid injection can improve further in the symptom of FS, there is also role of good physiotherapy course after this modality[37, 38].Evidence from aggregated published RCTs showed that the effectiveness of glenohumeral joint distension was similar to that of intra-articular corticosteroid injection, as well as that of most of the current conservative management methods.[39.] The limitations we found in our study were the difficulty in communication with patients from remote area. There follow-up was difficult and physiotherapy advised had poor compliance. Such patients were found randomly in both groups so this did not affect our comparative results.

CONCLUSION

The treatment with manipulation under anesthesia and intra-articular steroid significantly improve range of motion in frozen shoulder.

Author's Contribution:

Concept & Design of Study:	Shujaat Hussain
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Data Analysis:	M. Iqbal, Shujaat Hussain
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Conflict of Interest: The study has no conflict of interest to declare by any author.

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ACKNOWLEDGMENTS

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