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Editorial

Original Articles

Editorial

Depression, Peripheral Artery Disease and Exercise; Is there a link?

Mohsin Masud Jan
Editor

Depression may increase the risk for PAD (peripheral artery disease), which commonly results from narrowed leg arteries, a new study suggests.

The study results demonstrate that there is an association between depression and PAD. We know that if you have depression, your risk for PAD is likely related to poor health behaviors like smoking and physical inactivity. People who are depressed may be more likely to smoke and less likely to exercise and eat a healthy diet, all of which could raise the risk of heart disease and PAD.

The findings were presented at the American Heart Association's Arteriosclerosis, Thrombosis, and Vascular Biology 2012 Scientific Sessions in Chicago. In the study, 1,018 people with heart disease were followed for more than seven years. When the study began, 12% of people with depression had PAD, as did 7% of those who were not depressed. People who were depressed were more likely to be younger and female.

They were also more likely to have lower HDL ("good" cholesterol), high levels of C-reactive protein, which is a sign of inflammation in the body, and a history of heart attack, heart failure, or diabetes. They also tended to smoke and be physically inactive, and were less inclined to take their medications as directed.

7% of depressed people and 5% of those without depression had a PAD-related event during the study period. These included surgery to open blocked leg arteries or other treatments.

PAD occurs when arteries away from the heart become narrowed and blocked. The leg and pelvis arteries are most commonly affected. PAD involving the leg arteries can cause pain while walking, climbing stairs, or exercising. This pain usually stops during rest.

Risk factors for PAD are similar to those of heart disease, including smoking, diabetes, high blood pressure, and elevated cholesterol.

PAD treatment includes lifestyle changes -- such as eating a healthy diet, quitting smoking, and getting more exercise - that are aimed at reducing these risks. Medications to treat conditions that increase risk for PAD and/or surgery to open blocked leg arteries are also options. People having pain with walking or lesions on their feet, should be evaluated by a doctor to see if it is PAD.

Depression in itself cannot be called a red flag for PAD. But, we need to look at other risk factors in patients with depression. People who have depression are at increased risk for heart disease and PAD in the future, but at present, they are more at risk of having certain poor health behaviors that could increase their risk of heart disease.

Exercise helps people with heart failure feel a bit better, physically and emotionally, a new study shows. It may also lower a person's risk of dying or winding up in the hospital.

Up to 40% of people with heart failure grapple with depression. The combination often leads to poor health outcomes. One study found seriously depressed people with heart failure were more than twice as likely to die or be hospitalized over the course of a year compared to other people with heart failure who were not depressed. Whenever patients are more depressed, their motivation goes down. Their ability to keep up with their doctors' recommendations and do basic physical activities like walking goes down, thus making it a vicious cycle.

This study shows a non drug way to try to improve patients' mood and motivation. For this study, which is published in the journal of the American Medical Association, researchers assigned more than 2,322 stable heart failure patients to a program of regular aerobic exercise or usual care. Usual care consisted of information on disease management and general advice to exercise.

The exercise group started with a standard exercise prescription for patients in cardiac rehab: three, 30 minute sessions on either a treadmill or stationary bike each week. After three months, they moved to unsupervised workouts at home. At home, their goal was to get 120 minutes of activity a week. Just as happens in the real world, most exercisers fell short of their weekly goals. Despite the fact that they were not as active as they were supposed to be, they still had slightly better scores on a 63 point depression test than the group assigned to usual care. There was a little less than a one point difference between the two groups. But the differences persisted even after a year, leading researchers to think the result was not a fluke. And the exercisers were about 15% less likely to die or be hospitalized for heart failure compared with the group getting usual care.

Researchers think the differences between the two groups were small because most people in the study were not depressed to begin with. Only 28% had test scores high enough to indicate clinical depression. But the more depressed a person was, the more they had to gain from regular exercise. After a year, test scores of depressed patients were about 1.5 points better in the exercise group compared to those assigned to usual care.

We already know that exercise is beneficial in terms of improving cardiovascular fitness. Now we know that depression is also reduced in these patients after working out. For people who were more depressed, they experienced a greater reduction in their depressive symptoms with exercise, according to the study. The study shows exercise "is in the same ballpark" as other established treatments, particularly antidepressant medications.

This, places exercise as one of our most versatile tools to help combat a myriad of diseases, which now also includes depression and by its link, could also help reduce the incidence of Peripheral Artery Disease.

Original Article

Frequency and Awareness of Ante-Natal Care to Avoid Primary Cesarian-Section Among Multi-Parous Women of Karachi

Tafazzul H. Zaidi and Kiran Mehtab

ABSTRACT

Objective: To assess lack of antenatal visits as a reason of Primary Cesarean-Section in multi-parous women with previous S.V.D.

Study Design: Cross sectional study

Place and Duration of Study: This study was conducted at the Department of Community Medicine, Jinnah Postgraduate Medical Centre, Civil hospital and Sobraj Hospital, Karachi from May to August 2017.

Materials and Methods: A study was conducted on a sample of 130 women (undergone Primary cesarean section with previous S.V.D) taken through non probability purposive sampling from 3 hospitals of Karachi namely, Jinnah Postgraduate Medical Centre, Civil hospital and Sobraj hospital. A structured self-administered questionnaire was developed. An informed verbal consent was taken and a pilot study was conducted to assess the validity of the questionnaire. The questionnaire was then distributed, got filled, data was analyzed using SSPS version 16.0, with 95% confidence interval and 0.05 p-value as statistically significant.

Results: Out of the 130 primary caesarean deliveries during the study period 35.4% were indicated for mal-presentation, 25.4% for antepartum hemorrhage 20.0% for fetal distress, and 16.2% for pre-eclampsia. 73.8% (p-value= 0.035) patients had hypertension during pregnancy. When asked if these patients experienced any swelling in the hands or feet's during that time, a total number of 49.2% (p-value= 0.04) complained they had. 70.8% (p-value= 0.023) patients gave the history of fits during pregnancy. Antenatal clinics were frequented by only a mere 40.8% (p-value=0.005) of the patients. Among these 130 patients, reduced fetal movements were felt by 54.6% (p-value= 0.006) of the total consensus. A total of 52.3% (p-value= 0.00) were informed by their health worker about the abnormal position of their baby. It was also noted that 53.1 % (p-value= 0.00) of the patients were told by their doctor that they have a low lying placenta, and 56.9% (p-value= 0.00) of the total had an episode of severe vaginal bleeding at any time of pregnancy.

Conclusion: Previous vaginal delivery gives the family and the doctors a false sense of security that overshadows the need for vigilant antenatal and intra-partum care. The method of previous deliveries shouldn't be the primary criteria upon which the current delivery is decided. Rather, every pregnancy should be treated with as much concern and care as the first. (The physicians should display obligation in such circumstances and assess the pregnancy thoroughly before heading towards a massive scheme. Rather than promoting the doctors' own interests and convenience, Mothers' health and wellbeing should be considered the first priority and every possible measures should be taken to ensure that. The antenatal care should be the utmost preference and necessary investigations should be practiced. WHO recommends a minimum of four antenatal visits, comprising interventions such as tetanus toxoid vaccination, screening and treatment for infections, and identification of warning signs during pregnancy? With all the adequate steps taken, the rate and reasons of cesarean sections could be monitored and restricted hence progressing to initiate a huge stride for maternal and fetal health.

Key Words: Ante- Natal Care, Cesarean section, SVD, Antenatal care, Multipara, Mal-Presentation, Antepartum Hemorrhage

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INTRODUCTION

Department of Community Medicine, SMC, Jinnah Sindh Medical University, Karachi.

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Cesarean Section describes a procedure in which the fetus is delivered through incisions in the maternal abdominal and uterine walls. With the increasing risk of fetal mortality, C-section seems an appropriate choice to deal with maternal and fetal complications in a high-risk pregnancy. A study in India showed that the total cesarean rate in 2013 was 29.46%[1]. The rate of cesarean section in US in 2010 and 2011 was 32.8%[2]. According to a study in Pakistan, the rate of cesarean section was 27.94%, out of which 14.14% were elective and 85.86% were emergency C-sections[3]. These rates are significantly higher than the appropriate maximum

rate of 15%, above which more harm is done than good[4]. A previous concept that primary C-Section is of no much concern in parous women was disproved in a recent study[5] which showed the rate to be 13.3% against 18% in nulliparous women, which is not much different. In fact, increase in cesarean section rates is consistent with increase among parous women[1]. Dystocia with cephalopelvic disproportion (CPD) is the most important indication for nulliparous women, whereas placenta previa, hypertensive vascular disorder, mal-presentations and ruptured uterus are more common causes for C-section in multiparous women[6].

Multipara refers to those women who have delivered once or more after the age of viability. Dr. Solomon stated in his paper 'The dangerous multipara': "My object in writing this paper and giving it a sensational title is to remove if possible once and for all, from the mind of the reader, the idea that a primigravida means difficult labour, but a multipara means an easy one.[7] Primary caesarean section in the multipara means first caesarean section done in patients who had delivered vaginally once or more. Mainly the baby and the placenta are responsible for caesarean section in multipara[1]. It is a common belief amongst public that once a mother delivers her child or children normally, all her subsequent deliveries will be normal. As a result such multiparous mothers often neglect routine antenatal checkup[8].

Some indications for Primary Cesarean Section are:

- Fetal Mal-presentation: This refers most commonly to breech presentation, but also means any fetal orientation other than cephalic.
- Antepartum Hemorrhage: APH is bleeding from the genital tract during pregnancy from the 20th week till the onset of labour. It is caused by placental abruption or placenta previa.
- Non Reassuring EFM (electro fetal monitoring) STRIP: The fetal heart rate monitor pattern suggests the fetus may not be tolerating labour, but commonly this is a false-positive finding.

There is a false notion that multiparous women are less inclined to have a complicated pregnancy and delivery in comparison with a primipara, and this has primarily led to lack of care and antenatal follow up among them which ultimately directs them on the path of developing more severe complications at the time of delivery.

Cesarean delivery is one of the most commonly performed operations today[9]. Primary caesarean section in a multipara means first caesarean section done in the patients who had delivered vaginally once or more. Mainly the baby and the placenta are responsible for caesarean section in multipara[10].

MATERIALS AND METHODS

A cross sectional study was conducted on a sample of 130 women (multi-parous) (undergone Primary caesarean section) taken through non probability purposive sampling from 3 hospitals of Karachi namely, Jinnah Postgraduate Medical Centre, Civil hospital and Sobraj hospital, within a period of 4 months from May to August 2017.An informed verbal consent was taken and a pilot study was conducted to assess the validity of the questionnaire. A self-administered structured questionnaire was then distributed, got filled, and the data was analyzed using SSPS version 16.0, with 95% confidence interval and 0.05 p-value as statistically significant.

RESULTS

Out of the 130 primary caesarean deliveries during the study period 35.4% were indicated for mal-presentation, 25.4% for antepartum hemorrhage 20.0% for fetal distress, and 16.2% for pre-eclampsia. It was noted that 73.8% (p-value= 0.035) patients had hypertension during pregnancy. When asked if these patients experienced any swelling in the hands or feet's during that time, a total number of 49.2% (p-value= 0.04) complained of this. 70.8% (p-value= 0.023) patients gave the history of fits during pregnancy. Antenatal clinics were frequented by only a mere 40.8% (p-value=0.005) of the patients. Among these 130 patients, reduced fetal movements were felt by 54.6% (p-value= 0.006) of the total consensus. A total of 52.3% (p-value= 0.00) were informed by their health worker about the abnormal position of their baby. It was also noted that 53.1 % (p-value= 0.00) of the patients were told by their doctor that they have a low lying placenta, and 56.9% (p-value= 0.00) of the total had an episode of severe vaginal bleeding at any time of pregnancy.

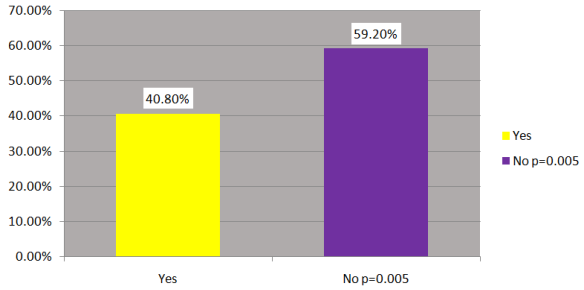

Figure No.1: Did you go for antenatal visits?

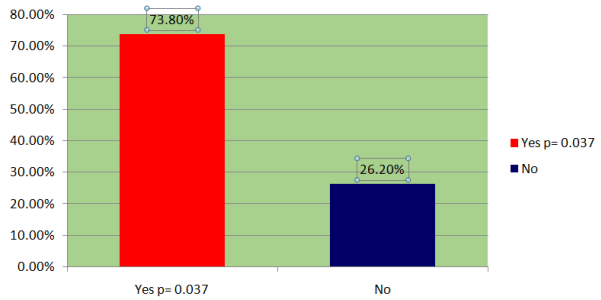

Figure No.2: Do you have hypertension during pregnancy?

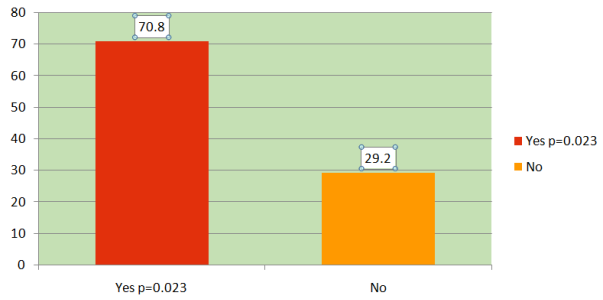

Figure No.3: Did you ever have fits during pregnancy?

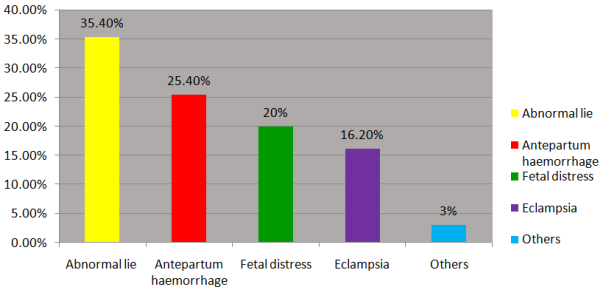

Figure No.4: What was the reason told by the doctor for C-section?

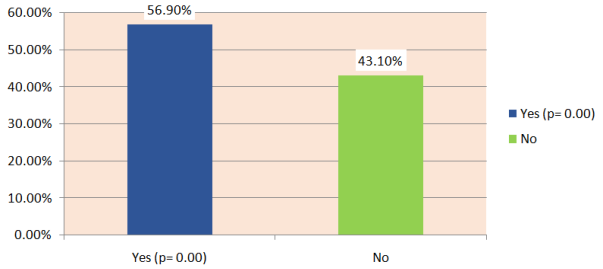

Figure No.5: Was there severe vaginal bleeding at any time of pregnancy?

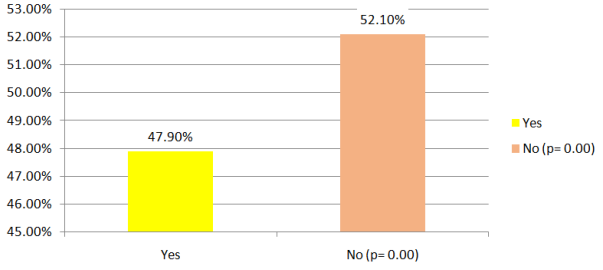

Figure No.6: Did your health worker inform you that position of your baby is abnormal?

DISCUSSION

Mal-presentation has been observed to be the leading cause of primary cesarean section in a multiparous woman. Here mal-presentation includes both an abnormal presentation- anything other than the back of the fetal head, and an abnormal lie- transverse or oblique lie.

The identification of mal-presentation as the most common cause of primary caesarean in a multipara is similar to studies done by Rao & Rampure[1] and Jacob & Bhargava[11]. Whereas, in another study, mal-presentation was ranked as the fourth most common cause[10]. Mal-presentation in a multiparous woman can be explained by the lordosis of the lumbar spine and the presence of a pendulous abdomen due to relaxed abdominal and uterine musculature. Additionally, in a multipara, engagement of the head usually doesn't take place before the onset of labour. Besides this, placental location is an important factor to the fetal presentation- it is known that placenta previa poses a significant risk to development of breech presentation and transverse lie, which could have been an underlying etiology in our study as 52.1% women were recorded to have a low-lying placenta. 47.7% women were informed about the abnormal positioning of the baby during the pregnancy. Consequently, 35.4% women were operated because of this reason whereas amongst the rest, either the head engaged at the time of labour or external cephalic version (ECV) was successful.

Antepartum hemorrhage (APH) ranked second as the most common cause of primary caesarean in multiparous woman. APH occurs secondary to placenta previa or placental abruption. One of the risk factors for placenta previa is multiparity, but age seems to play a greater role than parity[12]. Abruptio placentae is again more common in the multipara, being seen three times more often in those with parities greater than five, as opposed to primigravida[13].

Fetal distress was ranked as third most common cause of primary caesarean in multipara. The electronic fetal monitoring which is commonly used to detect fetal distress is known to have poor specificity resulting in increase in number of cesarean sections carried out for fetal distress[14,15]. It is considered prudent to perform a caesarean section rather than waiting and possibly endangering both mother and baby. In a study[12], it was found that 58% infants delivered via cesarean due to fetal distress were actually unaffected.

Pre-eclampsia was ranked as the fourth leading indication for primary caesarean in a multipara. Out of 130 women 96 were noted to be hypertensive during pregnancy, out of which 64 women had swelling on hands and face. Studies show that up to 22% of women with chronic hypertension and 50% of those with gestational hypertension eventually progress to preeclampsia[16, 17]. Preeclampsia if unchecked can lead to fits which is a potentially fatal situation for both mother and baby, hence, to avoid this, it is a common practice to deliver the baby as soon as it reaches term (37-42 weeks). However, active protection by thorough follow-ups is a very important element in prevention of preeclampsia[18].

According to WHO19 the minimum number of antenatal visits recommended are four, irrespective to the absence of any complications. A recent study in India showed that 68% women had not received any antenatal care[3]. Our study shows that 40.8% women

had only 1 antenatal visit, and 31.5% had 2 antenatal visits. In reality, only 19 out of 130 women actually visited 4 or more times. Thus lack of proper antenatal care could be the reason for the high number of hypertensive patients progressing to preeclampsia and moreover to a primary caesarean section.

Another point of interest noted was that 60.8% women had had previous instrumental vaginal deliveries. These women should be counseled that a previous instrumental delivery does not pose any risk of injury to the mother during subsequent delivery, but rather a vaginal delivery should be preferred as it prevents the complications of a caesarean section. In fact approximately 80% of women achieve a spontaneous vaginal delivery after an instrumental delivery[20,21,22] having heavier babies with very low overall rates of birth trauma or asphyxia[23].

According to a comparative study[2], multiparas are more prone to require caesarean section for mal-presentation and APH, whilst nulliparous more commonly required it for prolonged labour and cephalopelvic disproportion (CPD). Hence a cesarean section should not be disregarded just because a woman has had a previous vaginal delivery. Rather a multipara requires good antenatal care as it helps to detect threatening abnormalities that may have an adverse outcome.

CONCLUSION

Previous vaginal delivery gives the family and the doctors a false sense of security that overshadows the need for vigilant antenatal and intra-partum care. The method of previous deliveries shouldn't be the primary criteria upon which the current delivery is decided. Rather, every pregnancy should be treated with as much concern and care as the first. (The physicians should display obligation in such circumstances and assess the pregnancy thoroughly before heading towards a massive scheme. Rather than promoting the doctors' own interests and convenience, Mothers' health and wellbeing should be considered the first priority and every possible measures should be taken to ensure that. The antenatal care should be the utmost preference and necessary investigations should be practiced. WHO recommends a minimum of four antenatal visits, comprising interventions such as tetanus toxoid vaccination, screening and treatment for infections, and identification of warning signs during pregnancy? With all the adequate steps taken, the rate and reasons of cesarean sections could be monitored and restricted hence progressing to initiate a huge stride for maternal and fetal health.

Author's Contribution:

Concept & Design of Study:	Tafazzul H. Zaidi,
Drafting:	Tafazzul H. Zaidi
Data Analysis:	Kiran Mehtab, Tafazzul H. Zaidi,
Revisiting Critically:	Kiran Mehtab, Tafazzul H. Zaidi,
Final Approval of version:	Tafazzul H. Zaidi, Kiran Mehtab

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

REFERENCES

1. Rao JH, Rampure N. Study of Primary Caesarean Section in Multiparous Women. J Evol Med Dent Sci 2013;2(24):4414-4418.
2. Hamilton BE, Martin JA, Ventura SJ. Births: preliminary data for 2010. Natl Vital Stat Rep 2011;60(2):1-25.
3. Karim F, Ghazi A, Ali T, Aslam R, Afreen U, Farhat R. Trends and determinants of cesarean section. J Surg Pak 2011;16(1):22-7.
4. Althabe F, Belizan JF. Caesarean section: The paradox. The Lancet 2006;368:1472-3.
5. Ford J, Grewal J, Mikolajczyk R, Meikle S, Zhang J. Primary Cesarean among Parous Women in the United States, 1990-2003. Obstet Gynecol 2008; 112(6):1235-1241.
6. Khawaja NP, Yousaf T, Tayyeb R. Analysis of caesarean delivery at a tertiary care hospital in Pakistan. J Obstet Gynecol 2004;24:139 -141.
7. Solomon B. The dangerous multipara. Lancet. 1932;2:8-11.
8. Konar M, Sikdar K, Basak S, Lahiri D. Maternal mortality (ten years' survey in Eden Hospital). J Ind Med Assoc 1980;75(3):45-51.
9. Saluja JK, Roy PK, Mahadik K. Study of Primary Caesarean Section in Multiparous Women. NJIRM 2014;5(2):27-29
10. Desai E, Leuva H, Leuva B, Kanani M. A study of primary caesarean section in multipara. Int J Reprod Contracept Obstet Gynecol 2013;2(3): 320-324.
11. Jacob S, Bhargava H. Primary caesarean in multipara. J Obstet & Gyn Ind 1972;22(6): 642-50
12. Praagh IGV, Tovell HMM. Primary caesarean section in multipara. J Obstet Gynecol 1968;32(6): 813-24
13. Hibbard, J. Abruptio placentae preeclampsia and essential hypertension. J Obstet Gynaec Brit Comm 1962;69:282.
14. Shehata AI, Hashim TJ. Decrease in perinatal mortality and increase in caesarean section rates. Int J Gynecol Obstet 1995;48:261-267
15. Guihard P, Blondel B. Trends in risk factors for caesarean sections in France between 1981and 1995: lessons for reducing rates in the future. Bri J Obstet Gynaecol 2001;108:48-55
16. Chandiramani M, Shennan A. Hypertensive disorders of pregnancy: A UK-based perspective. Curr Opin Obstet Gynecol 2008;20:96-101.

17. Chappal LC, Enye ST, Seed P, Briley AL, Poston L, Shennan AH. Adverse perinatal outcomes and risk factors for preeclampsia in women with chronic hypertension: a prospective study. Hypertension 2008;51:1002-9.
18. Jasovic-Siveska E, Jasovic V, Stoilova S. Previous pregnancy history, parity, maternal age and risk of pregnancy induced hypertension. Bratisl Lek Listy 2011;112(4):188-91.
19. WHO. Provision of Effective Antenatal Care: Integrated Management of Pregnancy and Child Birth (IMPAC). Geneva, Switzerland: Standards for Maternal and Neonatal care (1.6), Department of Making Pregnancy Safer, World Health Organization; 2006.
20. Bahl R, Strachan B, Murphy DJ. Outcome of subsequent pregnancy three years after previous operative delivery in the second stage of labour: cohort study. BMJ 2004;328:311–4
21. Mawdsley SD, Baskett TF. Outcome of the next labour in women who had a vaginal delivery in their first pregnancy. BJOG 2000;107:932–4.
22. Bahl R, Strachan BK. Mode of delivery in the next pregnancy in women who had a vaginal delivery in their first pregnancy. J Obstet Gynaecol 2004; 24:272–3.
23. Kadar N, Romero R. Prognosis for future childbearing after mid-cavity instrumental deliveries in primigravidas. Obstet Gynecol 1983; 62:166-70.

Original Article

Quantification of Extended Spectrum β-Lactamase Producing Isolates among Gram Negative Bacteria in Hospitalized Patients with Blood Stream Infections

Muhammad Usman Anjum[1], Anjum Saeed[1], Surriya Yasmin[2] and Nazia Shams[1]

ABSTRACT

Objective: To quantify ESBL producing microorganisms among hospitalized patients with blood stream infections,
Study Design: Descriptive study
Place and Duration of Study: This study was conducted at the Department of Pathology, Frontier Medical College, Abbottabad from Jan 2016 to Dec 2016.
Materials and Methods: Bacterial isolates were recognized based on colony morphology and biochemical characteristics. Modified Kirby-Bauer method using Mueller Hinton agar was used to check for antibiotic sensitivity. ESBL producers were identified using double disc synergy test.
Results: Overall 152 samples yielded a growth of gram negative bacteria. Out of these 152 positive samples, 80% comprised of E. coli while 12% were K. pneumoniae, 05% were P. aeruginosa and 03% were P. mirabilus. The prevalence of ESBL producing bacteria was low, 1.97%. Most of them were observed in male patients as compared to female patients. Likewise, their incidence was similar among different age groups but there was no ESBL producing organism observed in patients who were less than 20 years of age. As per the site of involvement, ESBL producing bacteria were most commonly seen in specimens received from ICU followed by medical ward.
Conclusion: Infections caused by ESBL producing microorganisms are not uncommon in clinical practice. Detection of such bacteria is pivotal in both community and hospital acquired infections as rapid identification and characterization of such resistant bacteria will aid in minimizing the spread of these infections as well as in selecting appropriate antimicrobial therapy.
Key Words: ESBL, gram negative

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INTRODUCTION

β–lactam antibiotics are frequently used in the management of infectious diseases and therefore, emerging and increasing resistance to these drugs is common. Persistent exposure to β–lactam antibiotics has led to mutations and continued production of β–lactamases which has resulted in bacterial resistance to even newer groups of β–lactam antibiotics.[1,2] These enzymes have been labeled as extended spectrum β–lactamase (ESBL).

Infections with these ESBL producing microorganisms pose a new and significant risk in hospitalized patients globally. They lead to both hospital and community acquired infections and are associated with higher mortality.[3-5] The geographical distribution of such clinical isolates varies greatly depending on geography and institution. The prevalence of ESBL producing Enterobacteriaceae varies between 0 – 25% among different institutes in United States but the national average is 3%.[6] Similarly, ceftazidime resistance in K. pneumoniae isolates varies from 5% in non-intensive care unit to 10% in intensive care unit (ICU).[6] In Japan, there is a very low incidence of ESBL producing isolates among K. pneumoniae and E. coli where only 0.3% of K. pneumoniae and < 0.1% of E. coli isolates were ESBL positive.[7]

It is remarkable that certain specific ESBLs are solely present in certain geographical areas or regions. For example, infection with TEM-10 is quite new in Europe while it is responsible for many disparate outbreaks in United States for many years.[8-11] On the other hand, TEM-3 is found frequently in France but it is undetected in United States.[12] TEM refers to Temoniera who was a patient from Greece from whom this strain was first isolated.[13]

Indiscriminate and injudicious use of antibiotics especially broad spectrum cephalosporins is a major

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cause of emergence of ESBL producing microorganisms.[14] Duration of inpatient and specifically ICU stay, catheterization, mechanical ventilation and intubation, severity of disease and prior antibiotic use are few of the risk factors which are associated with the emergence of ESBLs.[6]

MATERIALS AND METHODS

This descriptive study was performed Department of Pathology, Frontier Medical & Dental College, Abbottabad from Jan 2016 to Dec 2016. Samples, received in the Pathology department for culture and sensitivity from hospitalized patients, were included. Bacterial isolates were recognized based on colony morphology and biochemical characteristics. Modified Kirby-Bauer method using Mueller Hinton agar was used to check for antibiotic sensitivity of the gram negative bacteria using a set of antibiotics comprising of imipenem, aztreonam, levofloxacin, amoxicillin with clavulanic acid, ceftazidime and cefoperazone with sulbactam. ESBL producers were identified using double disc synergy test as described by Jarlier et al.[15] Test organisms were swabbed on the surface of Mueller Hinton agar plate. A disc of amoxicillin and clavulanic acid (20µg and 10µg) was positioned in the center while cephalosporin (ceftriaxone, cefotaxime, and that of ceftazidime, 30µg each) and aztreonam (30µg) discs were placed around the central disc at a distance of 30mm. Extension of zone of inhibition around cephalosporin/aztreonam discs towards central disc were labeled as ESBL producers. E. coli ATCC 25922 was used as a negative while a recognized ESBL producer were used as positive control.[5]

RESULTS

Overall 152 samples yielded a growth of gram negative bacteria. Out of these 152 positive samples, 80% comprised of E. coli while 12% were K. pneumoniae, 05% were P. aeruginosa and 03% were P. mirabilus. The prevalence of ESBL producing bacteria was low, 1.97%. Most of them were observed in male patients as compared to female patients, Table 1.

Table No.1. Distribution of ESBL producing bacteria as per gender

Gender	Characteristics	Number	%age
Male	Total Isolates	97	63.82%
	ESBL Producing Isolates	02	1.31%
Female	Total Isolates	55	36.18%
	ESBL Producing Isolates	01	0.66%

Likewise, their incidence was similar among different age groups but there was no ESBL producing organism observed in patients who were less than 20 years of age, Table 2. As per the site of involvement, ESBL producing bacteria were most commonly seen in specimens received from ICU followed by medical ward, Table 3.

Table No.2: Incidence of ESBL producing bacteria among different age groups

Age, (in years)	Total Isolates	ESBL Producing Isolates
0 – 20	39, 25.66%	00, 00%
21 – 40	59, 38.82%	01, 0.65%
41 – 60	34, 22.37%	01, 0.66%
> 61	20, 13.15%	01, 0.66%
Total	152, 100%	03, 1.97%

Table No.3: Stratification of ESBL producing bacteria according to the site of isolation

Hospital Site	Total Isolates	ESBL Producing Isolates
ICU	68, 44.74%	02, 1.31%
Medical Ward	50, 32.89%	01, 0.66%
Surgical Ward	29, 19.08%	00, 00%
Gynecology Ward	05, 3.29%	00, 00%
Total	152, 100%	03, 1.97%

Both E. coli and K. pneumoniae were sensitive to imipenem and levofloxacin while E. coli showed moderate resistance to amoxicillin plus clavulanic acid and ceftazidime, Figure 1. P. aerugenosa was sensitive to most of the antibiotics. P. mirabilus was sensitive to levofloxacin and cefoperazone plus sulbactam while it showed moderate resistance to imipenem, aztreonam and amoxicillin plus clavulanic acid.

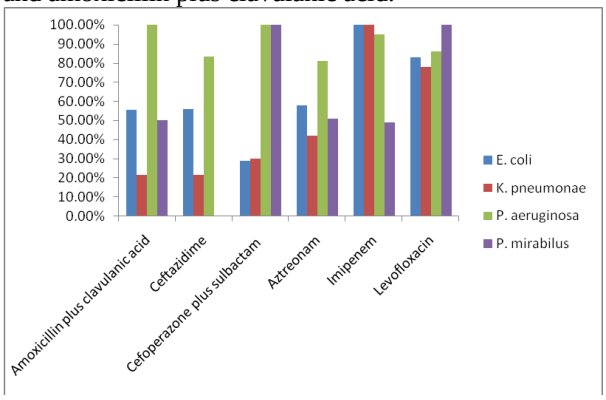

Figure No.1: Antibiotic sensitivity of gram negative bacteria

DISCUSSION

Resistance of infectious organisms to conventional antimicrobial drugs has become a global issue with serious consequences on the outcome of infectious diseases. Misuse or overuse of antibiotics has played a major role in acquiring this resistance to antibiotics.[2] There is a very high risk of treatment failure in patients who have acquired infections, which were caused by ESBL positive organisms, when given extended

spectrum β–lactam antibiotics. Thus, all microorganisms which were established for ESBL production should be reported as resistant to all extended spectrum β–lactam antibiotics irrespective of their antibiotic susceptibility test outcomes.[16]

The prevalence of ESBL producing bacteria was low (1.97%) in our study. Similarly, Gray et al have also reported a very low (0.7%) rate of ESBL positive bacteria in their study which was conducted in Malawi.[17] Likewise, only 3.8% of blood isolates in patients from Dakar, Senegal, were ESBL producing microorganisms.[18] Correspondingly, the rate of ESBL was 6% in Saudi Arabia according to Khanfar et al whereas 15.4% of these were detected among hospitalized patients while 4.5% were detected in out-patients.[19] But, on the other hand, the prevalence of ESBL positive bacteria was found to be 10-25% in Southern Europe while it was reported to be 25.8% amongst E. coli and K. pneumoniae isolates in Eastern Europe.[20, 21] The variable rate of ESBL producing microorganisms, being lower in low income counties and higher in higher income countries, could be due to the fact that poor quality or higher cost of antibiotic drugs in developing countries while their overuse in developed counties could lead to this discrepancy in results.[21]

The prevalence of E. coli was higher (80%) in our study. Khanfar et al also reported that majority (83%) of their isolates comprised of E. coli. [19] Likewise, most of the isolates were E. coli in a study conducted by Al-Zarouni et al in UAE.[22]

Knowledge of regional resistance patterns of pathogens, timely initiation of appropriate empirical antimicrobial therapy and strict enforcement of infection control measures could help not only to contain this emerging problem of antimicrobial resistance among microorganisms but also provide a cost effective way of reducing economic burden related to such infections, through prevention, on already over-burdened health system especially in developing countries.

CONCLUSION

Infections caused by ESBL producing microorganisms are not uncommon in clinical practice. Detection of such bacteria is pivotal in both community and hospital acquired infections as rapid identification and characterization of such resistant bacteria will aid in minimizing the spread of these infections as well as in selecting appropriate antimicrobial therapy.

Author's Contribution:

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Data Analysis:	Surriya Yasmin, Nazia Shams
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REFERENCES

1. Pitout JD, Laupland KB. Extended-spectrum beta-lactamase-producing Enterobacteriaceae: an emerging public-health concern. The Lancet Infect Dis 2008;8(3):159-66.
2. Shaikh S, Fatima J, Shakil S, Rizvi SMD, Kamal MA. Antibiotic resistance and extended spectrum beta-lactamases: Types, epidemiology and treatment. Saudi J Biological Sci 2015;22(1): 90-101.
3. Fennell J, Vellinga A, Hanahoe B, Morris D, Boyle F, Higgins F, et al. Increasing prevalence of ESBL production among Irish clinical Enterobacteriaceae from 2004 to 2008: an observational study. BMC Infect Dis 2012;12:116.
4. Kim B, Kim J, Seo MR, Wie SH, Cho YK, Lim SK, et al. Clinical characteristics of community-acquired acute pyelonephritis caused by ESBL-producing pathogens in South Korea. Infection 2013;41(3):603-12.
5. Sood S, Gupta R. Antibiotic Resistance Pattern of Community Acquired Uropathogens at a Tertiary Care Hospital in Jaipur, Rajasthan. Ind J Comm Med: Official Publication of Ind Assoc Prevent Soc Med 2012;37(1):39-44.
6. Bradford PA. Extended-Spectrum β-Lactamases in the 21st Century: Characterization, Epidemiology, and Detection of This Important Resistance Threat. Clinical Microbiol Reviews 2001;14(4):933-51.
7. Yagi T, Kurokawa H, Shibata N, Shibayama K, Arakawa Y. A preliminary survey of extended-spectrum beta-lactamases (ESBLs) in clinical isolates of Klebsiella pneumoniae and Escherichia coli in Japan. FEMS Microbiol letters 2000;184(1):53-6.
8. Barroso H, Freitas-Vieira A, Lito LM, Cristino JM, Salgado MJ, Neto HF, et al. Survey of Klebsiella pneumoniae producing extended-spectrum beta-lactamases at a Portuguese hospital: TEM-10 as the endemic enzyme. J Antimicrobial Chemotherap 2000;45(5):611-6.
9. Bradford PA, Cherubin CE, Idemyor V, Rasmussen BA, Bush K. Multiply resistant Klebsiella pneumoniae strains from two Chicago hospitals: identification of the extended-spectrum TEM-12 and TEM-10 ceftazidime-hydrolyzing beta-lactamases in a single isolate. Antimicrobial agents and chemotherapy 1994;38(4):761-6.
10. Liu PY, Gur D, Hall LM, Livermore DM. Survey of the prevalence of beta-lactamases amongst 1000

gram-negative bacilli isolated consecutively at the Royal London Hospital. J Antimicrobial Chemotherap 1992;30(4):429-47.

11. Naumovski L, Quinn JP, Miyashiro D, Patel M, Bush K, Singer SB, et al. Outbreak of ceftazidime resistance due to a novel extended-spectrum beta-lactamase in isolates from cancer patients. Antimicrobial agents and Chemotherap 1992;36(9):1991-6.
12. Nordmann P. Trends in β-lactam resistance among Enterobacteriaceae. Clin Infect Dis 1998;27 (Supplement_1):S100-S6.
13. Rawat D, Nair D. Extended-spectrum beta-lactamases in Gram Negative Bacteria. J Global Infect Dis 2010;2(3):263-74.
14. Rice LB. Successful interventions for gram-negative resistance to extended-spectrum β-lactam antibiotics. Pharmacotherapy: J Human Pharmacol Drug Therap 1999;19(8P2):120S-8S.
15. Jarlier V, Nicolas MH, Fournier G, Philippon A. Extended broad-spectrum beta-lactamases conferring transferable resistance to newer beta-lactam agents in Enterobacteriaceae: hospital prevalence and susceptibility patterns. Reviews of Infect Dis 1988;10(4):867-78.
16. National Committee for Clinical Laboratory Standards. Methods for dilution antimicrobial susceptibility tests for bacteria that grow aerobically. Approved standard M7–A5 and informational supplement M100–S10. National Committee for Clinical Laboratory Standards, Wayne, PA; 2000.
17. Gray KJ, Wilson LK, Phiri A, Corkill JE, French N, Hart CA. Identification and characterization of ceftriaxone resistance and extended-spectrum β-lactamases in Malawian bacteraemic Enterobacteriaceae. J Antimicrobial Chemotherap 2006;57(4):661-5.
18. Sire JM, Nabeth P, Perrier-Gros-Claude JD, Bahsoun I, Siby T, Macondo EA, et al. Antimicrobial resistance in outpatient Escherichia coli urinary isolates in Dakar, Senegal. J Infect Develop Countries 2007;1(3):263-8.
19. Khanfar HS, Bindayna KM, Senok AC, Botta GA. Extended spectrum beta-lactamases (ESBL) in Escherichia coli and Klebsiella pneumoniae: trends in the hospital and community settings. J Infect Develop Countries 2009;3(4):295-9.
20. Balode A, Punda-Polic V, Dowzicky MJ. Antimicrobial susceptibility of gram-negative and gram-positive bacteria collected from countries in Eastern Europe: results from the Tigecycline Evaluation and Surveillance Trial (T.E.S.T.) 2004-2010. Int J Antimicrobial Agents 2013;41(6): 527-35.
21. Tansarli GS, Poulikakos P, Kapaskelis A, Falagas ME. Proportion of extended-spectrum β-lactamase (ESBL)-producing isolates among Enterobacteriaceae in Africa: evaluation of the evidence—systematic review. J Antimicrobial Chemotherap 2014;69(5):1177-84.
22. Al-Zarouni M, Senok A, Rashid F, Al-Jesmi SM, Panigrahi D. Prevalence and antimicrobial susceptibility pattern of extended-spectrum beta-lactamase-producing Enterobacteriaceae in the United Arab Emirates. Medical principles and practice: Int J Kuwait Univ, Health Sci Centre 2008;17(1):32-6.

Original Article

Treatment of Large Proximal Ureteral Stone

Comparison the Efficacy of Extracorporeal Shock Wave Lithotripsy, Ureterolithotripsy and Laproscopic Ureterolithotomy in Treatment of Large Proximal Ureteral Stone

Sultan Mohammad Tareen and Abdul Razaque Nasir

ABSTRACT

Objective: To determine the usefulness of extracorporeal shock wave lithotripsy, ureterolithotripsy and laproscopic ureterolithotomy in treatment of large proximal ureteral stone.

Study Design: Comparative/prospective study

Place and Duration of Study: This study was conducted at the Department of Urology, Bolan Medical Complex Hospital, Quetta from 1st January 2018 to 30th June 2018.

Materials and Methods: In this study, 62 patients of both genders having large proximal stones >1cm in ureters were included. Patient's ages were ranging from 25 to 50 years. Patient's detailed history including age, sex and socio-economic status was examined. All patients had undergone extracorporeal shock wave lithotripsy, ureterolithotripsy and laproscopic ureterolithotomy treatment.

Results: There were 35 (56.45%) patients were men while 43.55% were women. 27 (43.55%) patients were aged between 25 to 35 years, 25 (40.32%) patients were ages between 35 to 45 years while remaining 16.13% were ages >45 years. 40 (64.52%) patients had urban area residency.25 patients had undergone treatment with shock wave lithotripsy, 20 patients had ureterolithotripsy and 17 patients were treated with laproscopic lithotomy treatment. Highest successful rate in stone clearance was resulted in patients whom had treated with laproscopic ureterolithotomy as 94.12%.

Conclusion: It is concluded that, the patients whom had treated with laproscopic ureterolithotomy was a highest success rate in clearance of stone. Laproscopic lithotomy shows better result than the other techniques.

Key Words: Extracoporeal shock wave lithotripsy, Ureterolthotripsy, Laproscopic ureterolithotomy, Large proximal stone

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INTRODUCTION

Worldwide, ureteral stone is commonly found in people and it causes acute pain and may lead to hydronephrosis and urinary tract infection. Ureteral stone may also the main cause of renal failure. Small size ureteral stone (<1 cm) is usually pass through the ureter into the bladder, but large proximal stones (>1cm) can take more than two to three weeks to release from the ureters from the bladder.[1] In very serious or bad condition the large stones in the uretus required surgical treatment for removal from the ureters.

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Medical expulsive therapy using alpha blockers and calcium channel blocker have been used for multiple years for the treatment of effected patients with ureteral stones, and that was resulted a highest stone clearance rate as compared to placebo.[2] Nevertheless, a current multicentre placebo control trialed examination resulted different benefits about the position of medical expulsive treatment.[3]

Surgical treatment is the better alternative treatment for removal of large proximal stones from the ureters. Moreover, it is controversial that which technique or method is best for the treatment of large proximal stones, some of researches shows that ureteroscopic treatment is more successful than the others.[4] American urological association and European urological association have advocated ureterolithotripsy and shock wave lithotripsy (SWL) as a first alternative treatment for the large proximal ureteral stone and in severe condition may treated with laproscopic uretero-lithotripsy method. In developing coutries, the success rate by ureterolithotripsy (URS) is high as compared to shockwave lthotripsy and mostly patients were treated with ureterolithotripsy for extraction of large stones.[5]

In our settings ureteroscopy is not commonly available, semi rigid and rigid ureterolithotripsy has been applied for treatment of large proximal stones. Percutaneous nephrolithotomy may cause the multiple surgical complications but laproscopic lithrotomy technique for treatment of large stone resulted less complications and high successful rate in clearance of stones from the ureter.[6]

Several studies have been conducted for examine the efficacy of laproscopic lithotomy and ureterolithotripsy in treatment of large proximal ureteral stones and resulted that laproscopic lithotomy is more efficient and results oriented as compared to URS.[7,8] Fang et al[9] reported that the clearance rate of stones from the ureters is high in LAP and was resulted LAP 100%, 88% URS.

MATERIALS AND METHODS

This comparative/prospective study was conducted at Department of Urology, Bolan Medical Complex Hospital, Quetta from 1st January 2018 to 30th June 2018. Sixty two patients of both genders having large proximal stones >1cm in ureters were included. Patient's ages were ranging from 25 to 50 years and patient's detailed history including age, sex and socio-economic status was examined. Patients having pregnancy, previous open surgery, ureteral stone with renal failure were excluded from the study. All patients had undergone extracorporeal shock wave lithotripsy, ureterolithotripsy and laproscopic ureterolithotomy treatment. All the data was analyzed by computer software SPSS 17.0.

RESULTS

Out of all 62 patients, 35 (56.45%) patients were men while 43.55% were women. 27 (43.55%) patients were aged between 25 to 35 years, 25 (40.32%) patients were ages between 35 to 45 years while remaining 16.13% were ages >45 years. 40 (64.52%) patients had urban area residency.25 patients had undergone treatment with shock wave lithotripsy, 20 patients had ureterolithotripsy and 17 patients were treated with laproscopic lithotomy treatment. 35 (56.45%) patients had found stone size 1.2 cm to 1.8cm and 27 (43.55%) patients had found >1.8cm (Tables 1-2).

Causes observed in patients as severe pain, hematuria, hydrenopherosis, previous stone treatment and family history of stone disease as 56/62 (90.32%), 37/62 (59.68%), 6/62 (9.68%), 5/62 (8.06%) and 10/62 (16.13%) respectively. Treatment duration mean time (minutes) were noted in all three procedures SWL, URS and LAP UL as 42.9±3.2, 71.2±4.9 and 137±2.7 respectively. 10 (40%) patients had overall stone removal whom treated with SWL, 11 (55%) found by URS and 94.12% (16) had overall stone removal whom treated with laproscopic ureterolithotomy. Highest successful rate in stone clearance was resulted in patients whom had treated with laproscopic ureterolithotomy as 94.12%. Forty five (72.58%) patients had length of hospital stay was < 1 day and 17 (27.42%) had hospital stay was 1 or more than 1 day after treated with SWL, URS and laproscopic ureterolithotomy procedure. Mean post operative pain on visual scale was noted as 1.4±0.9, 1.7±0.89 and 1.2±0.7 in SWL, URS and LAP UL. Opoid requirement was found in 1 (4%) patients in SWL group, 6(30%) patients in URS group and 9 (52.94%) patients required opoid treatment whom treated with laproscopic ureterolithotomy. We observed voiding symptoms in 10 (40%) patients in SWL group, 11(55%) in URS group and 8 (47.05%) found in laproscopic ureterolithotomy group. Patients' satisfaction rate was high in patients whom treated with URS and laproscopic ureterolithotomy as 90% and 88.23% (Tables 3-5).

Table No.1: Age, gender and residency wise distribution of patients

Characteristics	No.	%
Gender		
Male	35	56.45
Female	27	43.55
Age (years)		
25 -35	27	43.55
35 – 45	25	40.32
> 45	10	16.13
Residency		
Urban	40	64.52
Rural	22	35.48

Table No.2: Distribution of patients in treatment procedures

Procedure	No.	%
Extracorporeal shock wave lithotripsy	25	40.32
Ureterolithotripsy	20	32.25
Laproscopic ureterolithotomy	17	27.41

Table No. 3: Stone size findings

Stone size (cm)	No.	%
1.2 to 1.8	35	56.45
>1.8	27	43.55

Table No.4: Clinical examination of the patients

Treatments	Severe Pain	Hematuria	Hydronephrosis	Stone Treated History	Stone disorder in family
Shock wave lithotripsy (n=25)	18	10	2	0	4
Ureterolitho-tripsy (n=20)	22	15	2	3	2
Laproscopic ureterolitho-tomy (n=17)	16	12	2	2	4
Total (%age)	56 (90.32)	37 (59.68)	6 (9.68)	5 (8.06)	10 (16.13)

Table No.5: Findings of procedures

Findings	Shock wave lithotripsy (n=25)	Ureteroli-thotripsy (n=20)	Laprosc-opic uretero-lithotomy (n=17)
Mean time (minutes)	42.9±3.2	71.2±4.9	137±2.7
Stone removal	10 (40%)	11 (55%)	16 (94.12%)
Mean post operative pain on visual scale	1.4±0.9	1.7±0.89	1.2±0.7
Opoid requirement	1 (4%)	6(30%)	9 (52.94%)
Voiding symptoms	10 (40%)	11(55%)	8 (47.05%)

DISCUSSION

Ureteral stone is one of the most commonly found disorder in urological departments. Gradually technical advances have modified the treatment of upper urinary tract stones. Surgical treatment is the better alternative treatment for removal of large proximal stones from the ureters. Moreover, it is controversial that which technique or method is best for the treatment of large proximal stones, some of researches shows that ureteroscopic treatment is more successful than the others.[4] The main drawback of shock wave lithotripsy are long duration time for treatment and it requires auxiliary method.

Rigid ureterolithotripsy is safe and effective treatment procedure for large proximal ureteral stone and same as resulted in this research.[10] Some of studies shows that ureterolithotripsy procedure for treatment of removal of stone has high rate in clearance of stone as compared to ESW[11] and that findings was same as in our research that stone removal ratio was 55% and 40%. Another study conducted by Cut et al[11] also reported that URS and ESWL treatments have better advantages with no major difference in complications rate. Many of studies regarding ureteral stones resulted that stones observed at upper urinary tract may lead to severe complications.[12] The most common and severe complications found in URS treatment procedure is ureters avolution and perforation and studies shows that the incidence rate 0 to 1%.[13]

In our study, 35 (56.45%) patients were men while 43.55% were women. These results shows similarity to the some other study conducted by Asif et al in which the male ratio was high as compared to females.[14] Twenty seven (43.55%) patients were aged between 25 to 35 years, 25 (40.32%) patients were ages between 35 to 45 years while remaining 16.13% were ages >45 years. In this study we observed highest success rate was achived from laproscopic ureterolithotomy as 94.12% as compared to ESWL and URS procedure and some of studies shows the high rate of success resulted from URS as compared to ESWL and these results shows similarity to our study in which URS success rate in clearance of stone was 55% and in ESWL that was 40%.[15,16]

In the present study, we observed treatment duration mean time (minutes) were noted in all three procedures SWL, URS and laproscopic ureterolithotomy as 42.9±3.2, 71.2±4.9 and 137±2.7 respectively. Highest successful rate in stone clearance was resulted in patients whom had treated with laproscopic ureterolithotomy as 94.12%, these results showed similarity to some other studies in which time duration for treatment is high in laproscopic ureterolithotomy procedure.[17] Laproscopic ureterolithotomy procedure is best in treatment of those patients having complex and severe condition of stones.[18] We observed that 45 (72.58%) patients had length of hospital stay was < 1 day and 17 (27.42%) had hospital stay was 1 or more than 1 day after treated with SWL, URS and laproscopic ureterolithotomy procedure.

We also observed that, patients satisfaction rate was high in patients whom treated with URS and laproscopic ureterolithotomy as 90% and 88.23% , some other studies shows similarity to our results.[19] We observed voiding symptoms in 10 (40%) patients in SWL group, 11 (55%) in URS group and 8 (47.05%) found in laproscopic ureterolithotomy group and these results showed a bit similarity to some other studies conducted regarding treatment of large proximal stones.[20]

In our study the accuracy rate is better than the other procedures. Moreover, it is not a sufficient research due to small number of patients and many other conditions, we should have to do more work for better treatment and to reduce the mortality and morbidity and also to reduce the mortality and morbidity rate.

CONCLUSION

Treatment for large proximal ureteral stones acquired several treatment laps for removal of stones from the ureters. We concluded that the patients whom had treated with laproscopic ureterolithotomy were a highest success rate in clearance of stone. Laproscopic lithotomy shows better result than the other techniques, but with many of disadvantages in which increase in length of stay in hospital, very expensive than the other procedure and more time consuming. We should have to do more work for better treatment of this cure.

Author's Contribution:

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Data Analysis:	Abdul Razaque Nasir
Revisiting Critically:	Sultan Mohammad Tareen

Final Approval of version:	Sultan Mohammad Tareen

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REFERENCES

1. Eisner BH, Goldfarb DS, Pareek G, Pharmacologic treatment of kidney stone disease. Urol Clin North Am 2013;40:21-30.
2. Campschroer T, Zhu Y, Dujvesz D, Grobbee DE, Lock MT, Alpha blockers as medical expulsive therapy for ureteral stones. Cochrane Database Syst Rev 2014;4:CD008509.
3. Pickard R, Starr K, McLennan G, Lam T, Thomas R, et al. Medical expulsive therapy in adults with ureteric colic; a multicentre, randomized placebo controlled trial. Lancet 2015;386:341-9.
4. Bader MJ, Eisner B, Porpilia F, Preminger GM, Tiselius HG, Contemporary management of ureteral stones. EUR Urol 2012:61:764-72.
5. Marchini GS, Mello MF, Levy R, Vicentini FC, Torriceli FC, Eluf-Neto J, et al. Contemporary trends of Inpatient Surgical Management of stone disease; National Analysis in an Economic growth Scenario. J Endourol 2015;61:764-72.
6. Simforoosh N, Aminisharifi A. Laproscopic management in stone disease. Curr Opin Urol 2013;23:169-742.
7. Kumar A, Vasudeva P, Nanda B, Kumar N, Jha SK, Singh H, A prospective randomized comparison between laproscopic ureterolithotomy and semi rigid ureteroscopy for upper ureteral stones >2cm; A single center Experience. J Endourol 2015;29:47-51.
8. Ko YH, Kang SG, Park JY, Bae JH, Kang SH, Cho DY, et al. Laproscopic ureterolithotomy as a primary modality for large proximal ureteral calculi: Comparison to rigid ureteroscopic pneumatic lithotripsy. J Laproendosc Adv Surg Tech A 2011;21:7-13..
9. Kumar A, et al. A prospective randomized comparisom between SWL and semirigid ureteroscopy for upper ureteral stones <2cm:a single centre experience. J Endourol 2015;29: 47-51.
10. Zhang J, et al. Cost-effectiveness analysis of ureteroscopic laser lithotripsy and shockwave lithotripsy in the management of ureteral calculi in eastern china. Urol Int 2011;86:470-475.
11. Cui H, et al. Efficacy of the lithotripsy in treating lower pole renal stones. Urolithiasis 2013;41:231-234.
12. Lee SH, Kim TH, Myung SC, et al. Effectiveness of Flexible Ureteroscopic Stone Removal for treating Ureteral and ipsilateral Renal Stones: A Single-Centre Experience. Korean J Urol 2013; 54:377-82.
13. Matlaga B, Janren J, Meckely L. Economic outcomes of treatment for ureteral and renal stones: A systemic literature review. J Urol 2012; 188:449-454.
14. Asif IM, Abid H,et al . Treatment of large proximal stones: Extracoporeal shock wave, ureterolithotripsy, Laproscopic lithotomy 2017: 28(12):72-75.
15. Singh V, Sinnha RJ, Gupta DK, Kumar M, Akjtar A. Transperitoneal versus retroperitoneal laparoscopic ureterolithotomy: a prospective randomized comparison study. J Urol 2013:189: 940-5.
16. Zhou X, Ang G, Zhou R, Shi Z, Han C. Assessment of suitsbility of retroperitoneal laproscopic ureterolithotomy as a treatment for laproscopic ureterolithotomy as a treatment for complex proximal ureteral calculi. Minerva Urol Nefral 2014;66(4):213-6.
17. Aboumarzou OM, Kata SG, Keelay FX< Mc Clinton S, Nabia G, Exracrorporeal Shock wave lithotripsy (ESWL) versus ureteroscopic management for ureteric calculi. Cochrane Database Sys Rev 2012;5:CD006029.
18. Philppou P, Payne D, Davenport K, et al. Does previous failed ESWL have a negative impact on the outcome of ureteroscopy? A matched pair analysis. Urolithiasis 2013;41:531-8.
19. Doizi S, et al. Comparative study of the treatment of renal stones with flexible ureteroscopy in normal weight, obese and morbid obsess patients. Urol 2015;85:38-44.
20. Bosiol A, et al. A linkert analysis about double j stent related urinay aymptoms Questionnario (USSQ) after semirigid and flexible ureteroscopy. Eur Urol Suppl 2017;169(3);e398.

Original Article

Comparison of Mean Duration of Drain Removal in Quilting VS Non Quilting Wound Closure in Modified Radical Mastectomy

Afsheen Javaid, Nadeem Khurshaidi, Zahid Habib and Rufina Soomro

ABSTRACT

Objective: To compare mean time for drain removal with quilting and non-quilting wound closure techniques in modified radical mastectomy.

Study Design: Single-centered prospective randomized control study

Place and Duration of Study: This study was conducted at the Department of General Surgery, Liaquat National Hospital, Karachi Study duration lasted for 1 year from April 2016 to March 2017.

Materials and Methods: All patients who had a Modified radical mastectomy during this period were included in this study. Total 72 patients were included. 36 Patients were enrolled either in Group-A (quilting) or in Group-B (no quilting). Quilting was done in group-A. 2 Radevuac drains (flap drain & axillary drain) were placed in both groups. drains were removed when total drain output was 20cc or less per day. Final outcome was measured in term of total days of drain removal. Descriptive statistics were calculated. Stratification was done. Post stratification t test was applied. P-value ≤0.05 was considered as significant.

Results: Mean duration of flap drain removal in group-A was 8.52±5.15 days and 10.41±4.23 days in group-B. Mean duration of axillary drain removal in group-A was 12.91±5.54 days and 17.55±7.19 days in group-B. Mean total duration of drain removal was 14.63±5.09 days in group-A and 18.38±6.36 days in group-B. This mean difference of total duration of drain removal was found significant.

Conclusion: Quilting is an efficient method to significantly reduce the duration and volume of wound drainage.

Key Words: Drain Removal Time, Quilting, Non Quilting, Modified Radical Mastectomy.

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INTRODUCTION

Seroma is collection of serous fluid in dead space between subcutaneous flap and chest wall. This is one of most common and nauseate side effect of breast cancer surgery[1], with an unknown etiology. Incidence rate varies between 25 to 65 %[2] in mastectomy and axillary clearance and even some studies up to 85 %[3] despite of multiple trial of difficult techniques to reduce this morbidity like drains of various types, adhesives etc have been used. Though not life threatening but this bothersome complication has both physical, psychological as well as financial burden on patient. It is associated with pain, heaviness at surgical site ,swelling and morbidity of wound site infection and wound dehiscence[4].

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This all leads to multiple hospital outpatient clinic visits, delayed recovery time and delayed adjuvant treatments.[5]

Adjuvant treatment for breast cancer after most common procedure of modified radical mastectomy has significant role if given on time. Seroma and its effects i.e. prolong drain in place, delayed wound healing, secondary surgical site infection and pressure effect leading to flap necrosis is a commonest hurdle in start of adjuvant treatment.[6]

Multiple efforts yet not able to get exact pathogenesis of seroma. Common consideration is tissue acute inflammatory response secondarily to surgical assault[5,6.] Different theories were given for its etiology like Orteli[(7)] et al believed that it's due to fibrinolytic reaction, Petrek et al[(8)] purposed number and extent of axillary lymph node dissection as a causative factor, Hashemi et al [(9)]thought nature of surgery as a major factor. Mastectomy with axillary clearance has more rate of seroma production rather breast conservative surgery. But none of hypothesis is established as a known primary factor.

Due to unknown etiology different medical and surgical techniques were adopted to reduce this morbidity including use of steroids locally, chemical substances thromboxane, tranexamic acid and fibrin, use of

seclerosent agent and octreotide. No technique has been rewarding and so could not adopted as a routine practice[10].

Mechanical closure of dead space has been used in various areas by the Plastic Surgeons. The search of the method to decrease the dead space between skin and pectoralis major muscle gave an idea of a surgical technique modification for wound closure by mechanical closure of dead space, which showed significant reduction in time duration of drain removal, decrease repeated needle aspiration and decreased surgical site infection[11,12] this include subcutaneous fixation of tissue with underlying muscle causing close approximation of space known as Quilting. Since patients want to have drain removed early and we also want to avoid residual seroma formation to decrease physical and psychological disturbance in the patients.

There is no reliable data available in our country, this study was done to see the effectiveness of this quilting technique in post mastectomy patients.

MATERIALS AND METHODS

This was a single-centered prospective randomized control study over a 1-year period was conducted at department of general surgery Liaquat national hospital, Karachi from April 2016 to March 2017. The non-probability consecutive sampling was used for sampling. By taking mean and standard deviation in group 1 (9 ± 3)[11] days and in group 2 (11 ± 3)days[11], power of study 80% than at least a sample of 36 in each group will be required. The total sample size will be 72 patients.

Total 72 patients were included. 36 Patients were enrolled either in Group-A (Quilting) or in Group-B (non Quilting). An informed consent was taken prior to induction in the study.

Patients selected for this study were who has Primary breast cancer up to stage III, planned for a mastectomy with axillary dissection with Nodal status N1(clinically palpable mobile axillary nodes) or mastectomy with sentinel node biopsy and axillary clearance . Patients with Age group between 35-65 years, ASA 1 and ASA 2 with BMI<35Kg/m^2 were included in study. Patients BMI >35Kg/m^2,ASA 3 &4 ,Prior breast surgery ,Post neo-adjuvant patients , Stage 4 diseased patients , N2 & N3 nodal status (fixed axillary and supraclavicular node respectively) .On histology greater than 10 axillary lymph node positive for metastasis and pregnant patients were excluded from study.

Modified Radical Mastectomy was the surgical procedure for carcinoma breast involving both breast removal along with axillary clearance. Quilting was done as a surgical method to approximate skin flaps with underlying tissues with interruptible absorbable sutures in multiple layers.

Drains were removed when drain out was 20 ml or less in the last 24 hours. Duration of drain removal was noted as total number of days required to remove both drains

Mastectomy with axillary clearance was performed by consultant (with 20 years of experience) in breast surgery. Each patient enrolled in the study was eligible to be enrolled into either arm of the study following the opening of a sealed envelope which had a slip bearing the name of procedure (quilting or not) to be done. Quilting was done by suturing skin flaps with under lying muscle (pectoralis major) with interrupted vicryl 2/0 from cranial to caudal end of wound with 3cm between them, totaling some 3-5 rows for superior flap. Inferior flap was quilted with 1-3 rows from caudal to cranial fashion. In the Control group only simple wound closure by approximating flap with vicryl 2/0 and then skin closure. 2 Radevuac drains (flap drain & axillary drain were placed in both groups. Patient was followed post-operatively on every 3rd day until both drains were removed. Patient and one responsible attendant was taught to mark drain once in 24 hours with date. In case any patient forgot to mark drain then drain output from last OPD visit was measured and divided by number of days to get mean drain output of last 3 days. Results was compared on the basis of mean ml of drain output in total days. Drain was removed when the drain output was 20ml or less in 24 hrs. Final outcome was measured in term of total days, was calculated when both flap and axillary drain were removed. Group having less drain output in both drains and early drain removal showed better surgical technique.

Patients were divided in two groups, Group A (quilting) and Group B (non-quilting). Descriptive statistics were calculated using SPSS version 21. Qualitative variables were presented in terms of frequency and percentages. Quantitative variables were presented in term of mean and standard deviations. T test was applied to compare the mean duration of drain removal in two study groups. Stratification was done to see the effect of modifiers on outcome. Post stratification t-test was applied. P-value ≤ 0.05 was considered as significant.

RESULTS

Total 72 female patients with age between 35 to 65 years, who met the inclusion criteria were included in the study to compare mean time for drain removal with quilting and non-quilting wound closure techniques in modified radical mastectomy. Patients were divided in two groups, Group A (quilting) and Group B (non-quilting). 36 patients were included in each group.

The mean age of study subjects in Group A was 49.63±8.60 years while mean age in Group B was 51.41±9.79 years. The mean BMI for study subjects in group A was 25.30±3.70 kg/m^2 while mean BMI for study subjects in group B was 25.45±3.72 kg/m^2. Stratification was done to see the effect of modifiers on outcome. The mean duration of carcinoma in group A was 6.05±7.83 months while in group B it was

34.33±5.90 months. Most of the study subjects were found with T2 stage in both groups while ASA-II was also found most common.

The mean duration of flap drain removal in group A was 8.52±5.15 days while for group B it was 10.41±4.23 days. The mean duration of axillary drain removal for study subjects in group A was 12.91±5.54 days while in group B it was 17.55±7.19 days. In our study mean total duration of drain removal was 14.63±5.09 days in group A while in group B it was 18.38±6.36 days. Comparison of mean was done through t-test. P-value < 0.05 was taken as significance. The results showed that there was significant mean difference of total duration of drain removal in study groups (p=0.007). Stratification with respect to age, ASA status, BMI, stage and duration of carcinoma was done to control the effect of these factors on outcome (total duration of drain removal) among two study groups. Significant mean difference of total duration of drain removal in study groups for patients age>50 years (p=0.007), patients with ASA-II (p=0.037), patients with BMI≥25 kg/m^2 (p=0.040) and duration of carcinoma≤3 months (p=0.013) was observed.

Post stratification t-test was applied. P-value ≤ 0.05 was considered as significant.

Table No.1: Descriptive statics of parameters Age,BMI , duration Of cancer , ASA

Parameters		Mean ± SD	Median	Range	Minimum	Maximum
Age (years)	Group A (n =36)	49.63 ±8.60	50	30	35	65
	Group B	51.41 ±9.79	52.00	30	35	65
BMI Kg/m	Group A	25.30±3.70	25.30	13.20	18.60	31.80
	Group B	25.45±3.72	26.00	12.80	19	31.80
Duration of cancer (months)	Group A	6.05± 7.83	7.83	35	1	36
	Group B	4.33±5.90	2.00	23	1	24
duration of removal of flap drain (Days)	Group A	8.52 ± 5.15	7.50	23	2	25
	Group B	10.41±4.23	10.00	17	3	20
Duration for removal of axillary drain (Days)	Group A	12.91±5.54	11.50	24	3	27
	Group B	17.55±7.11	17.00	25	3	28
Mean total duration of drain removal	Group A	14.63±5.09		18	9	27
	Group B	18.38±6.36	18	20	8	28

RESULTS

Mean of total duration of drain removal		Mean	Median	Range	minimum	maximum	p-value ≤ 0.05* significant
In patients with ASA-I (n=44)	Group A	14.12±4.93	13.00	18	9	27	0.208**
	Group B	16.31±6.08	15.00	19	9	28	not significant
In patients with ASA-II (n=28)	Group A	15.81±5.51	15.00	17	9	26	0.037*
	Group B	20.07±6.00	22.00	19	8	27	significant
In patients with age <50 years (n=37)	Group A	14.25±5.25	12.50	18	9	27	0.349**
	Group B	16.00±5.96	16.00	19	8	27	Not significant
In patients with age >50 years (n=35)	Group A	15.12±5.03	14.00	15	10	25	0.007*
	Group B	20.53±6.06	22.00	18	10	28	Significant
In patients with BMI <25 kg/m^2 (n=27)	Group A	14.80±5.69	13	18	9	27	0.094**
	Group B	18.91±6.57	18.50	16	10	26	Not significant
In patients with BMI ≥25 kg/m^2 (n=45)	Group A	14.52±4.77	14.00	17	9	26	0.040*
	Group B	18.12±4.77	17.00	20	8	28	significant
In patients with T1 stage (n=6)	Group A	18.25±4.34	18.50	8	14	22	0.058**
	Group B	27.00±1.41	27.00	2	26	28	Not significant
In patients with T2 stage (n=42)	Group A	14.28±5.56	12.00	17	10	27	0.060**not
	Group B	17.76±6.04	17.00	19	8	27	significant
In patients with T3 stage (n=24)	Group A	14.00±4.19	15.00	13	9	22	0.092** not
	Group B	14.08±6.61	19.00	17	9	26	significant
Days	Group A	14.63±5.09	13.50	18	9	27	0.007*
	Group B	18.38±6.36	18.00	20	8	28	significant

DISCUSSION

Seroma is most common worrisome sequel that disturb both patient and surgeon with multiple visits that delay starting the adjuvant therapy and cause great patient's discomfort with possibility of increased surgical site infection.

After breast surgery there is collection of serous fluid between skin flaps and muscles. This is due to axillary dead space[13,14]. Manifold research work is done to identify cause but no conclusive pathogenesis is identified the one of the most likely cause for the accumulation of seroma is damage to axillary lymphatic channels[15.] However, fluid analysis showed contradictory results for lymphatic fluid and inflammatory exudate. Other proposed risk factors are high BMI, large breast size, smoking, extensive axillary nodal disease.[16,17]

In our study patients with BMI greater than 25, duration of cancer less than 3 months and ASA II has high rate of seroma formation rather low BMI, ASA I, age less than 50 years and carcinoma greater than 3 months.

Other supposed causative factor is electrocautery dissection that increases seroma production due to thermal trauma.[19] which causes activation of pro inflammatory cytokines. Diathermy is regularly used for adequate hemostasis and to reduce operating time. Comparison of electrocautery and an ultrasonic dissector showed that ultrasonic dissector appears to produce smaller volumes of pro-inflammatory cytokines and also has a reduced incidence of seroma formation.[20] Quilting is not a new idea. However most of these studies were non randomized. Suturing of skin flap to underlying muscle leads to abolition of dead space and causes early approximation of subcutaneous tissue with chest wall .This all leads to less fluid production and early removal of drains. As prolong drain insitu also causes increase fluid production due to tissue reaction. So, quilting not only reduce dead space but also helps in early removal of drain which is another causative factor for fluid production.[21]

Khater et al[11] explained the incidence of seroma in the quilting group was 20% versus 78.6% in the control group and significantly reduced the mean duration of drainage from 11 days in the control group to 9 in the intervention group ($P< 0.001$) A similar figure was reported by Sakkary MA[12] explained it with an overall incidence of 20% in the intervention group versus 50% in the control group ($P = 0.047$). and significant reduction in duration of drain removal from 13.4 to 5, $P< 0.001$ with a mean decrease from 2017.8mL in the control group to 524.8 in the intervention group ($P<0.001$). Coveney EC[22] and his coworkers described an closed suction drainage was significantly less ($P < 0.05$) in the group that had flaps sutured, 272 +/- 46 ml vs 393 +/- 39 ml. Also fewer patients in the flap sutured group developed seromas, 5 (25%) vs 17 (85%) chi 2 = 12.2 $P < 0.001$. a significant difference 25% in the suture group versus 85% in the control group.

In recent trial by Ten Wolde[23] and his coworkers in 2014showed decrease of seroma from 80.5% in the control group to 22.5% in the quilting group ($P< 0.01$) also had significant reduction in total drainage volume (from a mean of 1160 to a mean of 710) with a decrease of mean number of aspirations from 4.86 to 2.40 ($P = 0.015$) and the volume of aspirations from 1660mL to 611mL ($P = 0.05$). Seroma has significant association with extent of surgery i.e. mastectomy has great incidence of seroma rather than breast conservation. Similarly extensive axillary dissection and number of nodes removal is directly proportional to amount of seroma.

Purushothamet al. demonstrated in a controlled randomized study that the incidence of seroma was significantly lower with sentinel lymphnode (SLNB) axillary approach than with conventional axillary dissection[24].

Previous work in the literature have compared the effect of quilting versus conventional closure with drainage after mastectomy for breast cancer on patient outcome. However, these studies have limited impact due to small sample sizes, single centered and absence of randomization. Breast cancer surgeons appear to currently still favor conventional wound closure with drainage, although current evidence suggests better patient outcomes with quilting suture.[25]

Quilting give a large advantage over non-quilting in decreasing medical cost and improving the outcome by early hospital discharge ,less outpatients visits .It also helps in early start of adjuvant therapy by early drain removal and decreasing surgical site infection. Though it is also associated with prolong operative time and some surgeon yet not preferred this technique due to time shortage and fear of drain entrapment or formation of pockets which can lead to infection. No data is available on these queries and there was no such complication noted during our study trial.so, additional operative time may be not considered as important obstacle of performing flap fixation any more for breast cancer patients.

CONCLUSION

Quilting is an effective method in modified radical mastectomy to significantly reduce the postoperative seroma formation in addition to significantly reducing the duration and volume of fluid drainage in the grains by causing obliteration of dead space. Therefore, quilting of flaps is recommended as a routine step at the end of any mastectomy.

Author's Contribution:

Concept & Design of Study:	Afsheen Jabaid
Drafting:	Nadeem Khurshaidi
Data Analysis:	Zahid Habib, Rufina Soomro
Revisiting Critically:	Afsheen Jabaid, Nadeem Khurshaidi
Final Approval of version:	Afsheen Jabaid

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

REFERENCES

1. Chand N, Aertssen AMG, Royle G. Axillary "exclusion" A successful technique for reducing seroma formation after mastectomy an axillary dissection. Adv Breast Cancer Res 2013;2:1-6.
2. Gonzales EA, Saltzstein EC, Riender CS, Nelson BK. Seroma formation following breast cancersurgery. Breast J 2003;9(5):385-88.
3. Boostrom SY, Throckmorton AD, Boughey JC. Incidence of Clinically significant seroma after breast and axillary surgery. J Am Coll Surg 2009;208,(1).
4. Tadych K, Donegan DL. Post mastectomy Seromas and Wound Drainage. J Surg Gynacol Obstet 1987; 165(6):483-487.
5. Hashemi E, Kaviani A, Najafi M, Ebrahimi M, Hooshmand H, Montazeri A. Seroma formation after surgery for breast cancer. World J Surg Oncol 2004;2:44.
6. Sampathraju S, Rodrigues G. Seroma formation after Mestectomy:Pathogenesis and Prevention. Ind J Surg Oncol 2010;1(4):328-33.
7. Oertli D. Axillary lymphadenectomy. Chirurg 2000;78:196–202 6.
8. Petrek JA, Peters MM, Nori S, Knauer C, Kinne DW, Rogatko A. Axillary lymphadenectomy. A prospective randomized trial of 13 factors influencing drainage including early or delayed arm mobilization. Arch Surg 1990;125:378–82
9. Hashemi E, Kaviani A, Najafi M, Ebrahimi M, Hooshmand H, Montazeri A. Seroma formation after surgery for breast cancer. World J Surg Oncol 2004;2:44.
10. Wolde BT, Frist JH, Wildenberg VD, Mariel E, Gels K, Polat F, et al. Quilting prevent seroma formation following breast cancer surgery:Closing the dead space by quilting prevents seroma following axillary lymph node dissection and Mastectomy. Ann Surg Oncol 2014;21:802-7.
11. Khater A, Elnahas W, Roshdy S, Farouk O, Senbal R, Fathi A, et al. Evaluation of Quilting Technique for Reduction of Postmestectomy Seroma: a rendomized control study. Int J Breast Can 2015;2015 ID 2873986:6.
12. Sakkary MA. The value of mastectomy flap fixation in reducing fluid drainage and seroma formation in breast cancer patients. World J Surg Oncol 2012;10 10.1186/1477-7819-10-8)
13. Sohail S, Alam SN. Breast cancer in Pakistan: awareness and early Detection. J Coll Physician Surg Pak 2007;17:711-2
14. Wolde B. Ten, Vandan FJH, KeemersGels ME, Strobbe JA. Quilting prevents seroma formation following breast cancer Surgery: closing the dead space by Quilting prevents seroma following Axillary Lymph node dissection and mastectomy. Annals Surg Oncol 2014;21(3):802-807.
15. Bonnema J, Ligtenstein DA, Wiggers T, van Geel AN. The Composition of Serous Fluid after Axillary Dissection. Eur J Surg 1999;165(1): 9-13.
16. Kuroi K, Shimozuma K, Taguchi T, Imai H, Yamashiro H, Ohsumi S, Saito S. Effect of Mechanical Closure of Dead Space on Seroma Formation after Breast Surgery. Breast Cancer 2006;13(3):260- 265.
17. McCaul JA, Aslaam A, Spooner RJ, Louden I, Cavanagh T, Purushotham AD. Aetiology of Seroma Formation in Patients Undergoing Surgery for Breast Cancer. Breast 2000;9(3):144-148.
18. Jain K, Sowdi R, Anderson AD, MacFie J. Randomized Clinical Trial Investigating the Use of Drains and Fibrin Sealant Following Surgery for Breast Cancer. Bri J Surg 2004;91(1):54- 60.
19. Porter KA, O'Connor S, Rimm E, Lopez M. Electrocautery as a factor in seroma formation following mastectomy. Am J Surg. 1998;176(1): 8-11.
20. Kontos M, Kothari A, Hamed H. Effect of harmonic scalpel on seroma formation following surgery for breast cancer: a prospective randomized study. J BU ON.: official J Balkan Union Oncol 2007;13(2):223-30
21. Purushotham AD, McLatchie E, Young D, George WD, Stallard S, Doughty J, et al. Randomized clinical trial of no wound drains and early discharge in the treatment of women with breast cancer. Bri J Surg 2002;89(3):286-92.
22. Coveney EC, O'Dwyer PJ, Geraghty JG, O'Higgins NJ. Effect of closing dead space on seroma formation after mastectomy-a prospective randomized clinical trial. Eur J Surg Oncol 1993; 19:143-46.
23. ten Wolde B, van den Wildenberg FJ, Keemers-Gels ME, Polat F, Strobbe LJ. Quilting prevents seroma formation following breast cancer surgery: closing the dead space by quilting prevents seroma following axillary lymph node dissection and mastectomy. Annals Surg Oncol 2014;21(3):802-7.
24. Chen D, Li Z, Song J, Zheng X, Yu A. Systematic review and meta-analysis of the use of quilting to prevent seroma formation after axillary lymphadenectomy. Int J Clin Exp Med 2016;9(2): 760-72.
25. Larsen BB, Hugan C. Fixation of skin flaps in radical mastectomy by subcutaneous sutures; observations. AMA Arch Surg 1955;71:419-423.

Original Article

Seasonal Variation in Occurrence of GBS

Seasonal Variation in Occurrence of Guillian Barre Syndrome (GBS) in Local Population of Pakistan

Raja Zaigham Abbas, Maryam Javed, Usman Ali Khan, Fatima Javed and Muhammad Athar Javed

ABSTRACT

Objective: To report the effect of seasonal variation in a large cohort that are clinically diagnosed with GBS in tertiary care hospital which will serve as reference for region of Pakistan.
Study Design: Retrospective / cross-sectional study
Place and Duration of Study: This study was conducted at the Neurology Department, Mayo Hospital Lahore in collaboration with various private and public hospitals in Punjab from March 2013 to February 2015.
Materials and Methods: The Inclusion criteria was proven cases of GBS diagnosed according to the Ashbury et al. criteria for GBS based on clinical and electrophysiological findings requiring plasmapharesis. Exclusion criteria included patients of neuropathies associated with chronic inflammatory demyelination (CIDP), diabetes, and other metabolic, toxic and vasculitic neuropathies. A Performa containing demographic, clinical, CSF analysis and electrophysiological detail was designed which was filled by treating physician before requesting for plasmapheresis. The data was analyzed using SPSS version 17.
Results: A total of 185 patients were included in the study with 112(60.5%) males and 73(39.5%) females and M: F ratio of 1.53: 1. The mean age was 35.24(SD 15.51) with a range from 11-78 years. Ninety nine (53.5%) cases presented between 20- 40 years of age. The highest incidence of GBS (n=86, 46.5%) was seen during winter season (Dec - Feb), followed by 36(19.5%) in spring (March - May), 46 (24.9%) in rainy summer (June - Sept) or southwest monsoon period and only 17(9.2%) in post monsoon (Oct- Nov).
Conclusion: The present study provides data suggesting that there is significant (p=.000) seasonal variation in frequency of GBS patients with the highest frequency observed in winter. The study supports the finding GBS being more common in males as compared to females.
Key Words: Guillian Barre Syndrome (GBS), Seasonal variation, plasmapheresis

Citation of articles: Abbas RZ, Javed M, Khan UA, Javed F, Javed MA. Seasonal Variation in Occurrence of Guillian Barre Syndrome (GBS) in local Population of Pakistan. Med Forum 2018;29(8):20-23.

INTRODUCTION

GBS is usually a post infectious state whereby the immune system of a person while reacting against the pathogen also cross reacts with the host nervous system causing immune mediated nerve injury. It is usually an autoimmune mediated demyelinating polyradiculo-neuropathy that equally affects males & females. Multiple triggering events have been reported in its pathogenesis such as C jejuni, hepatitis, Epstein Bar virus, haemophilus influenza, cytomegalovirus and Zika virus infections[1-5].

Clinical features involve severe back pain and limb paresthesias over the limbs. Weakness begins in the most proximal muscles. Symmetric muscle weakness are accompanied by depressed or absent deep tendon reflexes. Legs are more typically involved than arms, which creates the illusion of an ascending paralysis. The weakness of oropharyngeal and facial muscles is observed in 50% of cases due to involvement of cranial nerves[6]. Other important clinical manifestations include areflexia, oculomotor weakness & ataxia[7-10]. It is also associated with numbness & tingling of feet[11].

Various studies on electro diagnosis, nerve conduction and F waves have been conducted with well documented results but the studies reporting the effect of seasonal variation on GBS are few. In Pakistan only two studies have been carried out to analyze the effects of seasonal variations on occurrence of GBS. Both have little cohort size and indicates varying results[12,13].

Retrospective studies have also been carried out in India & Iran show case clustering during winter season[14,15]. However a few other Indian & Iranians studies also show the maximum occurrence of disease during summer season[16,17]. Rebecca Prevots et al indicates that there are no seasonal variations noted in GBS patient in USA[18]. Because of the different seasonal conditions in different geographical regions it's very difficult to comment on geographical trends.

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MATERIALS AND METHODS

This retrospective cross sectional study was conducted at Mayo Hospital Lahore in collaboration with various private and public hospitals from March 2013 to February 2015. The study cohort involved 185 patients with the age limit >12-80 years involving both sexes. The inclusion criteria for diagnosis of GBS involve patients fulfilling the Ashbury and Cornblath's criteria of GBS and patients who required plasmapharesis. The exclusion criteria involved the patient with age less than 12 years, patients with different neuropathies like Chronic Inflammatory Demyelinating Polyneuropathy (CIDP), Diabetic peripheral neuropathy (DPN) & neuropathies due to toxic, metabolic, vasculitic and hereditary causes. A Performa containing demographic details, History & examination, EMG/NCS finding & CSF findings was filled by the physician at the time of primary plasmapharesis. Data was analyzed by using the SPSS version 17. Stastical significance was determined by the Pearson Chi-Square test.

RESULTS

Demographics: Out of 185 patients who were accessed 112 (60.5%) were male whereas 73 (39.5%) were female with the male to female sex ratio being 1.53:1 (Figure 1).

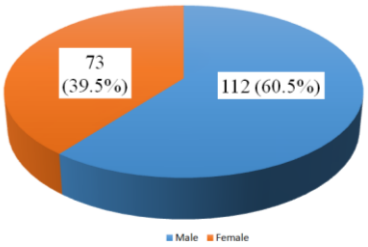

Figure No.1: Pie chart indicating male to female ratio in case of GBS

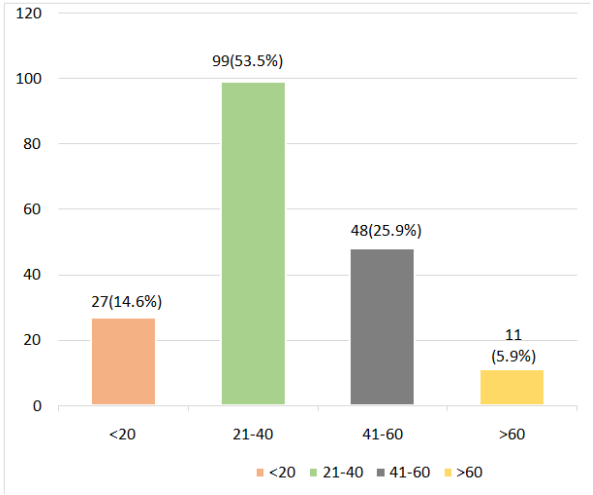

Figure No.2: Chart depicting frequency of GBS in various age groups.

The patient's age limit ranged from >12-80 years with the mean age of 35.24 years. The GBS analysis in various age groups showed the peak incidence in age group of 21-40 year (n= 99, 53.5%), followed by the age group of 41-60 (n=48, 25.9%), the age group <20 (n=27. 14.6%) with the least number of cases (n=11, 5.9%) were seen in patient aged >60 years **(Figure 2).**

Seasonal variations: The frequency of GBS in various months was observed and highest incidence (n=86, 46.5%) was seen in winter season from December to February, followed by summer season (n=46, 24.9%) from June to September, spring season (n=36, 19.5%) from March to May & lowest incident rate was seen in rainy season (n=17, 9.2%) in month of October & November as shown in Figure 3. The distribution of GBS in various season is depicted in Figure 4 which shows highest case clustering during winter season with the second peak was seen during summer season.

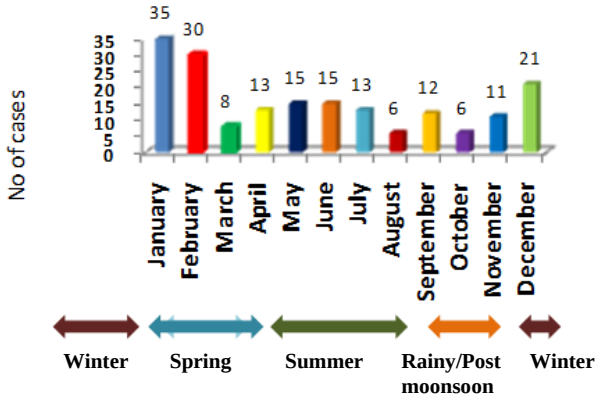

Figure No.3: Chart indicates the seasonal variations in case of GBS.

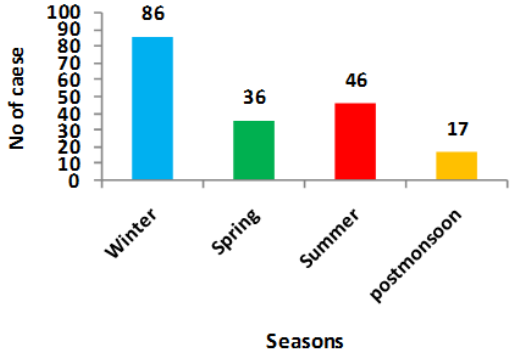

Figure No.4: Distribution of GBS in various seasons.

Statistical Analysis: Statically significance was determined by the Pearson Chi-Square test using SPSS 17. The value of X2= .000 shows significant variation in frequency of GBS with clear prediction that the highest incident is seen during winter season. The results of chi square test are highlighted in Table 1.

Table No.1: Result of Chi- Square test showing the frequency of GBS during winter season - Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	5.550E2a	33	.000
Likelihood Ratio	458.806	33	.000
Linear-by-Linear Association	50.204	1	.000
N of Valid Cases	185		

a. 34 cells (70.8%) have expected count less than 5. The minimum expected count is .55.

DISCUSSION

We did demographical profiling of patients who presented to out-patient department of neurology in Mayo Hospital Lahore with the diagnosis of GBS. Although disease is common throughout the year but the highest incident peak was observed during winter from December to February and the second peak was observed during summer season. The previous Pakistani study by Zaheer et al indicates major clustering of disease during summer season whereas another study by Yaqoob et al indicates the highest incident during spring & Rainy season[12,13] depicted in Table 2.

Table No.2: Seasonal Variation in GBS in different studies of the world.

Study group	Summer	Spring	Rainy/ fall	Winter
Local studies				
Present study (Pak) n=185	46 (24.9%)	36 (19.5%)	17 (9.2%)	86 (46.5%)
Zaheer et al (Pak) n =25	16 (64%)			9(26.5%)
Yaqoob et al (Pak) n =34	3 (8.82%)	11 (32.4%)	11 (32.4%)	9 (26.5%)
Asian studies				
Haghighi et al (Iran) n =389	90 (23.13%)	113 (29.04%)	71 (18.25%)	115 (29.56%)
Akbayram et al (Iran) n =25	10 (40%)	8 (32%)	5 (20%)	2 (8 %)
Geetanjali et al (India) n =65	27 (41.53%)	19 (29.23%)	8 (12.30%)	11(16.92%)
Sharma et al (India) n = 50	11 (22%)	20 (40%)		19 (38%)
Coe et al (Korea) n = 129	54 (40.90%)	25 (18.93%)	35 (26.51%)	15 (11.36%)
International studies				
Sivadon-Tardy et al (France)				60%
Rocha et al (Brazil)		62 %		
Larson et al (Norway)				Maximum
Arami et al (Saudi arabia) n =75	14 (18%)	15 (21%)	14 (18%)	32 (43%)
Louie et al (USA) n = 98	22%	20%	27%	31%
Rebecca et al	No seasonal Variations noted			

In Asian countries the studies have been conducted in India, Iran and Korea. From India Geetanjali et al indicates the highest incident rate (41.53%) during summer season[17] whereas Sharma et al showed the peak during spring season (40%)[14]. Coe et al from Korea showed the major outbreak during summer season[19]. These findings are strikingly different from our studies because of different geographical and climate conditions. The study from Iran however showed the results similar to our studies indicating maximum incidence during winter season shown in Table 2.

Studies from other parts of world like Saudi Arabia[20], Norway[21], USA[22] and France[23] also show peak clustering during winter season. In Brazil highest incident is observed during spring season[24]. One of the study from USA depicted that there is no seasonal variation noted in case of GBS[25]. Hence the review of all these studies indicates that it is hard to define any specific trend of seasonal variations for GBS patients because the climate conditions are strikingly different even in neighboring countries. So the study with larger cohort size and maximum time span may only serve as reference study for that area of the world.

Our study shows that there is significant (p=.000) variation in frequency of GBS patients with a clear predilection towards winter season. GBS is more common in males than females in our local population with maximum frequency between 20- 40 years of age. Larger studies are required to confirm our finding and possible association with upper respiratory tract infections such as influenza which are common during this season so that preventive measures can be taken to prevent this illness.

CONCLUSION

The present study provides data suggesting that there is significant (p=.000) seasonal variation in frequency of GBS patients with the highest frequency observed in winter. The study supports the finding GBS being more common in males as compared to females.

Author's Contribution:

Concept & Design of Study:	Raja Zaigham Abbas
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Revisiting Critically:	Fatima Javed, Muhammad Athar Javed
Final Approval of version:	Raja Zaigham Abbas

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

REFERENCES

1. Ropper AH. Ischemic compression paresthesias in Guillain-Barré syndrome. Arch Neurol 1991;48: 1261-2.
2. Jacobs BC, Rothbarth PH, Van der Meché FG, Herbrink P, Schmitz PI, De Klerk MA, et al. The spectrum of antecedent infections in Guillain-Barre syndrome a case-control study. Neurol 1998; 51(4):1110-5.
3. McCarthy N, Andersson Y, Jormanainen V, Gustavsson O, Giesecke J. The risk of Guillain–Barre syndrome following infection with Campylobacter jejuni. Epidemiol Infect 1999; 122(1):15-7.
4. Mori M, Kuwabara S, Miyake M, Noda M, Kuroki H, Kanno H, et al. Haemophilus influenzae infection and Guillain–Barré syndrome. Brain 2000;123(10):2171-8.
5. Rees JH, Soudain SE, Gregson NA, Hughes RA. Campylobacter jejuni infection and Guillain–Barré syndrome. New Eng J Med 1995;333(21):1374-9.
6. Hauser SL, Asbury AK. Guillain-Barre Syndrome & Other Immune-Mediated Neuropathies. Harrison's Principles of Int Med McGraw Hill 2009;(16):2667-2671.
7. Phillips MS, Stewart S, Anderson JR. Neuropathological findings in Miller Fisher syndrome. J Neurol, Neurosurg Psychiatr 1984; 47(5):492-5.
8. Ropper AH. Miller Fisher syndrome and other acute variants of Guillain Barre syndrome. Baillieres Clin Neurol 1994;3:95-106.
9. Yuan CL, Wang YJ, Tsai CP. Miller Fisher syndrome: a hospital-based retrospective study. Eur Neurol 2000;44(2):79-85.
10. Ropper AH. Unusual clinical variants and signs in Guillain-Barré syndrome. Arch Neurol 1986; 43(11):1150-2.
11. Amato AA. Guillain Barre syndrome & related disorders. Revista Mexicana de Neurociencia 2005; 6(5):455-69.
12. Zaheer M, Naeem M, Nasrullah M. Seasonal Variation and Sex Distribution in Patients with Guillain-Barre Syndrome. Pak J Neurolog Sci 2008;3:6-8.
13. Yakoob MY, Rahman A, Jamil B, Syed NA. Characteristics of patients with Guillain Barre Syndrome at a tertiary care centre in Pakistan, 1995-2003. J Pak Med Assoc 2005;55(11):493-496.
14. Sharma A, Lal V, Modi M, Vaishnavi C, Prabhakar S. Campylobacter jejuni infection in Guillain-Barré syndrome: A prospective case control study in a tertiary care hospital. Neurol Ind 2011;59(5): 717-721.
15. Haghighi AB, Banihashemi MA, Zamiri N, Sabayan B, Heydari ST, Safari A, et al. Seasonal variation of Guillain-Barre syndrome admission in a large tertiary referral center in southern Iran: a 10 year analysis. Acta Neurologica Taiwanica 2012; 21(2):60-321.
16. Akbayram S, Doğan M, Akgün C, Peker E, Sayın R, Aktar F, et al. Clinical features and prognosis with Guillain-Barré syndrome. Ann Ind Acad Neurol 2011;14(2):98-102.
17. Sharma G, Sood S, Sharma S. Seasonal, age & gender variation of Guillain Barre syndrome in a tertiary referral center in India. Neuroscience and Med 2013;4(01):23.
18. Prevots DR, Sutter RW. Assessment of Guillain-Barré syndrome mortality and morbidity in the United States: implications for acute flaccid paralysis surveillance. J Infect Dis 1997;175 (Supplement_1):S151-5.
19. Coe CJ. Guillain Barre Syndrome in Korean Children. Yonsei Med J 1989; 30: 81-87.
20. Arami MA, Yazdchi M, Khandaghi R. Epidemiology and characteristics of Guillain-Barre syndrome in the northwest of Iran. Annals Saudi Med 2006;26(1):22-27
21. Louie M, Gilchrist JM, Woodard C. Guillain-Barre syndrome: a 5-year Rhode Island hospital experience. Rhode Island Med 1994;77(5):135-140
22. Sivadon-Tardy V, Orlikowski D, Rozenberg F, Caudie C, Sharshar T, Lebon P, et al. Guillain-Barré syndrome, greater Paris area. Emerg Infect Dis 2006;12(6):990.
23. Larsen JP, Kvale G, Nyland H. Epidemiology of the Guillain-Barré syndrome in the county of Hordaland, Western Norway. Acta Neurolog Scandinavica1985;71(1):43-7.
24. Rocha MS, Brucki SM, Carvalho AA, Lima ÚW. Epidemiologic features of Guillain-Barre syndrome in Sao Paulo, Brazil. Arquivos de neuro-Psiquiatria 2004; 62(1):33-7.
25. Prevots DR, Sutter RW. Assessment of Guillain-Barré syndrome mortality and morbidity in the United States: implications for acute flaccid paralysis surveillance. J Infect Dis 1997; 175 (Supplement_1):S151-5.

Original Article

Gallstones and Hepatitis C Infection

Association Between Gallstones and Hepatitis C Virus Infection: A study of 600 Cases at Pak Red Crescent Medical & Dental Teaching Hospital

Aqeel Ahmad[1], Nasir Mahmood[2], Abid Hussain[1]

ABSTRACT

Objective: To compare the frequency of gallstones in patients with and without hepatitis C virus infection.
Study Design: Cross-sectional study
Place and Duration of Study: This study was conducted at the department of surgery & radiology, Pak Red Crescent Teaching Hospital, affiliated with Pak Red Crescent Medical & Dental College, Lahore from July 2016 to June 2018.
Materials and Methods: A total of 600 patients irrespective of age and sex were included in this by consecutive nonprobability sampling technique. All subjects were screened for Anti-HCV antibody by immune-chromatographic strip-test method. An equal number of patients with and without HCV infection were chosen in two different groups. Group I was seronegative and Group II was seropositive patients. Ultrasound scan of abdomen was performed on all the patients to see especially for gallstones. Data was collected for age, sex, presence or absence of gallstones, on a specially designed performa. Data was analyzed using SPSS version 21. Descriptive statistics & Chi-square test was used.
Results: Out of 600 patients, 414 (69%) were females and 186 (31%) were males. Mean age of the patients was 38 ± 1.28 years. Youngest patient was 17 years old and eldest was 90 years old. Males and females with Hepatitis C antibodies were 121 (40.33%) and 179 (59.66%) respectively. In Group II patients suffering from HCV infection had a significantly high frequency of gallstones (25.66%) as compared to HCV seronegative Group I (8.66%). P-value was significant (p=0.01).
Conclusion: There is a strong association of gallstone disease in patients suffering from HCV infection.
Key Words: Gallbladder, cholelithiasis, gallstones, Hepatitis C Virus, GBD.

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INTRODUCTION

Worldwide Hepatitis C virus infection is a major healthcare problem. It is estimated that approximately 180 million patients across the globe are infected with this virus.[1] According to world health organization (WHO), Pakistan has the world's second highest prevalence of hepatitis C, second only to Egypt.[2] Current prevalence of HCV in Pakistan is 8.64%,[3] high from previously reported prevalence rate of 4.8%.[4]
Some epidemiologic studies[5,6] reported that, HCV infection could also be an independent risk factor for gallstones.

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Only two studies were conducted in our country to investigated HCV infection as a solitary risk factor for gallstones.[5, 7]
We consistently found in our institution, lots of patients with cholelithiasis who also had HCV virus infection. Fact that HCV is an endemic in this region we planned a study, to see this association. We hypothesized that persons with HCV infection have a higher incidence of gallstone disease than those without HCV infection. The objective of the study was to compare the frequency of gallstones in patients with and without hepatitis C virus infection.

MATERIALS AND METHODS

This cross-sectional study was conducted from July 2016 to June 2018 in the department of surgery & radiology, Pak Red Crescent Teaching Hospital, affiliated with Pak Red Crescent Medical & Dental College, Lahore. The study was approved by the ethical review committee of our institution. In order to reduce the bias, all the scans were performed by the same

radiologist. All cases included in this study were referred for ultrasound scan of abdomen.

A total of 600 patients irrespective of age and sex were included in this by consecutive non-probability sampling technique. Patients with abnormal LFT's due to any cause other than Hepatitis C, abnormal lipid profile, sickle cell disease, thalassemia, history of gastric/bariatric surgery and patients taking contraceptives were excluded.

All subjects were tested for Anti-HCV antibody by strip method. An equal number of patients with and without HCV infection were chosen in two different groups. Group I was seronegative and Group II was seropositive patients. Ultrasound scan of abdomen was performed on all subjects, with special focus on hepatobiliary system. Special note was made of gallstones location whether in the gallbladder or in the bile duct, and presence or absence of cirrhosis.

Data was collected for age, sex, presence or absence of gallstones, on a specially designed proforma. Data was analyzed using SPSS version 21. Descriptive statistics were applied. Frequency and percentage were calculated for categorical variables like gender whereas mean and standard deviation were calculated. Chi-square test was used to determine the association of HCV infection with gallstones by comparing the frequency of gallstones in the two groups. p-value of <0.05 was considered significant.

RESULTS

A total number of 600 patients were included in the study which were divided into two groups. In group I, 300 patients were HCV seronegative and while in Group II 300 patients were HCV seropositive. Out of 600 patients, 414 (69%) were female and 186 (31%) were male. Mean age of the patients was 38 ± 1.28 years.

Table No. 1. Gender Distribution in study groups

Study Group	Gender		Total
	Male	Female	
Group I (HCV-ve)	65	235	300
Group II (HCV+ve)	121	179	300
Total	186	414	600
%	31	69	100

Table No.2: Frequency of gallstones in relation with gender in study groups

Study Group	Gallstones				Total
	Present		Absent		
	Male (%)	Female (%)	Male (%)	Female (%)	
Group I (HCV-ve)	5 (1.66)	21 (7)	60 (20)	214 (70.33)	300
Group II (HCV+ve)	16 (5.33)	61 (20.33)	49 (16.33)	174 (58)	300
Total (%)	21 (3.5)	82 (13.66)	109 (18.16)	388 (64.66)	600 (100)

Youngest patient was 17 years old and eldest was 90 years old. Male and females with Hepatitis C antibodies were 121 (40.33%) and 179 (59.66%) respectively. Gender distribution of both groups is given in table 1 and frequency of gallstone in relation with gender of both study groups is given in Table. 2.

Total presence of gallstone in both groups was 103 (17.6%) patients. In group I gallstones were found in 26 (8.66%) patients and in group II (HCV+ve) in 77 (25.66%) patients. Comparative frequency of gallstone in both groups is shown in table 3.

Table No. 3: Presence of gallbladder stone in study groups

Study Group	Gallstones		Total	p-value
	Present	Absent		
Group I (HCV-ve)	26	274	300	0.001
%	8.66	91.33	100	
Group II (HCV+ve)	77	223	300	
%	25.66	74.33	100	
Total	103	497	600	
%	17.6	82.83	100	

DISCUSSION

Gallstones are one of the most common biliary pathology and it has a prevalence of 10-15%. Cholesterol stone is one of the most common type. In the USA and Europe 80% stones are cholesterol or mixed, whereas in Asia 80% are pigment stones.

Transabdominal ultrasonography is one of the most common, rapid, noninvasive method of imaging the gallbladder, and this technique has contributed greatly to our understanding of the epidemiology and risk factors for gallbladder disease.[8,9]

The risk of gallbladder disease (GBD) increases with age. Traditionally it is associated with middle age females. Other potential risk factors for GBD include obesity,[10] rapid weight loss,[10] lower levels of physical activity,[11] pregnancy,[12] increasing number of live births,[13] oral contraceptive, estrogen replacement therapy,[14] diabetes mellitus,[13,15] abstinence from alcohol,[13,16,] smoking,[13] low total serum cholesterol levels,[13,17] low levels of coffee consumption,[19,20] and genetic factors.[21] However, some of these variables have not been consistently associated with GBD, and these risk factors may differ considerably among men and women.[13,17]

Liver cirrhosis is believed to be another major risk factor for gallstones,[21] and it increases the risk of gallstones two times more than other patients.[22,23] Formation of gallstones in cirrhosis are mainly due to, the changes in bile composition and impaired gallbladder motility.[22] Patients with cirrhosis are more likely to undergo cholecystectomy for emergent reasons

than those who do not have liver disease.[24] Moreover if cirrhosis is due to viral hepatitis C, the risk of gallstones becoming symptomatic is further increased than in those with alcoholic cirrhosis.[25]

Acalovschi et al. reported that HCV infection was a risk factor for gallbladder stones when comparing subjects without liver diseases.[26] Stroffolini et al, reported that gallstone prevalence was significantly higher in patients with HCV-related cirrhosis than in those with HBV-related or alcoholic cirrhosis.[27] The exact mechanisms behind the development of gallstones in HCV patients is not well understood.[28] Loriot et al. demonstrated that HCV can successfully infect gallbladder epithelial cells.[29] Many other studies also reported HCV can directly infect bile duct and gallbladder epithelial cells.[30,31] It might impair gallbladder epithelium lipid absorption and gallbladder muscle contractility function, resulting in increased propensity of development of gallstones. HCV infection is also known to have interactions with glucose and cholesterol metabolisms.[32,33] This metabolic disturbance could lead to alteration of bile composition that may contribute to the gallstones formation.

Acalovschi et al, reported 19% incidence of gallstones in HCV positive patients.[26] In present study We found that the risk of gallstones was significantly higher (25.66%) among HCV-infected patients compared with subjects without HCV infection (8.66%). Which is consistent with local [5, 7] and international data. [8, 21, 28, 34]

Bini EJ and McGready J, found that chronic HCV infection is strongly associated with GBD in men but not in women in the United States.[8] Chia-Yen Dai et al, also reported, the association between HCV infection and GB stones existed in males but not in females.[35] In current study we did not find this association. We found 20.33% of HCV positive females who had gallstone disease whereas incidence in HCV positive males was only 5.33%. We recommend further studies in different areas of our country to see this difference, that might be a regional one.

The risk of gallstones becoming symptomatic is higher in patients with cirrhosis due to viral hepatitis.[25] Furthermore patients with de-compensated liver cirrhosis are more susceptible to gallstone formation than patients with compensated liver cirrhosis.[36] It has major implications because cholecystectomy for symptomatic gallstones in patients with advanced liver disease is associated with a high risk of morbidity and mortality.[24,27] Further studies are required to clarify how this risk should be addressed in clinical practice.

This study has some limitations, sample size is not representative of the general population. The case and control patients were selected from those seeking medical care at our hospital. The patients with chronic HCV infection might have more abdominal imaging, leading to a higher likelihood of gallstones detection.

CONCLUSION

There is a strong association of gallstone disease in patients suffering from HCV infection. It may be HCV infection which is responsible for higher prevalence of gallstone disease in this region. Further studies are required to clarify how this risk should be addressed in clinical practice.

Author's Contribution:

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Data Analysis:	Abid Hussain
Revisiting Critically:	Aqeel Ahmad, Nasir Mahmood
Final Approval of version:	Aqeel Ahmad

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

REFERENCES

1. Mohd Hanafiah K, Groeger J, Flaxman AD, Wiersma ST. Global epidemiology of hepatitis C virus infection: new estimates of age specific antibody to HCV seroprevalence. Hepatol 2013; 57:1333-42.
2. Sievert W, Altraif I, Razavi HA, Abdo A, Ahmed EA, Alomair A, et al. A systematic review of hepatitis C virus epidemiology in Asia, Australia and Egypt. Liver Int 2011;31(2):61-80.
3. Arshad U, Ashfaq A. Epidemiology of hepatitis C infection in Pakistan: current estimate and major risk factors Crit Rev Eukaryot Gene Expr 2017; 63-77.
4. Ali SA, Donahue RM, Qureshi H, Vermund SH. Hepatitis B and hepatitis C in Pakistan: prevalence and risk factors. Int J Infect Dis 2009;13(1): 9-19.
5. Shah SI, Shah S, Hannan A. Hepatitis C–a risk factor for gallstone disease. J Ayub Med Coll Abbottabad 2014;26:84-7.
6. Tsai CH, Wu JS, Chang YF, Lu FH, Yang YC, Chang CJ. The number of metabolic abnormalities associated with the risk of gallstones in a nondiabetic population. PLoS One 2014;9:e90310.
7. Haq A, Shamim A, Ali M. Prevalence of Gallstone Disease in Patients of Hepatitis C Virus Infection. PJMHS 2017;3(11):1065-67.
8. Bini EJ, McGready J: Prevalence of gallbladder disease among persons with hepatitis C virus infection in the United States. Hepatol 2005;41:1029-36.
9. Kratzer W, Mason RA, Kachele V. Prevalence of gallstones in sonographic surveys worldwide. J Clin Ultrasound 1999;27:1-7.
10. Everhart JE. Contributions of obesity and weight loss to gallstone disease. Ann Int Med 1993;119:1029-35.
11. Leitzmann MF, Giovannucci EL, Rimm EB, Stampfer MJ, Spiegelman D, Wing AL, et al. The relation of physical activity to risk for symptomatic

gallstone disease in men. Ann Int Med 1998;128: 417-25.
12. Maringhini A, Ciambra M, Baccelliere P, Raimondo M, Orlando A, Tine F, et al. Biliary sludge and gallstones in pregnancy: incidence, risk factors, and natural history. Ann Int Med 1993; 119:116-20.
13. Everhart JE, Khare M, Hill M, Maurer KR. Prevalence and ethnic differences in gallbladder disease in the United States. Gastroenterol 1999; 117:632-9.
14. Uhler ML, Marks JW, Judd HL. Estrogen replacement therapy and gallbladder disease in postmenopausal women. Menopause 2000;7:162-7.
15. Ruhl CE, Everhart JE. Association of diabetes, serum insulin, and Cpeptide with gallbladder disease. Hepatol 2000;31:299-303.
16. Leitzmann MF, Tsai CJ, Stampfer MJ, Rimm EB, Colditz GA, Willett WC, et al. Alcohol consumption in relation to risk of cholecystectomy in women. Am J Clin Nutr 2003;78:339-47.
17. Attili AF, Capocaccia R, Carulli N, Festi D, Roda E, Barbara L, et al. Factors associated with gallstone disease in the MICOL experience. Multicenter Italian Study on Epidemiology of Cholelithiasis. Hepatol 1997;26:809-18.
18. Leitzmann MF, Willett WC, Rimm EB, Stampfer MJ, Spiegelman D, Colditz GA, et al. A prospective study of coffee consumption and the risk of symptomatic gallstone disease in men. JAMA 1999;281:2106-12.
19. Leitzmann MF, Stampfer MJ, Willett WC, Spiegelman D, Colditz GA, Giovannucci EL. Coffee intake is associated with lower risk of symptomatic gallstone disease in women. Gastroenterol 2002;123:1823-30.
20. Sarin SK, Negi VS, Dewan R, Sasan S, Saraya A. High familial prevalence of gallstones in the first-degree relatives of gallstone patients. Hepatol 1995;22:138-41.
21. Li X, Gao P. Hepatitis C Virus Infection Increases Risk of Gallstone Disease in Elderly Chinese Patients with Chronic Liver Disease. Scientific Reports 2018;8:4636.
22. Acalovschi M. Gallstones in patients with liver cirrhosis: incidence, etiology, clinical and therapeutical aspects. World J Gastroenterol 2014;20:7277–85.
23. Park JH, Kim TN, Lee SH. The prevalence and risk factors of gallstones in Korean patients with liver cirrhosis. Hepatogastroenterol 2013; 60:461–5.
24. Puggioni A, Wong LL. A metaanalysis of laparoscopic cholecystectomy in patients with cirrhosis. J Am Coll Surg 2003;197:921-6.
25. Acalovschi M, Blendea D, Feier C, Letia AI, Ratiu N, Dumitrascu DL, et al. Risk factors for symptomatic gallstones in patients with liver cirrhosis: a case-control study. Am J Gastroenterol 2003;98:1856-60.
26. Acalovschi M, Buzas C, Radu C, Grigorescu M. Hepatitis C virus infection is a risk factor for gallstone disease: a prospective hospital-based study of patients with chronic viral C hepatitis. J Viral Hepat 2009;16:860-6.
27. Stroffolini T, Sagnelli E, Mele A, Cottone C, Almasio PL; Italian Hospitals' Collaborating Group. HCV infection is a risk factor for gallstone disease in liver cirrhosis: an Italian epidemiological survey. J Viral Hepat 2007;14:618–23.
28. Wijarnpreecha K, Thongprayoon C, Panjawatanan P, Lekuthai N, Ungprasert P. Hepatitis C virus infection and risk of gallstones: A meta-analysis J Evid Based Med 2017;10(4):263-70.
29. Loriot MA, Bronowicki JP, Lagorce D, Lakehal F, Persico T, Barba G, et al. Permissiveness of human biliary epithelial cells to infection by hepatitis C virus. Hepatol 1999;29:1587-95.
30. Haruna Y, Kanda T, Honda M, Takao T, Hayashi N. Detection of hepatitis C virus in the bile and bile duct epithelial cells of hepatitis C virus-infected patients. Hepatol 2001;33:977-80.
31. Uchida T, Shikata T, Tanaka E, Kiyosawa K. Immunoperoxidase staining of hepatitis C virus in formalin-fixed, paraffinembedded needle liver biopsies. Virchows Archiv 1994;424:465-9.
32. Eguchi Y, Mizuta T, Ishibashi E, et al. Hepatitis C virus infection enhances insulin resistance induced by visceral fat accumulation. Liver Int 2009;29: 213–20.
33. Moucari R, Asselah T, Cazals-Hatem D, et al. Insulin resistance in chronic hepatitis C: association with genotypes 1 and 4, serum HCV RNA level, and liver fibrosis. Gastroenterol 2008;134:416-23.
34. Zhang FM, Chen LH, Chen HT, Shan GD, Hu FL, Yang M, et al. Hepatitis C Virus Infection Is Positively Associated with Gallstones in Liver Cirrhosis. Digestion 2016;93:221-8
35. Dai CY, Lin CI, Yeh ML, et al. Association between gallbladder stones and chronic hepatitis C: ultrasonographic survey in a hepatitis C and B hyperendemic township in Taiwan. The Kaohsiung Journal of Med Sci 2013;29(8): 430-5.
36. Li X, Wang Z, Wang L, Pan M, Gao P. Liver cirrhosis: a risk factor for gallstone disease in chronic hepatitis C patients in China. Medicine 2017;96(26):e7427.

Original Article

Study of Prevalence of Iron Deficiency Anaemia in Children with Chronic Diarrhoea

Abid Ali[1], Muhammad Idris Mazhar[2] and Mazhar Nazir Chattha[2]

ABSTRACT

Objective: To find out the prevalence of iron deficiency anaemia (IDA) in children, coming to hospital with chronic diarrhoea and to see risk factors in these children, like age, gender, socioeconomic status, education of mother, feeding habits and nutritional status.

Study Design: Analytical / cross-sectional study

Place and Duration of Study: This study was conducted at Department of Paediatrics, Islam Medical & Dental College, Sialkot from February 2009 to March 2010.

Materials and Methods: One hundred children were included on the basis of systemic random sampling method. Children with chronic diarrhoea (>14 days), both OPD and admitted patients, up to five years of age and either sex were included. The demographic profile was obtained like age, sex, detailed nutritional history, socioeconomic status, educational status of parents. Height and weight was recorded. Clinical assessment of hydration status, pallor and signs of malnutrition as well as other signs of systemic illness were recorded. The blood samples were taken for Hb and TIBC.

Results: There were 52 males and 48 females. Female children were having higher ratio of anaemia as compared to males (38/48 –79.2% versus 30/52–57.7%). Majority of children with lower socioeconomic status (45/56 – 80.4%) were anaemic. 83.3% of children of mothers with under primary or primary to middle education, were anaemic. The mothers who had better education (above middle class), 86.4% of their children were non anaemic. It was found that 20% of children of both genders were well nourished and among these, only 2 children were anaemic. The other 20 children (20%) had First degree malnutrition and among this group, 11 children (55%) were anaemic. Among the second degree malnutrition children (35), 30 children (85.7%) were anaemic. Another group of patients having 3rd degree malnutrition (25) of both genders, all children (100%) were anaemic. Only 15 children were on exclusive breast feeding (2 anaemic {13.3%}), 30 children on mixed (15 anaemic {50%}) and 55 children were on bottle feeding (51 anaemic {92.7%}). The difference for Hb level and TIBC were significant (<0.001).

Conclusion: Iron deficiency anaemia was a constant feature in all children having chronic diarrhea. Improving maternal education (literacy rate in general), socioeconomic status of the people, and promoting exclusive breast-feeding can dramatically improve the nutritional status and general well-being of children under 5 years of age in Pakistan.

Key Words: Prevalence, Iron deficiency anaemia, Children, Chronic diarrhoea

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INTRODUCTION

Chronic diarrhoea is one of the major causes of malnutrition in children and this leads to great mortality and morbidity in developing countries.[1] Dietary iron intake, socioeconomic status, education and poor hygiene have effect of prevalence of IDA among children in addition to impaired absorption of iron in chronic diarrhea.[2] Sialkot district has population of more than 3.5 million and this study was designed to measure magnitude of problem of IDA in children with chronic diarrhea. Some factors responsible for morbidity and mortality among the children with chronic diarrhoea are nutritional status of child, late weaning, no vaccination, nature of infection, no oral hydration therapy with ORS and presence of associated complications due to diarrhoea. The incidence of diarrhoea in Pakistani children under five years of age is 3 to 4 episodes per child per year maximum in first year. Among these children 90% children has acute watery diarrhoea and 10% children has persistent (chronic) diarrhoea.[3] Non-infective chronic diarrhoea is uncommon in Pakistan except in severe protein calorie

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malnutrition.[4] In Pakistan, IDA is the most prevalent nutritional deficiency among infants and children accounting for 83% of all anaemias. Prevalence rates vary from 60-80% among infants and children.[3]

The iron deficiency anaemia is secondary to many causes. However, in this study, the aim was to find out the incidence of IDA in children less than five years of age, coming to hospital with chronic diarrhea and to see risk factors in these children, like age, gender, socioeconomic status, education of mother, feeding habits and nutritional status.

MATERIALS AND METHODS

This study was conducted at Department of Paediatrics, Islam Medical & Dental College, Sialkot from February 2009 to March 2010. Patients taken from three hospitals; THQ Civil Hospital, Daska, Ali Hospital, Daska and City Hospital, Sialkot. One hundred children were included on the basis of systemic random sampling method. Children with chronic diarrhea (>14 days), both out-patient and admitted patients, up to five years age and either sex were included. Those having history of blood loss, serious co-morbid conditions like cardiac, respiratory, renal etc, and with haemolytic anaemia e.g. thalassemia and others, were excluded. Informed consent was taken from parents of children. All mothers/ attendants of 100 children were interviewed. The demographic profile was obtained like age, sex. Detailed nutritional history, socioeconomic status, educational status of parents, was obtained. The anthropometric measurements like height and weight of the children were taken. Clinical assessment of hydration status, pallor and signs of malnutrition as well as other signs of systemic illness were recorded. The blood samples for lab investigations were taken for Hb and TIBC. Nutritional status of children was assessed according to Modified Gomez Classification. The hydration status was reported using WHO classification and graphically presented. The mode of feeding was also studied and mentioned as exclusive breast feeding, mixed breast and bottle feeding and only bottle feeding. All the collected information were entered into SPSS and analyzed accordingly. The outcome variables were tested for significance by applying chi square test on qualitative variables and t-test on quantitative variables. P value <0.05 was considered significant.

RESULTS

There were 52 males and 48 females (Table 1). In order to measure the prevalence of IDA in the sample group, it was found that among 52 male children, 30 (57.7%) were anaemic. Similarly among 48 females, 38 children (79.2%) had IDA. The female children had higher ratio of anaemia as compared to males with p value 0.037 (Table 2). It was found that percentage of anaemia rose with increasing age with chi square value 14.77 and p value 0.003. Only 5 patients of both genders were of age group 37-60 months and all these were anaemic (Table 3). Regarding nutritional status of children in this study, it was found that 20% of children of both genders were well nourished and among these well nourished children, only 2 children were anaemic and 18 were not anaemic. The other 20 children (20%) had 1st degree malnutrition and among this group, 11 children (55%) were anaemic. Among the second degree malnutrition children (35), 30 children (85.7%) were anaemic. Another group of patients having 3rd degree malnutrition (25) of both genders, all (100%) were anaemic. The prevalence of IDA was observed more in malnourished children as compared to well nourished children and was significant with chi square value 49.28 and p value of <0.001 (Table 4).

The data collected about feeding pattern of mothers showed 15 children were on exclusive breast feeding, 30 were having mixed breast and bottle feeding and 55 children were on bottle feeding only. Among these, 2 (13.3%), 15 (50%) and 51 (92.7%) respectively were anaemic. The association of IDA with feeding habits was strongly associated with chi square value 43.34 and p value <0.001 (Table 5).

Table No.1: Distribution of children with chronic/ persistent diarrhea by age and sex (n = 100)

Age (months)	Male (n=52)		Female (n=48)	
	No.	%	No.	%
0 – 6	4	7.7	6	12.5
7 – 12	18	34.6	17	35.4
13 – 24	23	44.3	17	35.4
25 – 36	4	7.7	6	12.5
37 – 60	3	5.7	2	4.2

Chi square value = 1.77 **P value 0.778**

Table No.2: Distribution of children with chronic/ persistent diarrhea by sex and anaemia status

Sex	IDA (n=68)		Normal (n=32)	
	No.	%	No.	%
Male	30	44.2	22	68.7
Female	38	45.8	10	31.3

Chi square value = 4.35 **P value 0.037**

Table No.3: Distribution of children with chronic/ persistent diarrhea by age and anaemia status

Age (months)	IDA (n=68)		Normal (n=32)	
	No.	%	No.	%
0 – 6	3	4.4	7	21.8
7 – 12	22	32.4	13	40.7
13 – 24	33	48.6	7	21.8
25 – 36	5	7.3	5	15.7
37 – 60	5	7.3	-	-

Chi square value = 14.77 **P value 0.003**

In order to measure the prevalence of IDA in the sample group, the standard value of Hb was fixed below 12 g/dl and for TIBC above 450. The average Hb level for anaemic children was 8.34±1.03 g/dl and for

those who were not anaemic, the average Hb level was recorded 12.35±0.42 g/dl (Table 6).

The average TIBC level was recorded 657.7±81.2 mg/dl and for those who were not anaemic, the average TIBC level was 309.42_+ 61.13 mg/dl. The difference for Hb level and TIBC were significantly different, both with p value <0.001. All children who were anaemic with Hb below 12 g/dl were having there TIBC level above 450 mg/dl (Table 7).

Table No.4: Distribution of children with chronic/ persistent diarrhea by nutritional status as per modified Gomez classification and anaemia status

Nutritional status (%)	IDA (n = 68)		Normal (n=32)	
	No.	%	No.	%
≥ 80	2	2.9	18	56.3
70 – 80	11	16.2	9	28.1
60 – 70	30	44.2	5	15.6
<60	25	36.7	-	-

Chi square value = 49.28 P value 0.001

Table No.5: Distribution of children with chronic/ persistent diarrhea by feeding habits and anaemia status (n = 100)

Feeding habits	IDA (n = 68)		Normal (n=32)	
	No.	%	No.	%
Breast feeding	2	2.9	13	40.6
Bottle & breast feeding	15	22.1	15	46.9
Bottle feeding	51	75.0	4	12.5

Chi square value = 43.34 P value 0.001

Table No.6: Distribution of children with chronic/ persistent diarrhea by haemoglobin level

Haemoglobin level	IDA (8.34±1.03)	Normal (12.35±0.42)	Total
6.0 – 7.5	16	-	16
7.6 – 9.0	37	-	37
9.1 – 10.5	10	-	10
10.6 – 12.0	5	-	5
> 12	-	32	32
Total	68	32	100

Table No.7: Distribution of children with chronic/ persistent diarrhea by TIBC level

TIBC level	IDA (657.7±81.2)	Normal (309.42±61.13)	Total
700-900	16	-	16
600–700	37	-	37
450-600	15	-	15
<450	-	32	32
Total	68	32	100

DISCUSSION

Diarrhea accounted for 8% of death in children less than 5 years of age in 2016 worldwide.[5] Chronic diarrhoea is one of the major causes of malnutrition in children under two years of age and this leads to great morbidity and mortality in developing countries. It is responsible for more than 30% of diarrhoeal deaths in 1 to 11 months old infants in Pakistan.[6] The outcome of acute diarrhoea has improved significantly worldwide with use of oral rehydration solution (ORS). However, chronic diarrhoea is still harmful, because less than five years of age, 10% of acute episodes of diarrhoea turn into prolonged diarrhoea (chronic/persistent) in developing countries like Pakistan.[7] The incidence and mortality is especially high in infancy and more so in the presence of malnutrition and lack of breast feeding. Iron deficiency anaemia is very common among children with chronic and/or persistent diarrhoea due to malabsorption as well as inadequate dietary intake during diarrhoeal episodes. The socioeconomic status is contributory to IDA.[8]

Majority of the patients in our study (85%) were below 2 years of age. Majority of patients were below two years of age as seen in a Pakistani and Indonesian study.[9,10] There was no significant importance of sex regarding the prevalence of IDA among the children who have chronic or persistent diarrhoea. In current study 52% children are male and 48% children are female. The male to female ratio in our study is consistent with previous studies. The study by KCC foundation had male to female ratio of 52:48.[11] In a study by Lutter and reported that male to female ratio was 62.7% to 33.3%.[12] Our study showed majority of the patients (80%) having malnutrition with severe malnutrition in 25% of the patients. In a study by Akinbami et al[13] reported that 61% patients were malnourished while 80% of children in a study done by KCC Foundation were suffering from some degree of malnutrition. 64% of patients suffering from persistent diarrhea had PCM grade 3.[11] Stunted children are more likely to be suffering from anemia as seen in Pakistan and Nepal.[22]

From the data collection, the findings which were collected regarding socioeconomic status and education level, it was observed that poverty and maternal illiteracy were leading factors for promoting diarrhoea in under five years of age. Mode of feeding and food practices during diarrhoea, were directly related to level of maternal education. Almost half of the mothers were illiterate and only 22% of the mothers had middle or secondary school education. Ninety percent of the patients were coming from lower and middle class socio-economic status. In other studies done by Ali & Zuberi.[14] and Community Health Center, Agha Khan University Karachi also showed significant correlation with maternal education and low socio-economic status. Lower socioeconomic status and lower education was also associated with increased chances of anaemia in

rural area of Yemen[15] and also in Indonesia.[16] These factors were mainly responsible for increasing susceptibility to diarrhoea in developing countries like Pakistan.

In this research work, it was found that all patients who had persistent/ chronic diarrhoea had mild to moderate anaemia. Sixty seven percent of the patients had haemoglobin levels between 8-10 gm/dl while no patients had severe anaemia. A cross sectional case control study was done in Kinder Garten children of Gaza suffering from acute diarrhoea revealed that 21.8% had iron deficiency anaemia as compared to 14.8% of controls.[17] Children living in urban slums of Indonesia had increased chances of anaemia if suffering from diarrhoea.[10] The BRINDA Project also revealed that inflammation in the high and very high infection group isassociated with anaemia.[18] In a Nepalese study anaemia was present in 52% of children suffering from acute diarrhoea.[19] However a case control study in Karachi did not show significant effects of recurrent diarrhoea and respiratory infections on anaemia in children.[20]

The outcome of acute diarrhoea has improved significantly worldwide with use of oral rehydration solution. Chronic diarrhoea causes malnutrition which is a negative indicator for mortality.[21] To reduce the incidence of chronic diarrhoea and iron deficiency anaemia, it is recommended to improve education level of mothers (improved literacy rate), promoting exclusive breast feeding, and improving socioeconomic conditions of the people. This can dramatically affect the outcome and improvement of the general well being of the children under five years of age in Pakistan.

CONCLUSION

Persistent or chronic diarrhoea is becoming recognized as an important child health problem in developing countries like Pakistan. The incidence is much higher among the children age less than two years. In our study, iron deficiency anaemia was a constant feature in all children having chronic/persistent diarrhoea while TIBC was high in all patients. Male to female ratio remained 1:1 in almost all instances. Majority of the patients (85%) were below 2 years of age and 90% of the children were coming from lower and middle socio-economic status. Almost half of the mothers / attendants were illiterate and 22% had education level of middle and higher secondary school. Many of the patients (80%) had some degree of malnutrition, with 25% having severe malnutrition. Only 15% of the children had exclusive breast feeding while 55% had bottle feeding. Thirty percent of the patients had received mixed breast and bottle feeding.

Author's Contribution:

Concept & Design of Study:	Abid Ali
Drafting:	Muhammad Idris Mazhar
Data Analysis:	Mazhar Nazir Chattha
Revisiting Critically:	Abid Ali, Muhammad Idris Mazhar
Final Approval of version:	Abid Ali

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

REFERENCES

1. Tette EMA, Sifah EK, Nartey ET. Factors affecting malnutrition in children and the uptake of interventions to prevent the condition. BMC Pediatr 2015;15:189-95.
2. Bailey RL, West KP Jr, Black RE. The epidemiology of global micronutrient deficiencies. Ann Nutr Metab 2015;66(suppl 2):22-33.
3. Hanif SM, Maqbool S, Arif MA. A textbook of paediatrics. 5th ed. Lahore: Pak Book Corporation; 2008.p.493-556
4. Khan SR. Clinical paediatrics. 2nd Ed. Lahore: Pak Book Corporation 2008; 53-60.
5. Clark A, Black R, Tate J, Roose A, Kotloff K, Lam D, Steele D. Estimating global, regional and national rotavirus deaths in children aged <5 years: Current approaches, new analyses and proposed improvements. PLoS ONE 2017; 12(9): e0183392.
6. Rahman AE, Moinuddin M, Molla M, Worku A, Hurt L, Kirkwood B, Mohan SB, Mazumder S, Bhutta Z, Raza F, et al. Childhood diarrhoeal deaths in seven low-and middle-income countries. Bulletin of the World Health Organization 2014;92:664-71.
7. Khan SR, Jalil F, Zaman S, Lindblad BS, Karlberg J. Early child health in Lahore, Pakistan: X. Mortality Acta Paediatr 1993;82(Suppl 390): 109-17.
8. Idris M, Anis R. Iron deficiency anaemia in moderate to severely anaemic patients. J Ayub Medi Coll Abbottabad 2005; 17(3):45-7.
9. Ahmed M, Billoo AG, Murtaza G. Risk factors of persistent diarrhoea in children below five years of age. JPMA 1995;45(11):290-2.
10. Semba RD, de Pee S, Ricks MO, Sari M, Bloem MW. Diarrhea and fever as risk factors for anemia among children under age five living in urban slum areas of Indonesia. Int J Infect Dis 2008;12(1): 62-70.
11. KCC Foundation. Report of a scientific group 1999.
12. Lutter CK. Iron deficiency in young children in low-income countries and new approaches for its prevention. J Nutr 2008;138(12): 2523-8.
13. Akinbami FO, Elnour IB, Nirmala V. Chronic diarrhoea in children: a prospective analysis of causes, clinical features and outcome. Bahrain Med Bull 2001; 23(4): 45-9.

14. Ali NS, Zuberi RW. Association of Iron Deficiency Anaemia in children of 1-2 years of age with low birth weight, recurrent Diarrhoea or recurrent Respiratory Tract Infection-a myth or fact? JPMA 2003;53(4):133.
15. Al-Zabedi EM, Kaid FA, Sady H, Al-Adhroey AH, Amran AA, Al-Maktari MT. Prevalence and risk factors of iron deficiency anemia among children in Yemen. Am J Health Res 2014;2(5):319-26.
16. Howard CT, de Pee S, Sari M, Bloem MW, Semba RD. Association of diarrhea with anemia among children under age five living in rural areas of Indonesia. J Tropical Pediatr 2007;53(4):238-44.
17. -Al-Laham NA, Elyazji MS, Al-Haddad RJ, Ridwan FN. Possible hematological changes associated with acute gastroenteritis among Kindergarten children in Gaza. Ann Med Health Sci Res 2015;5(4):292-8.
18. Engle-Stone R, Aaron GJ, Huang J, Wirth JP, Namaste SM, Williams AM, et al. Predictors of anemia in preschool children: Biomarkers Reflecting Inflammation and Nutritional Determinants of Anemia (BRINDA) project. Am J Clin Nutr 2017;106(suppl_1):402S-15S.
19. Chandyo RK, Ulak M, Adhikari RK, Sommerfelt H, Strand TA. Prevalence of iron deficiency and anemia among young children with acute diarrhea in Bhaktapur, Nepal. Health Care 2015;3(3): 593-606.
20. Ali NS, Zuberi RW. Association of Iron Deficiency Anaemia in children of 1-2 years of age with low birth weight, recurrent diarrhoea or recurrent respiratory tract infection - a myth or fact? JPMA 2003;53(4):133-6.
21. Thapar N, Sanderson IR. Diarrhoea in children: an interface between developing and developed countries. Lancet 2004;363(9409):641-53.
22. Harding KL, Aguayo VM, Namirembe G, Webb P. Determinants of anemia among women and children in Nepal and Pakistan: An analysis of recent national survey data. Matern Child Nutr 2017;31:e12478.

Original Article

Detection of Suspected Placental Invasion by MRI - A Prospective Study in a Tertiary Care Hospital

Sadaf Nasir, Saleha Anwar and Bushra Rehan

ABSTRACT

Objective: To evaluate the diagnostic value of MRI features used for detecting suspected placental invasion.
Study Design: Prospective / Observational study
Place and Duration of Study: This study was conducted at the Radiology Department Liaquat National Hospital and Medical College, Karachi June 2015 to December 2017.
Materials and Methods: All the patients referred to MRI department for the evaluation of placental invasion over 18 months and then went for surgery were included in the study. MRI images of all the patients who met the inclusion criteria were evaluated for placental invasion according to the established MR criteria and the findings were correlated with surgical findings.
Results: Total 9 patients met the inclusion criteria with a mean gestational age of 32 weeks. All of these patients had placenta previa and history of multiple previous C-sections. Placental invasion was proven (both surgically and pathologically) in 5 cases (55%). Out of which 3 had pathologically proven increta (60%), one had pathologically proven accreta (20%) and one had pathologically proven percreta (20%). MR evaluation of these patients showed focal interruption of myometrial band, thick intra-placental bands, heterogenous signal intensity of placenta and focal uterine bulging. The MR features of 4 non-invasive placentas include prominent flow voids on fetal and maternal surface of placenta and focal interruption of retro-placental myometrial border. One of the patient had thin intra-placental band.
Conclusion: We found that focally interrupted myometrial border was found to be the least sensitive MR feature. Thick intra-placental bands, heterogenous placental signal intensity and disorganized intra-placental vessels were the sensitive MR features for invasion.

Key Words: MRI pelvis, placenta previa, placenta accrete, placenta percreta, placenta increta.

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INTRODUCTION

Placenta accreta is abnormal placentation in which placenta is either abnormally adherent or invaded into the uterine myometrium. It is further classified into three entities namely placenta accreta vera, placenta increta and placenta percreta, based on depth of placental invasion into the myometrium. 'Placenta accreta vera' refers to abnormally attached placenta to myometrium without definite evidence of invasion.'Placenta increta' refers to invasion of placenta into the myometrium, without crossing the serosal surface of placenta.' Placenta percreta' refers to invasion of placenta through whole thickness of myometrium with disruption of the serosal layer with or without invasion of adjacent pelvic viseras.[1,2]

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The two most common risk factors are placenta previa and previous cesarean section and its prevalence is rising because of the rising percentage of cesarean section and advanced maternal age.[3,4]
Accurate prenatal diagnosis allow optimal obstetric management. Ultrasound remains the first line modality for the diagnosis of placenta accreta. MRI is used in equivocal cases for the evaluation of posterior placentas.[1,2,3]
The aim of our study is to evaluate the diagnostic value of MR features for detecting suspected placental invasion in our population.

MATERIALS AND METHODS

The design of our study is prospective observational. All patients who came to our institution with suspicion of invasive placenta from June 2015 to December 2017 were included in the study. Pelvic MRI of all of these patients was performed using 1.5T MR unit (Toshiba).
MR protocol used includes: fast spin echo T2 weighted images in axial, sagittal and coronal planes, T1 weighted images in axial and sagittal planes, STIR in axial, sagittal and coronal planes. For all the above-mentioned sequences the slice thickness was 4mm –

5mm with a 1mm gap and FOV was 350- 400mm. To reduce the respiratory artifacts we use the breath holding technique. We did not use any intravenous MR contrast. All MR images were reviewed according to the established MR criteria for placental invasion previously described in literature. It includes following features: (1) focal uterine bulging (a focal outward bulge or disruption of normal pear shaped myometrium of uterus), (2) heterogenous signal intensity of placenta (due to intra-placental hemorrhages), (3) dark thick intra-placental bands (nodular or linear areas of low SI on T2 weighted images, usually extend from the uterine–myometrial surface and have varying thickness and random distribution), (4) focally interrupted myometrial border (lack of myometrium at the site of placental invasion), (5) tenting of urinary bladder wall (represents bladder wall invasion) and (6) direct invasion of pelvic organs.

MRI findings were correlated with surgical findings and/or surgical pathology. Those patients whose surgical record were not available for correlation were excluded from the study.

Statistical analysis was performed using SPSS for windows version 2

RESULTS

11 pregnant patients underwent MRI for suspicion of placental invasion with a mean gestational age of 32.7 weeks and mean age of the women was 31.7(+-2.4) years. 2 (18%) out of 11 patients were excluded from the study due to unavailability of surgical records, as these patients were lost to follow up. The rest of 9 patients were followed till their time of delivery. All these patients had placenta previa and history of multiple C-sections (table 1). 5 (55%) out of 9 patients had proven placenta accreta either surgically or pathologically and all these patients underwent hysterectomy. In 4 (44%) out of 9 patients no placental invasion was found at surgery and the placenta was removed manually without any bleeding complication so there was no need of hysterectomy in these patients. Out of 5 positive cases 3 patients had pathologically proven placenta increta, one patient had pathologically proven percreta and one had pathologically proven accrete vera.

MR evaluation of cases is summarized in table 2. MRI of all invasive placentas shows thick dark intra-placental bands, heterogenous placental signal intensity and focal interruption of retro-placental myometrial band. Focal uterine bulging was seen in 3 out of 5 patients. There is invasion of placenta into adjacent pelvic organs in one patient. MRI evaluation of non-invasive placentas show focal interruption of retro-placental myometrial band in 3 patients and thin dark deep intra-placental band in 1 patient.

Table No.1: Details of patients with placenta previa and history of multiple C-sections

Patients age in yrs (n=9)	Gestational age in weeks	Placental previa	Previous C-section
35	30	Complete, central	2
28	31	Anterior, marginal	3
33	35	Complete, posterior	3
32	34	Complete, posterior	3
30	32	Complete, posterior	1
32	33	Complete, central	2
29	33	Posterior, marginal	2
35	30	Complete, posterior	3
32	37	Complete, anterior	4

Table No.2: Details of patients underwent hysterectomy

Patient's age in years	Surgical/ H/P diagnosis of placenta	MRI findings					
		Focal uterine bulging	Heterogenous SI of placenta	T2 dark bands	Focal inter-ruption of myometrium	Tenting of UB	Infiltration of pelvic organs
35	Percreta	Yes	Yes	Large	Yes	Yes	Yes
28	Normal	No	No	Small	Yes	No	No
33	Increta	Yes	Yes	Large	Yes	No	No
32	Increta	Yes	Yes	Large	Yes	No	No
30	Normal	No	No	No	Yes	No	No
32	Increta	No	Yes	Large	Yes	No	No
29	Normal	No	No	No	No	No	No
35	Accreta vera	No	Yes	Small	Yes	No	No
32	Normal	No	No	No	Yes	No	No

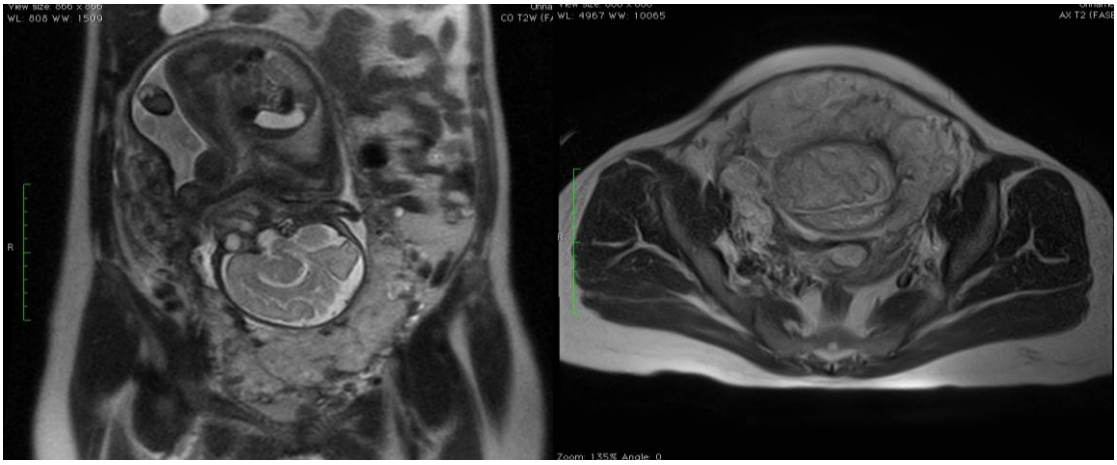

Figure No.1: T2 weighted coronal and axial MRI images of one the patient with invasive placenta, showing heterogeneous placenta with focal uterine bulging and multiple thick intra-placental bands

Diagnostic value of 5 observed MRI-features in invasive and non-invasive placentas is demonstrated in table 2. Dark deep intra-placental bands and heterogenous signal intensity of placenta are the 2 most significant MR features for detecting placental invasion (p-value = 0.008 for each feature) and the focal interruption of retro-placental myometrial band was found to be the least sensitive MRI feature (p-value=0.444).

DISCUSSION

Placenta accreta this risk increases to 67% in women with placenta previa along with previous three or more cesarean sections[7]. A pregnancy following a previous placenta accreta is at increased risk for severe placental attachment. It occurs when the chorionic villi (CV) of placenta invades the myometrium abnormally due to defect in the decidua basalis[5]. Placenta accreta is used as a broad term for invasive placentation and is classified on the basis of the degree of myometrial invasion into 3 entities namely: Placenta accrete vera, Placenta increta and Placenta percreta. In placenta accrete vera, the mildest form, chorionic villi are attached to the myometrium but do not invade the muscles. In placenta increta chorionic villi invades the myometrium partially while in placenta percreta, the most severe form, there is complete invasion of myometrium through uterine serosa into adjacent pelvic organs[4, 5].

Previous cesarean delivery and placenta previa are the two most common risk factors for placenta accreta[6]. In women with placenta previa there is 24% risk of placenta accreta and maternal outcomes such as recurrent accreta, uterine rupture, and peri-partum hysterectomy [(8)] . In our study all patients with invasive placentas had history of at least 2 previous C-sections which itself is a grave risk factor.

The accurate prenatal diagnosis of invasive placenta reduces the morbidity, complication rate and length of hospital stay as it allows optimal obstetric management (deciding the time of delivery and site of surgical incision), proper patient's counselling and planning for the type of resources needed at the time of delivery (including arrangement of blood products, recruitment of skilled surgical and anesthesia team, possible intervention guided procedures like uterine artery embolization and post operative intensive care unit[1,3].

Grey scale and color Doppler ultrasound of placenta remains the most commonly used and first line imaging modalities for the diagnosis of placental invasion as it is inexpensive, widely available and cost effective[2,4]. As ultrasound is operator dependent there is a wide variation in accuracy of grey scale and color Doppler ultrasonography in prenatal diagnosis of placenta accreta with sensitivity varying 33% to 100%[9-14]. There are limitations of ultrasound in diagnosis of placental invasion in cases of large body habitus and posterior placenta resulting in equivocal ultrasound findings [(3,4)]. Magnetic resonance imaging (MRI) is another diagnostic tool and has been widely used for further improving the prenatal diagnosis of placenta and acts as a problem-solving tool in cases of equivocal ultrasound findings[15]. Several MR features have been described in literature for the diagnosis of placenta accreta and among these features some are consistently associated with placental invasion[1-4].

In 2013 Alamo et al[3] stated that the combination of four imaging features increases the specificity of MRI. These four features are the T2-hypointense intra-placental bands, a focally interrupted myometrial border, infiltration of the pelvic organs and tenting of the bladder wall, the so-called "gold combination" in their study. In our study the tenting of urinary bladder wall and infiltration of pelvic organs were found only in one patient with surgically proven placenta percreta where as the focal uterine bulging and focal interruption of myometrium are found to be sensitive MR features in diagnosing placental invasion. The results of Alamo, et al.[3] suggests that reorganisation of myometrium/

placental interface to comment on focal interruption of myometrium requires experience in evaluation of placental MR studies and they recommend to perform MRI for placental invasion before 35 weeks of gestational age for better diagnosis.

In concordance with the MR imaging findings of Derman et al. in 2011[2] and Lax et al[16], we also found the thick dark intra-placental bands and heterogenous signal intensity in all invasive placentas.

Mansur, et al in 2011[4] conclude that MRI hand in hand with ultrasound is important for accurate diagnosis of placenta previa and seriously coexisting placenta accrete.

CONCLUSION

In conclusion we found thick dark intra-placental bands, heterogenous signal intensity of placenta and focal uterine bulging as the most reliable MR features. Focal interruption of retro placental myometrium was also identified at the sites of placental invasion but it was also seen in non-invasive placentas probably due to marked thinning of myometrium at the site of previous scar.

Author's Contribution:

Concept & Design of Study:	Sadaf Nasir
Drafting:	Saleha Anwar
Data Analysis:	Bushra Rehan
Revisiting Critically:	Sadaf Nasir, Saleha Anwar
Final Approval of version:	Sadaf Nasir

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

REFERENCES

1. Baughman WC, Corteville FE, Shah RR. Placenta accreta: spectrum of ultrasound and MR imaging findings. Radio Graphics 2008;28(7):1905-1916.
2. Derman AY, Nikac V, Haberman S, Zelenko N, Opsha O, Flyer M. MRI of placenta accreta: a new imaging perspective. AJR 2011;197:1514-1521.
3. Leonor A, Anaye A, Rey J, Denys A, Bongartz G, Terraz S, et al. Detection of suspected placental invasion by MRI: Do the results depend on observer experience? Eur J Radiol 2013;82: 51-57.
4. Mansour SM, Elikhyat WM. Placenta previa-accreta: Do we need MR imaging? The Egyptian J Radiol Nuclear Med 2011;42:433-442.
5. Verghare B, Singh N, George RAN, Gilvas S. Ind J Radiol Imag 2013;23(4):379-385.
6. Millar DA, Chollet JA, Goodwin TM. Risk factors for placenta previa – placenta accrete. Am J Obstet Gynaecol 1997;177: 210-214
7. Clark SL, Koonigh PP, Prelan JP. Placenta previa/accreta and prior cessarean section. Obstet Gynecol 1985; 66: 89-92
8. Eshked T, Weintrab AX, Sergienleo R, Sheiner E. Placenta accreta: Risk factors, perinatal outcomes and consequences for subsequent births. Am J Obstet Gynaecol 2013;208(3): 219e1-219e7.
9. Lam G, Kuller J, McMahon M. Use of magnetic resonance imaging and ultrasound in the antenatal diagnosis of pla- centa accreta. J Soc Gynecol Investig 2002; 9:37–40.
10. Finberg HJ, Williams JW. Placenta accreta: prospective diagnosis in patients with placenta previa and prior cesare- an section. J Ultrasound Med 1992; 11:333–343.
11. Levine D, Hulka CA, Ludmir J, Li W, Edelman RR. Placenta accreta: evaluation with color Doppler US, power Doppler US, and MR imaging. Radiol 1997; 205:773–776.
12. Chou MM, Tseng JJ, Ho ESC. Prenatal diagnosis of placenta previa accreta by transabdominal color Doppler ultra- sound. Ultrasound Obstet Gynecol 2000;15:28–35.
13. Comstock CH, Love JJ, Bronsteen RA, et al. Sonographic detection of placenta accreta in the second and third trimesters of pregnancy. Am J Obstet Gynecol 2004;190:1135–1140.
14. Wong HS, Zucollo J, Parker S, Burns K, Tait J, Pringle KC. Antenatal diagnosis of non-previa placenta increta with histological confirmation. Ultrasound Obstet Gynecol 2006; 27:467–469.
15. Warshak CR, Eskander R, Hull AD, Sciocia AL, Matterey RF, Benischke K, et al. Accuracy of ultrasonography and magnetic resonance imaging in the diagnosis of placenta accreta. Obstet Gynaecol 2006; 108:573-81.
16. Lax A, Prince MR, Mennitt KW, Schwebach JR & Budorick NE. the value of specific MR features in the evaluation of suspected placental invasion. Magn Reson Imaging 2007; 25:87-93.

Original Article

Awareness of Iodized Salt

Frequency and Awareness of Iodized Salt among the General Population of Karachi

Kiran Mehtab and Tafazzul H. Zaidi

ABSTRACT

Objective: To assess the frequency of people using iodized salt and to assess the awareness of people about its harmful effects.

Study Design: Cross-sectional study

Place and Duration of Study: This study was conducted at the Department of Community Medicine, Jinnah Postgraduate Medical Centre, Karachi from February to May 2018.

Materials and Methods: A study was conducted on a sample of 384 individuals. The sample was taken through Non-Probability Purposive Sampling from all the districts of Karachi. An informed verbal consent was taken from the people. A self-administered structured questionnaire was developed for the interview, Pilot study was conducted to assess the authenticity of the questionnaire. The questionnaire was then distributed, got filled, data was entered and analyzed using SPSS version 20, with 95% confidence interval and 0.05 p-value was taken as statistically significant.

Results: A total of 384 adults were interviewed. Out of them 21.6% were males and 78.4% were females. Only 36.5% people were using the iodized salt while the majority i.e. 63.5% were using the salt devoid of iodine. 42.7% of the individuals knew that not using iodized salt can cause diseases, on the contrary, a significant amount i.e. 57.3% of the persons were unaware that iodine deficiency can lead to pathological issues as well. Only 47.4% people knew that iodized salt is beneficial for pregnant ladies, while just 37.5% of the respondents were aware that goiter is caused by iodine deficiency. 57.6% of the public knew that surgery is suggested by the doctor for goiter. On the other hand, only 32.0 % individuals were aware that iodine deficiency can cause stunted growth. And just **18.2%** people believed that iodine deficiency can cause delayed puberty.

Conclusion: The study concluded that majority of population had meager knowledge of the benefits of iodized salt and are not well aware of the outcomes of its deficiency. The main factor responsible for iodine deficiency is a low dietary supply of iodine.

Key Words: Iodine, Benefits, Deficiency, Goiter, Mental retardation, General Public

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INTRODUCTION

Iodine plays the pivotal role in metabolism of the body since it is the key component of the thyroid hormone (T3,T4).[1] Thyroid hormone is essential for normal development, growth, neural differentiation, and metabolic regulation.[2,3] Deficiency of thyroid hormone makes a person suffer in various ways. The action of thyroid hormones (THs) in the brain is strictly regulated, since these hormones play a crucial role in the development and physiological functioning of the central nervous system (CNS).[4] The establishment of the essential link among iodine deficiency, thyroid function and brain development has emerged from a fascinating combination of clinical, epidemiologic and experimental studies. The central human phenomenon that focuses this relationship is the condition of endemic cretinism, described from the Middle Ages and characterized in its fully developed form by severe brain damage, deaf mutism and a spastic state of the hands and feet.[5]

It is demonstrated that iodine deficiency can be considered as sole cause of many thyroid abnormalities including mental disorders. Iodine deficiency of sufficient degree to cause hypothyroidism during fetus life and early infancy will be accompanied with brain abnormality possibly to the stage of mental retardation.[6]

Not everyone has an ample access to the natural sources of iodine. 2 billion individuals worldwide have insufficient iodine intake, with those in south Asia and sub-Saharan Africa particularly affected. Iodine deficiency has many adverse effects on growth and development.[7]

The adverse effects of iodine deficiency (ID) intellectual impairment, damaged reproduction, goiter and hypo- and hyperthyroidism are well known and easily corrected with salt iodization, but they continue to impair health and socioeconomic development, with

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more than two billion people at risk worldwide. During the major global expansion of salt iodization over the past four decades, much of Europe has remained iodine deficient.[8]

Therefore, these ailments can be avoided by adding iodine artificially in the diet to cater for the deficiency. Universal salt iodization (USI) and iodine supplementation are highly effective strategies for preventing and controlling iodine deficiency. USI is now implemented in nearly all countries worldwide, and two-thirds of the world's population is covered by iodized salt. [9]

Iodine deficiency early in life impairs cognition and growth, but iodine status is also a key determinant of thyroid disorders in adults. Severe iodine deficiency causes goitre and hypothyroidism because, despite an increase in thyroid activity to maximize iodine uptake and recycling in this setting, iodine concentrations are still too low to enable production of thyroid hormone. In mild-to-moderate iodine deficiency, increased thyroid activity can compensate for low iodine intake and maintain euthyroidism in most individuals, but at a price: chronic thyroid stimulation results in an increase in the prevalence of toxic nodular goitre and hyperthyroidism in populations.[10]The iodine content of the Pakistani diet is significantly lower than the intakes recommended by the U.S. Food and Nutrition Board (150 μg/d) and the International Commission of Radiological Protection Board (200 μg/d). The iodine intake of the Pakistani population needs to be improved substantially[11]

MATERIALS AND METHODS

A Cross-sectional survey was conducted on a sample of 384 individuals. The sample was taken through Non-Probability Purposive Sampling from five districts of Karachi, within a study period of four months from February to May 2018. An informed verbal consent was taken from the people. A self-administered structured questionnaire was developed for interview. Pilot study was conducted to assess the authenticity of the questionnaire. The questionnaire was then distributed, got filled, data was entered and analyzed using SPSS version 20, with 95% confidence interval and 0.05 p-value was taken as statistically significant.

RESULTS

A total of 384 adults were approached. Out of them 21.6% were males and 78.4% were females. Only 36.5%people were using the iodized salt while the majority i.e. 63.5% were using the salt devoid of iodine.42.7%of the individuals knew that not using iodized salt can cause diseases, on the contrary, a significant amount i.e. 57.3% of the persons were unaware that iodine deficiency can lead to pathological issues as well. Only 47.4% people knew that iodized salt is beneficial for pregnant ladies, while just 37.5% of the respondents were aware that goiter is caused by iodine deficiency. 57.6% of the public knew that surgery is suggested by the doctor for goiter. On the other hand, only 32.0 % individuals were aware that iodine deficiency can cause stunted growth. And just 18.2% people believed that iodine deficiency can cause delayed puberty.

Table No.1: Questionnaire

S.No	Questions Asked	Yes %	No %	Chi-square	p-value	Mean	Confidence interval 95%
1	Do you use the salt promoted by the Govt.?	36.5	63.5	91.904	0.000	1.635	1.59-1.68
2	Do you know by not using iodized salt can cause diseases?	42.7	57.3	23.659	0.000	1.573	1.52-1.62
3	Do you think iodized salt is beneficial for pregnant ladies?	47.4	52.6	8.015	0.005	1.525	1.48-1.58
4	Do you know that lump in neck is caused by not using iodized salt?	37.5	62.5	9.034	0.003	1.625	1.58-1.67
5	Do you know that surgery is suggested by the doctor for neck swelling?	57.6	42.4	.047	0.829	1.424	1.37-1.47
6	Do you know that iodine deficiency can cause stunted growth?	32.0	68.0	26.273	0.000	1.680	1.63-1.73
7	Do you know that iodine deficiency can cause delayed puberty?	18.2	81.8	31.124	0.000	1.818	1.78-1.86

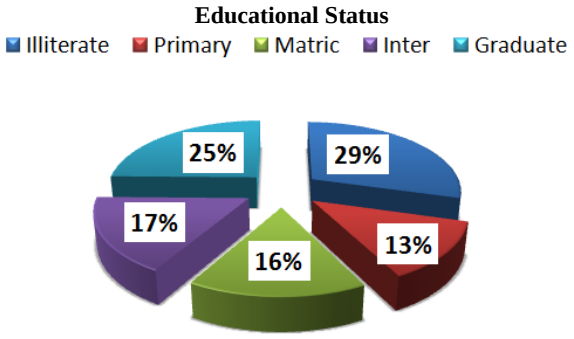
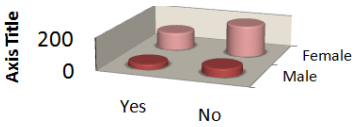


Figure No.1: The frequency of individuals belonging to different educational statuses participating in the study (N=384)

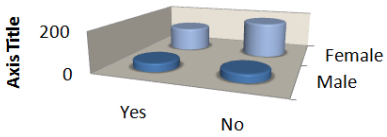
Do you use the salt promoted by the Govt.?



	Yes	No
Male	31	52
Female	109	192

Figure No.2: The frequency of individuals using iodized salt promoted by the government (N=384)

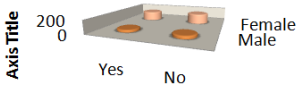
Do you know by not using iodized salt can cause diseases?



	Yes	No
Male	42	41
Female	122	179

Figure No.3: The frequency of individuals knowing the pathological consequences of not using the iodized salt (N=384)

Do you think iodized salt is beneficial for pregnant ladies?



	Yes	No
Male	38	45
Female	144	157

Figure No.4: The frequency of individuals considering iodized salt beneficial for pregnant ladies (N=384)

Do you know lump in neck is caused by not using iodized salt?

	Yes	No
Male	31	52
Female	113	188

Figure No.5: The frequency of individuals knowing the lump in neck as one of the consequences of not using the iodized salt (N=384)

Do you know that iodine deficiency can cause stunted growth?

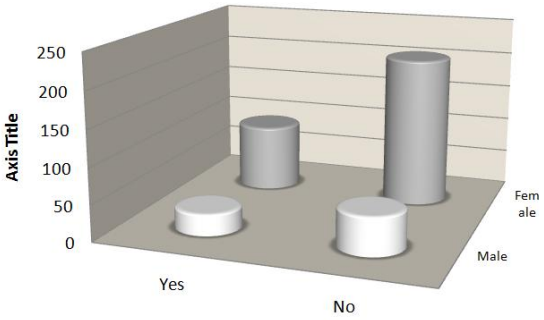
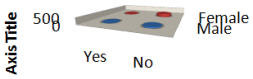


Figure No.6: The frequency of individuals knowing stunted growth as one of the outcomes of iodine deficiency (N=384)

Do you know that iodine deficiency can cause delayed puberty?



	Yes	No
Male	16	67
Female	54	247

Figure No.7: The frequency of individuals knowing delayed puberty as one of the aftermaths of iodine deficiency (N=384)

DISCUSSION

The non-metal iodine is needed for the synthesis of thyroid hormone. Since the metabolism of our body is dependent heavily over this hormone, therefore, the deficiency of iodine makes a person suffer in various ways ranging from the most visible manifestation goiter, to cretinism and reduced metabolic activities etc. When it come to the treatment, all of the aforementioned sufferings can be costly, time consuming and at times non-treatable too e.g. cretinism. Therefore, it is quite justified to say that the mere use of an iodized salt is the best, handy and cheapest method of avoiding all the diseases mentioned previously.

It is estimated that 1,570 million people are at risk of iodine deficiency. Because of the wide spectrum of disorders that IDD includes, and lack of any obvious association between iodine deficiency and its health effects, IDD is not perceived as a major public health problem. Approximately 2.2 billion (2200 million) of the world population are living in the area with Iodine deficiency (ID), most of them in the developing countries[1]. In IRAN about 2 million are exposed to Iodine deficiency. Most of the complications of ID are not curable, especially brain damage. On the other hand, adding iodine to daily salt is a suitable program for decreasing iodine deficiency [12]

Goiter is the most visible manifestation of IDD. Endemic goiter results from increased thyroid stimulation by thyroid stimulating hormone (TSH) to maximize the utilization of available iodine and thus represents mal adaption to iodine deficiency. However, the most damaging disorders induced by iodine deficiency are irreversible mental retardation i.e. cretinism. While conventionally associated with cretinism and goiter, iodine deficiency has broad effects on central nervous system development that can occur in the absence of either condition. Any maternal iodine deficiency results in a range of intellectual, motor, and hearing deficits in offspring. This loss in intellectual capacity limits educational achievement of populations and the economic prowess of nations[13]

Iodine is also essential for pregnant ladies. In pregnancy, the recommended mean daily iodine intake is of 220-250 microgram were estimated to correspond to a median UI concentration of about 150 microgram. In countries where the iodine intake is sufficient, most mothers have median breast milk iodine concentration (BMIC) greater than the concentration (100-120 microgram l- 1) required meet an infant's needs. The median UI concentration during infancy that indicates optimal iodine nutrition is estimated to be > or = 100 microg l- 1. In iodine-sufficient countries, the median UI concentration in infants ranges from 90-170 microg, suggesting adequate iodine intake in infancy.[14]

Certain studies illustrate the true status of some parts of the world with respect to iodine intake. 2 billion individuals worldwide have insufficient iodine intake, with those in south Asia and sub-Saharan Africa particularly affected[5] .One study showed that the iodine status of women in one region of New South Wales was low. These data add support to the need for a national approach to address iodine intake which includes an accompanying consumer education campaign[6] yet another the study demonstrated that the children on the island of Tanna were in a state of moderate iodine deficiency[15]

In the district of Bargarh, Orissa state, India a knowledge-attitude-practices (KAP) study was conducted along with a prevalence study of iodine deficiency disorders (IDD) between 1998-99 and this showed some astonishing results that only 37% of the males and 29.3% of the females perceived goiter as a disease. Less than 5% of both sexes knew how goiter is caused. Only 16.4% used iodized salt regularly[16]

In the past 80 years, salt has proved a reliable, safe, cheap and stable carrier to correct iodine deficiency on a large scale. The advantages of salt as a carrier largely outweigh its drawbacks, and today iodized salt is available to over one billion people[17]

Auditory disturbances may be present in iodine deficient children. Continuous iodine supplementation permanently improves the auditory thresholds of iodine deficient children[18] Moreover, another study concluded that iodized salt is an effective means of improving iodine status[19]

Successful experience from developed countries needs to be adapted to the developing country context. The increasing availability of processed foods in Pakistan provides an opportunity to increase iodine intake. However, the impact of this intervention remains to be quantified. [20]

The goal of our study is to figure out the perception of general population about the usage of iodized salt. We aimed at the people belonging to different areas of Karachi. Individuals pertaining to any age group were randomly approached.

The purpose of this study was to determine the concepts and the myths prevalent amongst the males and females of the society about the salt having iodine in it, whether the individuals know the beneficial effects or they deem it something harmful.

This study was planned to determine whether the general people have this much awareness or not. Our study brought into light that out of 384 being questioned only 36.5% were using an iodized salt. Amongst the rest, a significant number of the respondents didn't even know about this entity. While the remaining scarce amount of individuals had other reasons of not using the iodized salt including unwillingness, unaware of the benefits, unavailability etc.

Even some of our respondents complained that no one has ever informed them about the salt, had they been educated earlier they would have commenced using it straightaway. Even though the majority of public didn't have the knowledge about the iodized salt but the general attitude was a bit enthusiastic to know about it and a reasonable amount of individuals were keen to switch to iodized salt as soon as possible. By far the people were co-operative in answering the questions, but were felt a bit annoyed when the information about their children was probed.

For the upcoming researchers we strongly suggest that they should carry out the survey at villages and at other deprived areas, since we feel that the uneducated class is at a greater risk of iodine deficiency owing to their Ignorance. Moreover, we believe that both the genders

should be targeted equally in order to highlight the level of ignorance amongst the two so that appropriate measures can be taken.

CONCLUSION

The study concluded that majority of population has meager knowledge of the benefits of iodized salt and are not well aware of the outcomes of its deficiency. The most damaging disorders induced by iodine deficiency are irreversible mental retardation in children which is irreversible. Iodine Deficiency is a major public health problem in Pakistan and is a threat to the social and economic development of the country. The main factor responsible for iodine deficiency is a low dietary supply of iodine.

Author's Contribution:

Concept & Design of Study:	Kiran Mehtab, Tafazzul H. Zaidi
Drafting:	Kiran Mehtab
Data Analysis:	Kiran Mehtab
Revisiting Critically:	Tafazzul H. Zaidi, Kiran Mehtab
Final Approval of version:	Kiran Mehtab, Tafazzul H. Zaidi

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

REFERENCES

1. Gereben B, et al. Cellular and molecular basis of deiodinase-regulated thyroid hormone signaling. Endocr Rev 2008;29(7):898–938.
2. Cheng SY, Leonard JL, Davis PJ. Molecular aspects of thyroid hormone actions. Endocr Rev 2010;31(2):139–170
3. Bernal J. Thyroid hormone receptors in brain development and function. Nat Clin Pract Endocrinol Metab 2007;3(3):249–259.
4. Osama MA, El-Gareib AW, El-bakry AM, Tawab SMA, Ahmed RG. Thyroid hormones states and brain development interactions. Int J Develop Neurosci 2008;26(7):825-826.
5. Hetzel BS. Iodine and Neuropsychological Development. J Nutr 2000;130(2):493–495.
6. Mansourian AR. A review on the metabolic disorders of iodine deficiency. Pak J Biol Scie 2011;14(7):412-424.
7. Ahad F, Ganie SA. Iodine, Iodine metabolism and Iodine deficiency disorders revisited. Indian J Endocrinol Metab 2010;14(1):13–17.
8. Zimmermann MB, .Andersson M. Prevalence of iodine deficiency in Europe in 2010. Annals d'Endocrinologie 2011;72(2):164-166.
9. Andersson M, Benoist BD. Epidemiology of iodine deficiency: Salt iodization and iodine status. Clin Endocrinol 2010;24(1):1–11.
10. Zimmermann MB, Boelaert K. Iodine deficiency and thyroid disorders. Lancet 2015;3(4)-286-295.
11. Akhter P, Rehman KU, Orfi SD, Ahmad N. Assessment of iodine levels in the Pakistani diet. Nutr 2004;20(9):783–787.
12. Khajedaluee M, Rajabian R, Seyyednozadi M. Education Achievements and Goiter Size Ten Years After Iodized Salt Consuming. Int J Prev Med 2013;4(8):876-80
13. Redman K, Ruffman T, Fitzgerald P, Skeaff S. Iodine Deficiency and the Brain: Effects and Mechanisms. Critical Reviews in Food Sci Nutr 2016;56(16):
14. Zimmermann MB. Breast Milk Iodine Concentration Is a More Accurate Biomarker of Iodine Status Than Urinary Iodine Concentration in Exclusively Breastfeeding Women. Pub Health Nutr 2007;10(12):1584-95.
15. Li M, McKelleher N, Moses T, Mark J, Byth K, Ma G, Eastman CJ. Iodine nutritional status of children on the island of Tanna, Republic of Vanuatu. Pub Health Nutr 2009;12(9):1512-8.
16. Mohapatra SS, Bulliyya G, Kerketta AS, Geddam JJ, Acharya AS. Elimination of iodine deficiency disorders by 2000 and its bearing on the people in a district of Orissa, India: a knowledge-attitude-practices study. Asia Pac J Clin Nutr 2001;10(1): 58-62.
17. Zahnmed SM. Bürgi H, Zimmermann MB. Salt as a carrier of iodine in iodine deficient areas 2005; 115(8):648-50.
18. Azizi F, Mirmiran P, Hedayati M, Salarkia N, Noohi S, Rostamian D. Effect of 10 yr of the iodine supplementation on the hearing threshold of iodine deficient schoolchildren. J Endocrinol Invest 2005;28(7):595-8.
19. Wu T, Liu GJ, Li P, Clar C. Iodized salt for preventing iodine deficiency disorders. Cochrane Database of Systematic Reviews 2002;(3):1-3.
20. Spohrer R, Garrett GS, Timmer A, Sankar R, Kar B, Rasool F, et al. Processed foods as an integral part of universal salt iodization programs: a review of global experience and analyses of Bangladesh and Pakistan. Food Nutr Bull 2012;33(4 Suppl):S272-80.

Original Article

Frequency of Non-Alcoholic Fatty Liver Disease in Obese and Non-Obese Diabetics and Its Relation to Duration of Diabetes Mellitus

Shazia Siddiq[1], Kausar Malik[2] and Faiza Batool[2]

ABSTRACT

Objective: To find out the frequency of non-alcoholic fatty liver disease in obese and non-obese diabetics and its relation to duration of diabetes mellitus.

Study Design: Cross sectional study

Place and Duration of Study: This study was conducted at the Department of Medicine, Sheikh Khalifa Bin Zaid Al-Nahyan hospital Rawlakot from July 2017 to December 2017.

Materials and Methods: Patients with type 2 diabetes mellitus presenting to outpatient department were enrolled and their age, weight, height and duration of diabetes mellitus were noted. Body mass index (BMI) was calculated using formula BMI = (weight in kilograms) / (height in meters^2). Ultrasound abdomen was used to detect the presence and absence of fatty liver disease. SPSS version 20 was used for analysis of data. Chi-square test was applied to assess the significance of difference of fatty liver disease in normal weight, over weight, class I obese, class II obese and class III obese diabetics and relation of duration of diabetes mellitus with presence or absence of fatty liver disease.

Results: Out of 200 patients 10% were of normal weight, 44% were overweight and 41% had class I obesity while none had class II or class III obesity. Incidence of fatty liver was 50% in patients with normal weight, 76% of patient who were over-weight and 97% of patients with class I obesity. Also its incidence was 71% in patients with duration of disease between 1 to 4 years, 91% amongst patient with duration of diabetes between 5 to 8 years and 100% of patients with duration of diabetes between 9 to 12 years.

Conclusion: In type 2 diabetic patients Frequency of non-alcoholic fatty liver disease is high in patients who are obese as compared to patients who are non-obese and its incidence increases with increase in duration of diabetes

Key Words: Nonalcoholic fatty liver disease, Diabetes mellitus, Body mass index

Citation of articles: Siddiq S, Malik K, Batool F. Frequency of Nonalcoholic Fatty Liver Disease in Obese and Non-Obese Diabetics and Its Relation to Duration of Diabetes Mellitus. Med Forum 2018;29(8):42-45.

INTRODUCTION

Nonalcoholic fatty liver disease (NAFLD) is a major public health problem these days. It include steatosis, Nonalcoholic steatohepatitis (NASH), fibrosis, cirrhosis and ultimately hepatocellular carcinoma.[1]

About three decades ago Ludwig et al delineate liver lesions similar to alcohol associated lesions within liver in patients who did not take alcohol and called it NAFLD.[2]

Its definition needs (a) demonstration of steatosis in liver, either by ultrasonography or liver biopsy (b) other causes for fat accumulation in liver are excluded e.g. alcohol consumption, use of steatogenic medication or hereditary disorders.[3]

In USA it is most common chronic liver disease and is increasing in Asia pacific region including South Asia.[1,4] Almost 15-40% of general population are affected by NAFLD and its prevalence is expanding worldwide.[1,5] The community prevalence of NAFLD in South Asia and South East Asia ranges from 5-30%. Recently a hospital based study in Pakistan had shown a frequency of approximately 14%.[6]

In most of patients, metabolic risk factors causing NAFLD are obesity, diabetes mellitus, and dyslipidemia.

Mostly patients with NAFLD do not develop symptoms and mostly recognized when routine laboratory assessment shows deranged liver function tests. Liver enzymes alanine aminotransferase and aspartate aminotransferase are increased. However, these enzymes may not be increased in all cases of NAFLD, and their level does not exactly foretell about inflammation and cirrhosis [7]

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MATERIALS AND METHODS

A cross-section study was carried out for six month at Sheikh Khalifa Bin Zaid Al-Nahyan Hospital Rawlakot (from July 2017 to December 2017). It includes all patients with type 2 diabetes mellitus presenting to outpatient department. Their age, weight, height and duration of diabetes mellitus was noted. Body mass index (BMI) was calculated using formula BMI = (weight in kilograms) / (height in meters^2). Their liver function test (LFTS) and fasting lipid profile was performed.

They were given appointment for ultrasound abdomen for presence and absence of fatty liver disease. They were grouped according to BMI as Normal Weight (BMI 18.5–24.9), Over Weight (BMI 25 -29.9), class I obesity (BMI 30 -35), class II obesity (BMI 35-40) and class III (BMI > 40). They were also grouped according to duration of diabetes into 3 groups. Group 1 included patients with duration of diabetes between 1 to 4 years, Group 2 duration of diabetes was from 5 to 8 years and in group 3 duration of diabetes was 9 to 12 years.

Data was entered in SPSS version 20. Chi-square test was applied to assess the significance of difference of fatty liver disease in normal weight, over weight class I obese, class II obese and class III obese diabetics and relation of duration of diabetes mellitus with presence or absence of fatty liver disease.

RESULTS

Out of 200 patients 65 (32.5%) were male and 135 (67.5%) were females. Mean age was 55 years. 10% of patients were normal weight, 44% were overweight and 41% had class I obesity while none had class II or class III obesity.

Table No.1: Weight * fatty liver Cross tabulation

			Fatty liver		Total
			Present	Absent	
Weight	Normal weight	Count	11	11	22
		Expected Count	18.2	3.9	22.0
	Over weight	Count	70	22	92
		Expected Count	75.9	16.1	92.0
	Class 1 obesity	Count	84	2	86
		Expected Count	71.0	15.0	86.0
Total		Count	165	35	200
		Expected Count	165.0	35.0	200.0

Fatty liver disease was present in 165 patients and incidence of fatty liver was 50% in patients with normal weight, 76% of patient who were over-weight and 97% of patients with class I obesity and the difference in incidence was statistically significant. When duration of diabetes was compared with presence or absence of fatty liver disease, it was found that Non-alcoholic fatty liver disease was present in 71% of patients with duration of disease between 1 to 4 years, 91% amongst patient with duration of diabetes between 5 to 8 years and 100% of patients with duration of diabetes between 9 to 12 years and results were statistically significant.

Table No.2: No. of years* fatty liver Cross tabulation

			Fatty liver		Total
			Present	Absent	
No. of years	1 to 4 years	Count	69	28	97
		Expected Count	80.0	17.0	97.0
	5 to 8 years	Count	76	7	83
		Expected Count	68.5	14.5	83.0
	9 to 12 years	Count	20	0	20
		Expected Count	16.5	3.5	20.0
Total		Count	165	35	200
		Expected Count	165.0	35.0	200.0

DISCUSSION

Nonalcoholic fatty liver disease is a frequent disorder in which there is collection of fat in the liver cells in those who do not take much amount of alcohol. Injury to liver ranges from benign deposition of fat to steatohepatitis, advanced fibrosis and cirrhosis. It is more prevalent in patients who have insulin resistance due to overweight/obesity, type 2 diabetes mellitus (T2DM), dyslipidemia and the metabolic syndrome.[8] Insulin level in type 2 diabetes mellitus is either normal or increased but there is resistance to insulin action. This results in lipolysis, which result in fat deposition especially in patients in whom diabetes mellitus is not controlled .Free fatty acids are mobilized after lipolysis , which enter the liver cells and is, used for synthesis of triglycerides which results in deposition of fat in liver resulting in steatosis. Free fatty acids cause damage to cells and swelling of mitochondria, increase fragility of lysosomes, decrease in activity of enzymes, and integrity of membrane is impaired. The damage to cell resulting in inflammation ultimately causes cell death and fibrosis. Free fatty acids are increased in liver tissue of patients with obesity. so both diabetes mellitus and obesity cause increase in liver fibrosis through different mechanism however, their effect is increased when they both occur in the same person.[9] Our study has shown that frequency of nonalcoholic fatty liver disease was 82% in type II diabetes mellitus which was greater than the prevalence stated in normal population by shoba luxmi et al (60.8%)[10] , 55% in Saudi Arabia[11]and 49%in India [12]

Babusik P found that disparity in NAFLD prevalence among South Asians and Arabs residing in Kuwait was not significant. Factors predictive for developing liver steatosis are gender, history of diabetes mellitus and abdominal obesity delineate by waist circumference.[13] However, compared to non-Hispanics, subjects from Central American heritage were over three times as likely to have NAFLD compared to non-Hispanics.[14] Subjects with low physical activity levels were at increased risk for NAFLD (aOR = 4.52, 95% CI, 1.21-16.82) as compared to more active counterparts. When income was compared Families in whom income was low were twice as likely to have NAFLD then families with higher income[15].

Shoba luxmi et al also showed that BMI was 30 in patients who have fatty liver disease and 23 in patients without fatty liver. Also level of HBA1c, liver enzymes, total cholesterol, triglycerides (TG), low-density lipoprotein (LDL) were high and HDL was low in patients with fatty liver disease as compared to patient without fatty liver disease[10].

In our study 10% of patients with diabetes mellitus have normal BMI, 44% were overweight and 41%have class I obesity while none have class II or class III obesity. Incidence of fatty liver was 50% in patients with normal weight, 76% in patient who were over-weight and 97% in patients with class I obesity.

Cazzo E, et al compared the histological changes in patients with obesity who are either diabetic or non-diabetic who had Roux-en-Y gastric bypass. Obese Non-diabetics have less histological abnormalities, regarding steatosis, fibrosis as compared to obese diabetics who have increased frequency of moderate forms of steatosis and fibrosis. [15]

Ostovaneh MR, et al found that NAFLD is strongly related to central obesity as compared to increase BMI. 22.1% of patients with BMI < 30 had NAFLD[16] which is less than our patients with Diabetes mellitus in whom incidence of fatty liver was 50% in patients with normal weight, 76% in patient who were over-weight.

BMI and waist circumstance was low in patients with lean-NAFLD but visceral adiposity index was high as compared to overweight-obese controls. Level of TG, total cholesterol and LDL was high in Lean-NAFLD, a finding similar to overweight-obese NAFLD patients.[17] Factors associated with NAFLD in non-obese but over weight Asia-Pacific subjects are differential distribution of visceral adipose tissue, recent weight gain, diet high in cholesterol and genetic susceptibility. Also resistance to insulin may be an important mechanism. Since NAFLD is the manifestation of metabolic syndrome in liver, it predicts the future development of type 2 diabetes, metabolic syndrome and cardiovascular disease.[18]

Similarly Du T et al found that presence of NAFLD may prone the study population to develop diabetes without other metabolic risk factors. These features like obesity, hypertension, hyperlipidemia and NAFLD are common in diabetic population and significantly increase the risk of developing diabetes, [19.] While transient remission of NAFLD significantly decreased the risk of developing T2DM.[20, 21]

When relation of duration of diabetes was compared with development of fatty liver disease, it was found that fatty liver disease was present in 71% of patients with duration of disease between 1 to 4 years, 91% amongst patient with duration of diabetes between5 to 8 years and 100 % of patients with duration of diabetes between 9 to 12 years.

One of limitation of our study was that the ultrasonography was used for the diagnosis of NAFLD but it could not be confirmed by liver biopsy. However, in clinical practice ultrasonography is commonly used for diagnosis of NAFLD and can identify steatosis

CONCLUSION

Frequency of NAFLD is high in type 2 diabetic patients who are obese as compared to patients who are non-obese weight reduction will result in decrease in incidence of fatty liver disease in diabetes mellitus. Also its frequency increases with increase in duration of diabetes mellitus.

Author's Contribution:

Concept & Design of Study:	Kausar Malik, Shazia Siddiq
Drafting:	Shazia Siddiq, Faiza Batool
Data Analysis:	Kausar Malik
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Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Kistler KD, Brunt EM, Clark JM, Diehl AM, Sallis JF, Schwimmer JB. Physical activity recommendations, exercise intensity, and histological severity of nonalcoholic fatty liver disease. Am J Gastroenterol 2011;106:460-8.
2. Ludwig J, Viggiano TR, McGill DB, Oh BJ. Nonalcoholic steatohepatitis: Mayo Clinic experiences with a hitherto unnamed disease. Mayo Clin Proc 1980;55: 434-8.
3. Chalasani N, Younossi Z, Lavine JE, Diehl AM, Brunt EM, Cusi K, et al. The Diagnosis and Management of Non-Alcoholic Fatty Liver Disease: Practice Guideline by the American Association for the Study of Liver Diseases, American College of Gastroenterology, and the American. Gastroenterological Assoc Hepatol 2012.

4. Amarapurkar DN, Hashimoto E, Lesmana LA, Sollano JD, Chen PJ, Goh KL. How common is non-alcoholic fatty liver disease in the AsiaPacific region and are there local differences? J Gastroenterol Hepatol 2007; 22: 788-93.
5. Hou XH, Zhu YX, Lu HJ, Chen HF, Li Q, Jiang S, et al. Non-alcoholic fatty liver disease's prevalence and impact on alanine aminotransferase associated with metabolic syndrome in the Chinese. J Gastroenterol Hepatol 2011; 26: 722-30.
6. Niaz A, Ali Z, Nayyar S, Fatima N. Prevalence of NAFLD in Healthy and Young Male Individuals. ISRN Gastroenterol 2011; 2011: 363546.
7. Mofrad P, Contos MJ, Haque M, et al. Clinical and histologic spectrum of nonalcoholic fatty liver disease associated with normal ALT values. Hepatol 2003;37:1286-92.
8. Neuschawander-Tetri BA. Non-alcoholic steato-hepatitis and the metabolic syndrome. Am J Med Sci 2005; 330: 326 – 35.
9. Angulo P, Keach JC, Batts KP, Lindor KD. Independent predictor of liver fibrosis in patients with nonalcoholic steatohepatitis. Hepatol 1999; 30:1356-62.
10. Association of Non Alcoholic Fatty Liver with type 2 Diabetes Mellitus Shobha Luxmi, JLUMHS 2008.
11. Akber DH, Kawther AH. Non-alcoholic fatty liver disease in Saudi type-II diabetic subjects attending a medical outpatient clinic. Diabetes Care 2003;26: 3351-65.
12. Gupte P, Amarapurkar D, Agal S, Baijal R, Kulshreshtta P, Pramik S, et al. Non-alcoholic steatohepatitis in type 2 diabetes mellitus. J Gastroenterol Hepatol 2004;19:854-8.
13. Babusik P, Bilal M, Duris I. Nonalcoholic Fatty Liver Disease of Two Ethnic Groups in Kuwait: Comparison of Prevalence and Risk Factors. Med Princ Pract 2012;21:56–62
14. Botero P. Predictors of Non-Alcoholic Liver Disease in Ethnically Diverse Overweight Children and Adolescents**.** Curr Pediatr Rev 2018.
15. Cazzo E, et al Influence of type 2 diabetes mellitus on liver histology among morbidly obese individuals. A cross-sectional study. Sao Paulo Med J 2016.
16. Ostovaneh MR, et al. Nonalcoholic Fatty Liver: The Association with Metabolic Abnormalities, Body Mass Index and Central Obesity--A Population-Based Study. Metab Syndr Relat Disord 2015.
17. Feng RN, et al Lean-non-alcoholic fatty liver disease increases risk for metabolic disorders in a normal weight Chinese population. World J Gastroenterol 2014.
18. Liu CJ. Prevalence and risk factors for non-alcoholic fatty liver disease in Asian people who are not obese. J Gastroenterol Hepatol 2012.
19. Du T, et al Combined influence of nonalcoholic fatty liver and body size phenotypes on diabetes risk. Cardiovasc Diabetol 2015.
20. Yamazaki H, Tsuboya T, Tsuji K, Dohke M, Maguchi H. Independent Association Between Improvement of Nonalcoholic Fatty Liver Disease and Reduced Incidence of Type 2 Diabetes. Diabetes Care 2015;38(9):1673-1679.
21. Fukuda T, Hamaguchi M, Kojima T, Mitsuhashi K, Hashimoto Y, Ohbora A, et al. Transient remission of nonalcoholic fatty liver disease decreases the risk of incident type 2 diabetes mellitus in Japanese men. Eur J Gastroenterol Hepatol 2016; 28(12):1443-1449.
22. Wang Z, et al. Prevalence of nonalcoholic fatty liver disease and its metabolic risk factors in women of different ages and body mass index. Menopause 2015.

Original Article

A Retrospective Study on Efficacy of Transpupillary Diode Laser Retinal Photohotocoagulation for Treatment of Retinal Tears

Ali Afzal Bodla and Muhammad Afzal Bodla

ABSTRACT

Objective: To evaluate the efficacy and safety of trans pupillary diode laser retinopexy for the management of retinal tears as an outpatient ophthalmic procedure.

Study Design: Retrospective study

Place and Duration of Study: This study was conducted at the Multan Medical and Dental College and Bodla Eye Care, Multan from January 2018 to June 2018.

Materials and Methods: The long wave 810nm diode laser retinopexy was done instead of conventional argon laser retinopexy as an outpatient procedure. A moderate spot size between 300 to 400 microns with diode laser (810) was used to treat patients with breaks in attached retina. Powers between 400 and 800 mW produced an adequate burn in all cases. Pre and post laser anterior and posterior segment examination was done for any signs of inflammation, and PVR. Follow up was conducted, for over a period of six months, to ascertain for adequate chorio-retinal adhesions.

Results: A total of 13 patients were recruited in the study starting from February 2018 till July 2018. There were 13 eyes in total with the mean age of 57.8 years. Pre laser VA of 7 eyes was between 6/6 to 6/12 and 6 eyes had a visual acuity of 6/18 to 6/60. Post laser VA, improved to 6/6 to 6/12 in 10 eyes as associated vitreous haemorrhage resolved, and remained between 6/18 to 6/60 in 3 eyes. Out of 13 eyes, none of the eyes, developed anterior segment inflammation while mild posterior segment inflammation, was noticed in one eye. None of the eyes developed PVR. Excellent chorio-retinal adhesion was achieved in 12 out of 13 eyes. One eye with failure needed, scleral buckling procedure, this was with pre clinical rhegmatogenous retinal detachment having U shaped retinal tear.

Conclusion: Our study looked at the efficacy and safety of transpupillary diode laser which had been the main stay treatment for retinal tears prior to introduction of Argon laser primariloy used for the mentioned procedure now a days.Excellent chorio-retinal adhesion was achieved in 12 out of 13 eyes. There was no element of proliferative vitreo retinopatrhy noticed in either eye as a result of the procedure. Results of diode laser were found to be at par with Argon and definitely superior to trans sclera cryopexy. Cryopexy is known to cause scleral thinning, proliferative vitreo retinopatrhy, tissue necrosis along with breakdown of blood aqueous barrier and none of these complications are associated with diode laser.

Key Words: Diode laser, Retinopexy, Retinal Tears.

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INTRODUCTION

Photocoagulation for the treatment of retinal conditions has been used for over 40 years.[1,2] Meyer-Schwickerath initially used focused sunlight to produce retinal lesion, but this method was superseded by a modified Beck arc.[3,4]

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The development of the xenon arc photocoagulator provided a source of broadband optical radiation, which was effective in producing full-thickness chorioretinal lesions.[2,5] Xenon arcs devices were of proven effectiveness in the treatment of proliferative diabetic retinopathy and were commonly used for retinal therapeutic procedures. Continuous-wave argon and Krypton broadly used, were similar in terms of both efficacy and safety, though they had several inherent disadvantages. Laser energy was generated within relatively bulky gas-filled tubes, electrical energy consumption was high, and the efficiency of electric-optical conversion is low.

Advances in semi-conductor technology have allowed the development of infrared diode lasers (750-950mm) measuring a few millimeters in size. [6,7] These are used

in compact disc players and have important applications in the fields of optical printing and communications. [8]

The recent availability of laser diode with an output power of 1-3 W has stimulated interest in their potential applications in ophthalmic surgery. They are compact (9 x 2mm) and easily portable, they may be powered by either a standard 13A power supply or a 6 V battery, and no ancillary cooling facilities, are needed. Microscopical analysis of diode laser retinal lesion, demonstrated them to be similar to those produced by conventional clinical photocoagulators and, in particular, to those induced by argon lasers. The physical parameters of the exposures, such as power levels, exposure durations and spot sizes, were also similar. [9]

Pilot clinical studies in the past, in which a number of retinal vascular conditions, were treated with diode lasers have demonstrated comparable results to the most frequently used Argon. [9,10]

Transpupillary diode laser photocoagulation, is an alternate to broadly used argon laser retinopexy as well as cryopexy. Over a period of last few years there has been a consistent decrease in the use of Diode but Authors believe that even to this day it can be used effectively and safely as an alternate to Argon Laser for the treatment of retinal tears.

MATERIALS AND METHODS

A study of patients that had diode laser retinal laser photocoagulation between January 2018 to June 2018 with the semiconductor infrared diode laser was performed. These patients presented with identified retinal tears with or without associated vitreous haemorrhage. Inclusion criteria was patients presenting with atrophic retinal breaks associated with visible vitreous traction of flashing lights, horse shoe retinal tears with posterior vitreous detachment, symptomatic patients with retinal breaks present in the areas of lattice degeneration, retinal tears with or without posterior vitreous detachment with areas of sub retinal fluid around it.

Study proforma included age, sex, demographic area, pre and post laser visual acuity, presence or absence of vitreous haemorrhage as well as size, shape and location of retinal tears. A detailed account was noted of any associated sub retinal fluid around the break. Post treatment findings were presence or absence of adequate chorioretinal adhesion. Presence of any secondary retinal inflammation especially proliferative vitreoretinopathy. Patients with vitreous haemorrhage underwent an Oculus B-Scan using 12 MHz probe to identify for any other areas of retinal elevation.

Diode laser photocoagulation system used is manufactured by Nidek Inc ,Japan. A transpupillary approach was used for the treatment with patient's eye to be treated well dilated using topical phenylephrine 2.5% or Tropicamide 0.5% or both. Alcaine, Alcon topical anaesthetic drops were used with the Volk Mainster Wide Field Lens 160 degrees couple with preservative free Viscotears. Following the treatment patients were prescribed guttae Flouromethalone FML (Allergan Inc) Eye Drops four times a day for a week along with guttae Diclofenac Sodium (Ocufen Allergan Inc) three times a day for the same perioed.

Authors used a spot size between 300 to 400 microns in the form of confluent burns in three rows on the attached retina 360 degrees around breaks. It was made sure that appropriate blanching of retina was observed during the procedure. Follow up was for a period ranging from one to six months with dilated fundus examination and a close observation of the treated area. Post op examination proforma was meticulously filled for post laser visual acuity, degree of anterior and posterior segments inflammation, any presence of proliferative vitreortinopathy in and around treated area and extent of chorioretinal adhesion.

RESULTS

A total of 13 eyes of 13 patients underwent transpupillary diode laser retinopexy for the treatment of retinal tears. Patients had a variable follow up ranging between one to six months. All patients were recruited as per mentioned inclusion criteria. There were 8 (61.5%) males and 5(38.4%) female patients. The mean age at presentation was 57.8±9.3 years (range 36-69 years). The indication of treatment was retinal tear with or without an area of subretinal fluid. 3 (23.0%) out of 13 patients had an area of less than one disc diameter of subretinal fluid along with the retinal tear margin and 1 (7.6%) had an area of approximately three disc diameters of subretinal fluid. This particular patient, subsequently turned out to be a treatment failure and required sclera buckling. Slight discomfort was mentioned by majority of the patients following on the day of treatment. Only three out of thirteen patients complained of severe pain and subsequently required oral NSAID. 7 (53.8%) patients had an associated posterior vitreous detatchment at the time of presentation, and 5 (38.4%) were pseudophakic. Refracttive correction revealed an overwhelming majority of low to high myopes as expected i.e. 9 (69.2%). 8(61.5%) had breaks in the superior while 5 patients had breaks in the inferior quadrants. 5(38.4%) patients had mild to moderate amount of vitreous haemorrhage and all of them had a posterior vitreous detatchment at the time of presentations. All these patients underwent an ophthalmic B-scan. Patients were seen on day 1 and 7 following the procedure to determine for any possible complication as well as progression to retinal detatchment. Post laser VA, improved to 6/6 to 6/12 in 10 eyes due to resolution of vitreous haemorrhage, and remained between 6/18 to 6/60 in 3 eyes. The reason of reduced vision was preexisting retinal atrophy, mild amblyopia and

epiretinal membranes. 1 (6.7%) out of 13 eyes developed moderate vitritis post laser which resolved with the use of topical steroids. Post laser proliferative vitreoretinopathy was not identified in any patient. One eye progressed to development of retinal detatchment on account of significant pre existing subretinal fluid and subsequently required sclera buckling. Rest of 12 eyes preceded to have excellent chorioretinal adhesions with flat retina and did not required any subsequent intervention. Statistical analysis was not applied to the nature of study and number of patients enrolled.

DISCUSSION

Argon laser is the mainstay of treatment when it comes to retinal photocoagulation.[12] Authors believe that Diode laser can still be used as an alternate to Argon in order to achieve similar results. Diode laser is relatively inexpensive with less maintenance issues. [11,13] In pure socioeconomic areas as where we practice i.e. Southern Punjab , it still holds its importance as an alternate to relatively expensive Argon laser. Due to increased spectrum of absorption in the retinal tissue it potentially can be associated with side effects as foveal burns, visual field defects and retinal fibrosis leading to proliferative vitreoretinopathy but these complications can be avoided with adequate choice of power settings. [14,15]

This study includes, the post laser analysis of 13 eyes who underwent transpupillary diode laser retinopexy, for the treatment of retinal tears presenting to outpatient departments at Multan Medical and Dental College and Bodla Eye Care, Multan. Transpupillary diode laser proved to be an effective and safe option, compareable by all standards to Argon for the adequate treatment of mentioned pathology. It certainly holds clinical advantage on trans scleral diode laser retinopexy and cryopexy. Cryotherapy is known to be associated with an increase in the breakdown of the blood- retinal barrier, one of the contributors to PVR, the major cause of surgical failure after scleral buckling surgery. [16,17] Cryopexy has its drawbacks including development of postoperative cystoid macular edema, dispersion of retinal pigment epithelial cells,and breakdown of the blood-retinal barrier, resulting in an increase in the potential for stimulation of proliferative vitreoretinopathy (PVR). [18]

Authors propose that transpupillary diode laser is still a valid alternative to Argon and cryotherapy.[19] Some of the old data suggests that for transscleral photocoagulation with the diode laser, emitting light in the near infrared range (810 to 840nm) and its ability to penetrate the retinal pigment epithelium can have practical and theoretical advantages in terms of formation of adequate chorioretinal adhesions. [19,20]

In their study, Benner et al performed transpupillary retinopexy in the rabbit eye with the three laser-indirect Ophthalmoscopic delivery systems (argon, krypton, and diode), as well as with the transscleral diode laser. [9,21] They found the lesions to be clinically and histologically comparable. Higher power settings and longer burn duration were required for more lightly pigmented eyes, for burns without scleral depression, and for burns created with either the diode laser-indirect ophthalmoscopic or the transscleral diode delivery system. Some retinal hole formation and scleral thinning were observed histologically. [9] These iatrogenic breaks were similar to those encountered in transpupillary laser delivery and were attributed to delivering higher pulses of energy at a high a power settings and at relatively shorter durations. This is something which can always be avoided in clinical settings and hence subsequent side effects. Careful attention must be used when treating over areas of pigmentry variation to avoid a Bruch's membrane rupture. [22]

Keeping in view the above study authors performed transpupillary diode laser photocoagulation at a mild to moderate settings in 13 eyes, which were followed over a period of 1 to 6 months. In our study group with all being highly pigmented eyes, it was in fact easier to produce adequate retinal burns at lower power settings. Follow up results were found to be satisfactory in all possible aspects. Apart from one case, none others required further intervention. All other cases showed excellent chorio-retinal adhesion, with closure of the retinal tears. No signs of persisting anterior and or posterior segment inflammation were noted, and none of the eyes, developed proliferative vitreortinopathy.

Authors have found this treatment modality to be inexpensive ,less time consuming, precise, effective, and reliable. In conclusion, we believe though obsolete in the modern world, it continues to have its pivotal role in rural and developing economies where Argon laser is not assessable for every patient.

CONCLUSION

Our study looked at the efficacy and safety of transpupillary diode laser which had been the main stay treatment for retinal tears prior to introduction of Argon laser primariloy used for the mentioned procedure now a days.Excellent chorio-retinal adhesion was achieved in 12 out of 13 eyes. There was no element of proliferative vitreo retinopatrhy noticed in either eye as a result of the procedure. Results of diode laser were found to be at par with Argon and definitely superior to trans sclera cryopexy. Cryopexy is known to cause scleral thinning, proliferative vitreo retinopatrhy, tissue necrosis along with breakdown of blood aqueous barrier and none of these complications are associated with diode laser.

Author's Contribution:

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Data Analysis:	Ali Afzal Bodla
Revisiting Critically:	Ali Afzal Bodla, Muhammad Afzal Bodla
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Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Haller JA, Lim JI, Goldberg MF. Pilot trial of transscleral diode laser retinopexy in retinal detachment surgery. Arch Ophthalmol 1993; 111:952–956.
2. Sasoh M, Smiddy WE. Diode laser endophotocoagulation. Retina 1995;15:388–393.
3. Mahmoud AO, Kyari F, Ologunsua Y. Initial experience with the utility of the infrared diode laser in Kaduna, Nigeria. Nigerian J Ophthalmol 2002;1:37–44.
4. Ulbig MW, Hamilton AM. Comparative use of diode and argon laser for panretinal photocoagulation in diabetic retinopathy. Ophthalmologe 1993;90:457–462.
5. Lock JH, Fong KC. Retinal laser photocoagulation. Med J Malaysia. 2010;65:88–94.
6. Soman M, Ganekal S, Nair U, Nair KGR. Effect of panretinal photocoagulation on macular morphology and thickness in eyes with proliferative diabetic retinopathy without clinically significant macular edema. Clinical Ophthalmol 2012;6:2013–2017.
7. Ford JA, Lois N, Royle P, Clar C, Shyangdan D, Waugh N. Current treatments in diabetic macular oedema: systematic review and meta-analysis. BMJ Open 2013;3(e002269).
8. Kolar P. Risk Factors for Central and Branch Retinal Vein Occlusion: A Meta-Analysis of Published Clinical Data. J Ophthalmol 2014;2014 doi:1155/2014/724780.
9. Benner JD, Huang M, Ishigooka H, et al.Binocular indirect laser ophthalmoscope and diode trans scleral laser photocoagulation in the rabbit.Invest ophthalmol Vis Sci 1991;32 (suppl):27-64.
10. Nussbaum JJ, Pruett RC, Delori FC. Historic perspectives. Macular yellow pigment. The first 200 years. Retina 1981;1(4):296–31
11. Gaasterland DE, Pollack IP. Initial experience with a new method of laser transscleral cyclophoto-coagulation for ciliary ablation in severe glaucoma. Trans Am Ophthalmol Soc 1992; 90:225–246.
12. Jennings T, Fuller T, Vukich JA, Lam TT, Joondeph BC, Ticho B, et al. Transscleral contact retinal photocoagulation with an 810-nm semiconductor diode laser. Ophthalmic Surg 1990; 21(7):492–496.
13. 13-Haller JA, Lim JI, Goldberg MF. Pilot trial of transscleral diode laser retinopexy in retinal detachment surgery. Arch Ophthalmol 1993; 111(7):952–956.
14. Raymond GL, Lavin MJ, Dodd CL, McLeod D. Suture needle drainage of subretinal fluid. Br J Ophthalmol 1993;77(7):428–429.
15. Steinmetz CG. Reaction of the sclera to cryosurgery. Int Ophthalmol Clin 1967;7(2): 395–403.
16. Glaser BM, Vidaurri-Leal J, Michels RG, Campochiaro PA. Cryotherapy during surgery for giant retinal tears and intravitreal dispersion of viable retinal pigment epithelial cells. Ophthalmol 1993;100(4):466–470.
17. Vogel A, Dlugos C, Nuffer R, Birngruber R. Optical properties of human sclera, and their consequences for transscleral laser applications. Lasers Surg Med 1991;11(4):331–340.
18. McHugh DA, Schwartz S, Dowler JG, Ulbig M, Blach RK, et al. Diode laser contact transscleral retinal photocoagulation: a clinical study. Br J Ophthalmol 1995;79:1083–1087.
19. McHugh JD, Marshall J, Ffytche TJ, Hamilton AM, Raven A, et al. Initial clinical experience using a diode laser in the treatment of retinal vascular disease. Eye (Lond) 1989;(5):516–527.
20. Abramson DH, Servodidio CA, Nissen M. Treatment of retinoblastoma with the transscleral diode laser. Am J Ophthalmol 1998;126:733–735.
21. Parvaresh MM, Modarres M, Falavarjani KG, Sadeghi K, Hammami P. Transscleral diode laser retinal photocoagulation for the treatment of threshold retinopathy of prematurity. J AAPOS 2009;13:535–538.
22. Paysse EA, Miller A, Brady McCreery KM, Coats DK. Acquired cataracts after diode laser photocoagulation for threshold retinopathy of prematurity. Ophthalmol 2002;109:1662–5.

Original Article

Experience with Reverse Sural Artery Flap for Distal Leg and Foot Coverage

Moiz Sadiq[1], Fahad Hanif Khan[1], Bushra Zulfiqar[1] and Syed Sheeraz ur Rahman[2]

ABSTRACT

Objective: To analyze the complications associated with use of reverse sural artery flap to provide soft tissue coverage for lower third of leg and heel defects.

Study Design: Retrospective study

Place and Duration of Study: This study was conducted at the Plastic Surgery Department at Liaquat National Hospital from February 2014 to December, 2016

Materials and Methods: Patient demographics, physical and clinical examination retrieved. Doppler ultra sonography was used to identify perforating vessels to aid in the planning of a pivot point. The skin island was outlined to match the recipient site defect than the flap was dissected and inset done. Patients were followed for 1 month and outcomes were recorded.

Results: There were 136 patients were included with lower third of leg and heel wound and exposed structures like tendons, bone, nerve and vessels. Out of 136 cases 44 (32.4%) cases had complications. Complete flap necrosis was occurred in 19.1% cases, infection occurred in 11% and partial flap necrosis occurred in 8.1% cases.

Conclusion: The distally based reverse sural artery flap is a better option for coverage of soft tissue defects in the distal 3rd of the leg and proximal foot.

Key Words: Soft-tissue defects; Reverse sural artery flap; Flap necrosis; Ankle coverage; Complications

Citation of articles: Sadiq M, Khan FH, Zulfiqar B, Rahman SS. Experience with Reverse Sural Artery Flap for Distal Leg and Foot Coverage. Med Forum 2018;29(8):50-53.

INTRODUCTION

Due to an increase in high-energy trauma, the management of soft-tissue defects in the lower limbs has become a very frequent procedure[1]. The limited option of pliable soft tissue coverage in the distal third of the leg, ankle and foot presents a challenge for the reconstruction in this region of the body. The reconstructive options of such defects get even narrower in resource constrained environment where the choice of free tissue transfer is not an option because of the infrastructural challenges and limitation of manpower with requisite skills for microvascular surgeries[2,3]. The soft tissue defects of this region presents a challenging problem because of the paucity of local tissue and poor circulation of skin[2]. Various forms of coverage including muscle, fascial or free flaps are used for reconstruction. Each has their specific indications and inherent disadvantages[2]. Microsurgical reconstruction of lower extremity wounds requires long operative times, a stable patient, and technical expertise[4].

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There is limited expertise with free tissue transfers in many developing countries necessitating consideration of other options for the closure of such defects[3].

A simpler method for reconstruction of the lower leg, heel, and foot is the reverse sural fasciocutaneous flap[4]. The versatility and reliability of sural artery flap have made it a popular option for the reconstruction of such defects[3]. It has become popular since introduction by Donski and Fogdestam, followed by the detailed anatomical description by Masquelet, et al[4]. Among the main indications for the sural fasciocutaneous flap are soft-tissue defects of the heel and the lateral or medial perimalleolar regions [5, 6]. Multiple case series report the reverse sural fasciocutaneous flap as a reliable solution to a variety of reconstructive needs, with low complication rates[4]. In young patients with traumatic injuries, low complication rates have been reported[4]. This flap has a reliable and constant blood supply from multiple sources with a broad range of rotation and provides a less bulky coverage compared to free flap[5]. Distally based fasciocutaneous flaps supplied by vascular axis around sural nerve are extensively researched and constitute another important alternative to lower third and foot reconstruction[2].

In one of the studies involving 166 patients, this procedure was uneventful in 142 (85.5%) cases and 24 (14.5%) cases had some complications. Infection or discharge occurred in 12 (7.2%) cases, partial flap necrosis occurred in 10 (6.0%) cases, with resulting need for minor surgery (debridement and split thickness graft)[2]. In another study of 20 patients, satisfactory healing of the flaps was in 17 (85%) patients. Five

(25%) patients had varying range of minor dehiscence and necrosis of some part of the flap. Three (15%) patients had complete flap necrosis necessitating debridement and secondary wound cover with split thickness skin graft.[3]

MATERIALS AND METHODS

All patients who came to Plastic Surgery Department at Liaquat National Hospital from February 2014 to December, 2016, with lower leg wounds fulfilling the criteria below were selected for the study.

Inclusion criteria:

a) Patients of either gender
b) Patients with age 20 – 60 years
c) Patients with lower third of leg and heel wound, with exposed underlying structures (tendon, bone, nerve, vessel).
d) Size of flap was according to size of defect.
e) Wounds with no evidence of infection (confirmed by wound culture and sensitivity).

Exclusion criteria:

a) Patients who had segmental bone defect and required reconstruction with vascularized bone graft.
b) Patients with poly trauma having severe head injuries along with lower leg injuries
c) Scars and vascular injury at the donor site
d) Prior operations of the leg with impairment of blood supply.
e) Infected wound

After explaining the procedure and written informed consent was taken. Patient demographics, location of wound, time between injury and wound, dimension of wound, and postoperative complications were recorded in a predesigned performa by the principal investigator. X-rays of the injured limb were done to rule out underlying fracture and in case of fracture, fixation was done prior to the procedure. The procedure was performed by the consultant plastic surgeon having experience of at least 5 years.

Patients were followed for 1 month in the clinic and outcomes were recorded. Outcome was assessed in terms of complications, which included wound infection, flap necrosis and need for secondary soft-tissue coverage.

Data was complied and analyzed using SPSS (Statistical Package for Social Sciences) version 18. Effect modifiers were controlled by the stratification of age, gender, site of wound, dimensions of flap, and size of wound to see their effect on outcome by using chi-square test, with 95% confidence interval.

RESULTS

There were 136 patients with lower third of leg and heel wound who had exposed structures (tendons, neurovascular structure or bone). The mean age of the patients was 43 ± 11.01 years, similarly mean size of wound and time interval between injury to wound coverage was 1.51 ± 0.50 cm and 72.4 ± 21.07 minutes respectively.

Out of 136 patients 75 (55.15%) were female and 61 (44.85%) male. Regarding site of wound, 51.47% was on heel and 48.53% on distal third of leg. Tendon was the most commonly exposed structure in the wound followed by bone as presented in figure 2.

Frequency of complications in management of soft tissue coverage of lower third of leg and heel with reverse sural artery flap are presented in table I. Out of 136 cases, 44 (32.4%) cases had complications. Complete flap loss occurred (total flap necrosis) in 19.1% (26/136) cases as compared to partial flap loss (necrosis of more than 1/3 of total flap size), which occurred in 8.1% (11/136) cases. There were statistically insignificant results when rate of complication was compared to age (p-value: 0.09), gender (p-value: 0.4), wound size (p-value: 0.2) or site (p-value: 0.6).

Table No.I: Complications observed with reverse sural artery flap

Complications	N (%)
Partial Flap Necrosis	11 (8.1)
Infection	15 (11)
Complete flap Necrosis	6 (19.1)

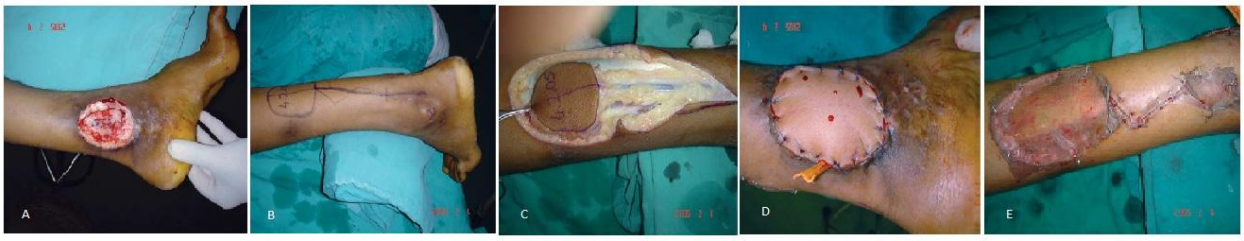

Figure No.I: Defect on the lateral malleolus of left leg (A), was covered with reverse sural flap as marked and dissected in B and C, respectively. Flap had nice tension free inset (D) and donor site was split thickness skin grafted (E).

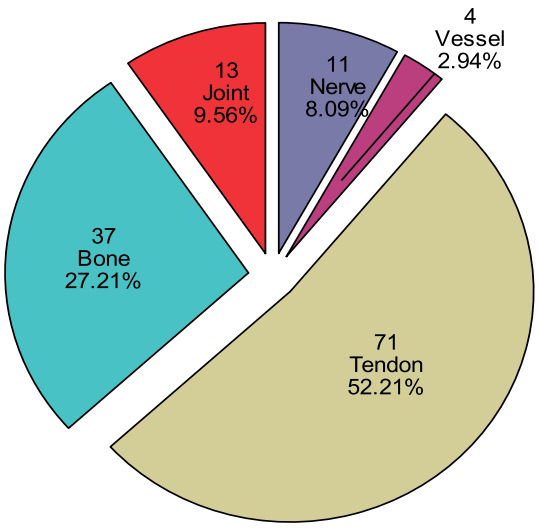

Figure No.2: Structures exposed in the wound (n=136)

DISCUSSION

Reconstruction of the lower leg and foot continues to be one of the most challenging tasks for a plastic surgeon. An unreliable lower limb subdermal plexus results in poor wound healing when cutaneous flaps are used[7]. Following developments in flap surgery, pedicled fasciocutaneous flaps and free flaps had been used. The introduction of distally based sural fasciocutaneous flap provides reliable and effective method to cover skin defects of distal leg, foot and ankle[8].

Fasciocutaneous flaps, first introduced by Ponten in 1981[9], are in use for the reconstruction of soft tissue defects of lower 1/3 of leg and foot. Reversed island flaps like, peroneal artery flap, anterior tibial artery flap, and posterior tibial artery flap can be transferred to the ankle or foot. However, it needs sacrifice of a major artery that constitutes a potentially serious disadvantage. Masquelet et al.[10] in 1992 first described distally based sural artery flap. The distally based superficial sural artery flap is perfused by median superficial artery with reverse flow, as this artery has septocutaneous perforators from peroneal artery.

The aetiology for lower limb wound includes road traffic accidents, non-healing skin wounds, chronic venous ulcers, chronic osteomyelitis in diabetics, contractures, gangrene, unstable scars, cancer resections, and electrical burns[11, 12].

In our study the average age of the patients was 43.24 ± 11.01 years. Out of 136 patients 75 (55.15%) were female and 61 (44.85%) male. Wound on heel was observed in 51.47% and on third of leg 48.53%. While in Olawoye et al[3] study the mean age of the patients was 30 years with a range of 7–58 years. There were 13 (65%) males and 7 (35%) females with a ratio of 1.9:1. The defect was located in the distal third of the leg in 13 patients (65%), ankle in 4 patients (20%), heel in 2 (10%) and dorsum of the foot in 1 patient (5%). In Thawerani et al[13] study 40 patients aged 7 years to 65 years were included with a mean age of 24 years. Among them, 37(92.5%) were males and 3 (7.5%) were females.

In this present study 32.4% cases had complications. Complete flap necrosis occurred in 26 (19.1%) cases, infection in 15 (11%) and partial flap necrosis in 8.1% (11) cases. In another study the complication rate reported was 59% (41 in 70 flaps), partial necrosis was noted in 17% and complete necrosis in 19% flaps [(14)]. Akhtar et al[15] in his study observed flap survival in 78.5%, partial necrosis in 16.5% and complete necrosis in 9.5%.

In Thawerani et al study[13] complications were observed in 8 cases who were operated initially. One patient each developed infection, discharging sinus & complete flap necrosis (7.5%). Two patients each developed partial flap necrosis (5%) and partial graft rejection (5%), respectively; and late recurrent ulcer on the flap occurred in one patient (2.5 %).

In a study, done in 2011 for 166 patients, this procedure was uneventful in 142 (85.5%) cases and 24 (14.5%) cases had some complications. Infection/discharge occurred in 12(7.2%) cases, Partial flap necrosis occurred in 10 (6.0%) cases, with resulting need for minor surgery (debridement and split thickness graft)[2]. In another study of 20 patients, satisfactory healing of the flaps was in 17 (85%) patients. 5 (25%) patients had varying range of minor dehiscence and necrosis of some part of the flap. 3 (15%) patients had complete flap necrosis necessitating debridement and secondary wound cover with split thickness skin graft [(3)]. In Ajmal et al[16] study out of 25 flaps, 20 showed complete survival (80%). Partial flap loss was found in 2 patients (8%), marginal flap necrosis in 2 patients (8%) and complete loss in 1 patient (4%). Hollier L et al[17] in 2002 studied the same flap in 11 patients and observed partial necrosis in 1 patient. He emphasized a broad inferolateral pedicle and the importance of including the short saphenous vein. Singh and Naasan[18] used the reverse sural artery flap to cover acute open fractures of the lower leg. Two out of seven patients had a partial necrosis of the distal tip of the flap.

CONCLUSION

The distally-based reverse sural artery flap is a good available option for coverage of soft tissue defects in the distal 1/3rd of the leg and proximal foot. The main advantages of the reverse sural artery flap are that it can be done in a single stage, is a reliable alternative to free tissue transfer and carries minimal donor site morbidity. In addition, it has a reliable and constant blood supply with a broad range of rotation and provides a less bulky coverage compared to free muscle flaps. It has lesser complications, is less time consuming and has high patient's satisfaction. The result of the study also

provides a base line data so that in future further studies can be done on the basis of this data.

Author's Contribution:

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

REFERENCES

1. Ignatiadis AI, Tsiampa VA, Galanakos SP, Georgakopoulos GD, Gerostathopoulos NE, Ionac M, et al. The reverse sural fasciocutaneous flap for the treatment of traumatic, infectious or diabetic foot and ankle wounds: a retrospective review of 16 patients. Diabetic Foot Ankle 2011;2:5653-58.
2. Kansal S, Goil P, Singh J. Surgical review: the versatile reverse flow sural artery Xap for lower 1/3 leg and foot defects: clinical series. Eur J Orthop Surg Traumatol 2011;21:553–56.
3. Olawoye OA, Ademola SA, Iyun K, Michael A, Oluwatosin O. The reverse sural artery flap for the reconstruction of distal third of the leg and foot. Int Wound J 2012:6:1-6.
4. Parrett BM, Pribaz JJ, Matros E, Przylecki W, Sampson CE, Orgill DP. Risk Analysis for the Reverse Sural Fasciocutaneous Flap in Distal Leg Reconstruction. Int Wound J 2009;123:1499-504.
5. Awerani SH, Ansari MN, Siddiqui N. Minimizing complications in reverse sural artery flaps free muscle flaps. Pak J Surg 2011;27(1):2-7.
6. Luna RA, Martinez VM, Saddi FH, Lopez VF, Gutie´rrez del CM. Versatility of the sural fasciocutaneous flap in coverage defects of the lower limb. Injury 2007;38:824-31.
7. Hallock GG. Lower extremity muscle perforators flap for lower extremity reconstruction. Plast reconst Surg 2004;114:1123–30.
8. Mozafari N, Moosavizadeh SM, Rasti M. The distally based neurocutaneous sural flap: a good choice for reconstruction of soft tissue defects of lower leg, foot and ankle due to fourth degree burn injury. Burns 2008;34(3):406–11.
9. Ponten B The fasciocutaneous flap. Its use in soft tissue defects of the lower leg. Br J Plast Surg 1981;34:215
10. Masquelet AC, Ramana MC, Wolf G. Skin island flaps supplied by the vascular axis of the sensitive superficial nerves: anatomic study and clinical experience in the leg. Plast Reconstr Surg 1992;89:1115-18.
11. Chen SL, Chen TM, Chou TD, Chang SC, Wang HJ. Distally based sural fasciocutaneous flap for chronic osteomyelitis in diabetic patients. Ann Plast Surg 2005;54(1):44–8.
12. Pirwani MA, Samo S, Soomro YH. Distally based sural artery flap: A workhorse to cover the soft tissue defects of lower 1/3 tibia and foot. Pak J Med Sci 2007;23:103–10.
13. Thawerani S, M. Najeeb Ur Rab Ansari, Nasreen Siddiqui. Minimizing complications in reverse Sural Artery flaps. Pak J Surg 2011;27(1):2-7.
14. Baumeister SP, Spierer R, Erdmann D, Sweis R, Levin LS, Germann GK. A realistic complication analysis of 70 sural artery flaps in a multimorbid patient group. Plast Reconstr Surg 2003;112: 129–40.
15. Akhtar S, Hameed A. Versatility of the sural fasciocutaneous flap in the coverage of lower third leg and hind foot defects. J Plastic, Reconst & Aesthetic Surg 2006;59: 839–45.
16. Ajmal S, Khan MA, Khan RA, Shadman M, Yousof K, Iqbal T. Distally based sural fasciocutaneous flap for soft tissue reconstruction of the distal leg, ankle and foot defects. J Ayub Med Coll Abbottabad 2009;21(4):19-23.
17. Hollier L, Sharma S, Babigumira E, Klebuc M. Versatilityof the sural fascocutaneous flap in the coverage of lower extremity wounds. Plast Reconstr Surg 2002;110:1673-76.
18. Singh S, Naasan A. Use of distally based superficial sural island artery flaps in acute open fractures of the lower leg. Ann Plast Surg 2001;47:505–10.

Original Article

Perceived Stress and Sources of Stress Among Medical Undergraduates of Fatima Jinnah Medical University, Lahore, Pakistan

Rabia Javed, Maryam Nawaz and Samina Asghar

ABSTRACT

Objective: To find out level of perceived stress and the probable stressors.
Study Design: Observational / descriptive / cross-sectional survey Study
Place and Duration of Study: This study was conducted at the Department of Obse and Gynae, Fatima Jinnah Medical University, Lahore during the period of one month of March 2016.
Materials and Methods: Using convenient sampling, 387 medical students completed the PSS-10 and a 30 item stress questionnaire. The data was analyzed with SPSS-22 software. ANOVA techniques were used to analyze differences in mean perceived stress score amongst different classes. Binary Logistic Regression Analysis was performed to determine core stress factors. P-Value was set at 0.05.
Results: The total response rate was 99.25%(397/400). The total mean PSS was 20.84 (SD=6.44) and was significantly highest amongst 1st year students with a score of 23.54 (SD=7.04). The prevalence of academic, psychological and health related stressors were 39%, 30% and 31% respectively.
Conclusion: A high level of perceived stress was noted among fresh enrolling MBBS students. Academic stressors were the most frequent stressors. It is important for medical educators to appreciate the level of stress and its various causes among medical undergraduates. So, we suggest early guidance and regular assessments of stressors which will help prepare students for stressful career of a health professional.
Key Words: Perceived Stress, Medical Students, Academic Stressors

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INTRODUCTION

Perceived stress is the perception of a person that his/her workload exceeds the ability to handle. It is a growing concern worldwide that medical education puts considerable stress on students affecting the overall quality of life[1]. The quality of life is adversely affected by the pressure of studies, hectic lecture routines and long hospital stays that leaves the students with negative behavioral changes, few good social contacts and poor psychosocial well-being[2,3]. The medical professionals strive for better life quality of their patients while their own life routines contradict the definition of a healthy ideal lifestyle[4]. Various stressors are reported among medical students which include types and frequency of assessments, living conditions in hostel, substandard nutrition, learning environment, working relationships etc.[3,5]. The students who are more stressed show poor academic performance which eventually leads to them becoming less competent doctors[6].

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Exposure to various stressors causes depression which affects the mental functioning of medical students and eventually leads to ill health, burnouts and suicidal thoughts among them[7]. There is a dangerously high percentage of medical students who have attempted or have thought of attempting suicide[8]. It is therefore important to assess stress and its various causes because if these are not dealt with immediately, it may lead to disastrous results. Studies have been carried out in different countries like UK, USA, Sweden, Germany, New Zealand, Brazil and India on prevalence of stress .Varying degrees of stress were reported because these researches were carried out using different instruments to calculate stress or it could be a real difference due to different socio-demographic backgrounds[9,10,11,12,14]. Different Studies carried out in India, Bangladesh, Greece and Pakistan has used Perceived stress Scale (PSS) to assess levels of stress[11,12,13,15,19]. It is a globally used scale to measure perception of psychological stress[15]. According to a research conducted in CMH, Lahore, Pakistan, a mean PSS score of 30.84 was calculated[16]. Local epidemiological data about academic, social, psychological and health problems among medical undergraduate students is very negligible in number and there is relative deficiency of information about stress and its various sources among medical undergraduates in Pakistan. To the best of author's knowledge, no such study has been carried out in Fatima Jinnah Medical University (FJMU). The

current study, therefore, was carried out among medical undergraduates of FJMU to find out the prevalence of perceived stress among the medical students and to identify the major stressors affecting medical students.

Hypothesis: 1. There is positive correlation between perceived stress and initial academic years

2. Majority of probable stressors affect the academic performance of the medical students.

MATERIALS AND METHODS

It was an observational descriptive cross-sectional survey study carried out during the month of March in 2016 in FJMU after ethical committee approval. A sample size of 390 was calculated (78/year) for the study with anticipated response rate of 90%. Randomized non-probability convenient sampling was done. The participants were requested to fill 2 questionnaires - PSS-10 and a 30 item stressor questionnaire listing potential stressors. PSS-10 contains 10 statements which are rated on a 5-pointlikert scale and the responder has to tell whether they had these thoughts ranging from never, almost never, sometimes, fairly often and very often (0, 1, 2, 3, 4 respectively) during the past month. The scores are calculated by summing up the responses giving a maximum score of 40. Items 4, 5, 7, and 8 are positively stated and their scores are calculated by reverse coding the items (0 = 4, 1 = 3, 2 = 2, 3 = 1, 4 = 0). The stress questionnaire has been taken from a similar research conducted in Nepal by Sreeramareddy et al after little modification [21]. A total of 30 potential stressors were enlisted. They were divided into three different categories namely academic, psychosocial and health related. For each potential stressor, the occurrence frequency was categorized as 'rarely/never', 'sometimes' and 'always/often' and given score of 0, 1 and 2 respectively using a Likert scale (1-10).

All the participants were told about the purpose and objectives of the study. Confidentiality was guaranteed. Participants were given option of either acceptance or refusal of participation in the research survey. Questionnaires were given to students and the completed questionnaires were collected by the researchers.

The data was analyzed using SPSS-22 software. Mean perceived stress score was calculated and also the percentage frequency of occurrence for each potential stressor. ANOVA techniques were used to analyze differences in mean perceived stress score amongst different classes. Binary Logistic Regression Analysis was performed in general to specific approach to determine core stress factors. P-Value was set at 0.05.

RESULTS

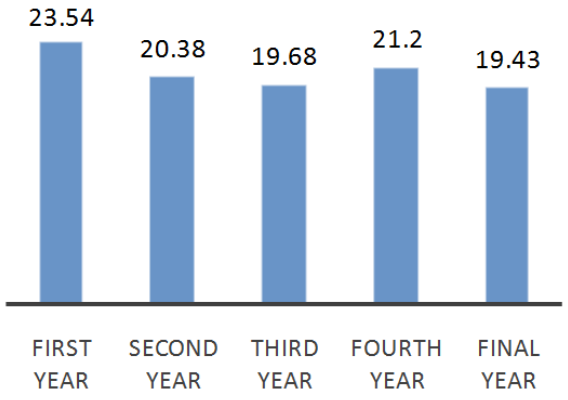
Demographic Characteristics: Out of 400 students, 397 completely filled and returned the research questionnaire giving a total response rate of 99.25%. (98.74% for 1st, and 97.5% for 2nd and 100% for 3rd, 4th and final years). The mean age of the responders was 20.43 (SD=0.81) with 18.45(SD=0.78), 19.51 (SD=0.85), 20.71(SD=0.80), 21.63(SD=0.93), 22.54 (SD=0.69) for 1st, 2nd, 3rd, 4th and final year respectively. All the respondents were female as FJMU is an all women university.

Table No 1: Differences in Mean Perceived Stress Score amongst Different Classes (By ANOVA Technique)

Year of Study		Mean Difference
First Year	Second Year	3.423*
	Third Year	4.133*
	Fourth Year	2.608*
	Fifth Year	4.383*
Second	First	-3.423*
	Third	.710
	Fourth	-.815
	Fifth	.960
Third	First	-4.133*
	Second	-.710
	Fourth	-1.525
	Fifth	.250
Fourth	First	-2.608*
	Second	.815
	Third	1.525
	Fifth	1.775
Fifth	First	-4.383*
	Second	-.960
	Third	-.250
	Fourth	-1.775

(By using ANOVA Technique)

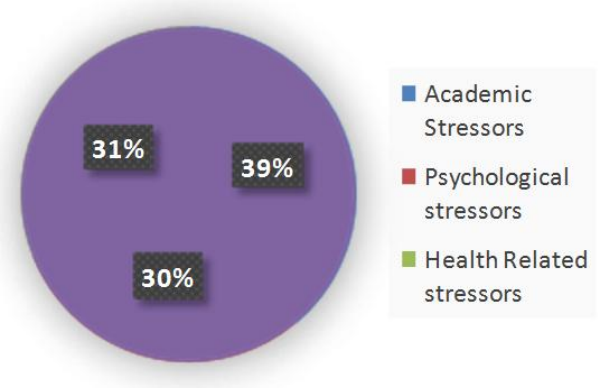
Perceived Stress: The total mean perceived stress score was 20.84 (SD = 6.44) with a median of 21.20 (Graph 1). Stress amongst 1st year medical students was significantly higher and different from other years (Table 1). Hence our hypothesis that undergraduates from initial years are more stressed was proved.



Graph No 1: Mean Perceived Stress Score of Individual Years

First year medical students showed highest level of stress

Most Potential Stressors: Most potential stressors were related to the academic domain with an overall prevalence of 39% followed by health related stressor with a prevalence of 31%. Psychological stressors accounted for 30% prevalence rate (Graph 2). The potential stressors were 'Performance In Examinations', 'Frequency Of Examinations', 'Accommodation Away From Home', 'Nutrition', 'Sleeping Difficulties', 'Satisfaction With Quality Of Food In Mess'. The most potential stressors in each year were all related to the academic domain. Hence our hypothesis that most potential stressors are related to academic domain was proved. (Table 2)



Graph No 2: Prevalence of Most Potential Stressors:

Table No. 2: Most Potential Stressors (year wise)

Year of	Stressor	P-
1st year	Frequency of	.008
	Lack of time for	.010
2nd Year	Frequency of	.011
	Class Attendance	.020
3rd Year	Frequency of	.001
	Performance in	.001
4th Year	Performance in	.027
	Frequency of	.015
Final Year	Performance in	.003
	Frequency of	.009

(Using step-wise Binary Logistic Regression Analysis)s

DISCUSSION

The perceived stress among year 1-5 of MBBS students of FJMU was evaluated and the sources of stress were identified. Perceived stress was calculated using Perceived Stress Scale-10 (PSS-10) questionnaire[15]. This scale was chosen for the present research because of its documented reliability and viability[17]. The total mean perceived stress score in our study was 20.84 (SD=6.44). Various studies have been done to assess perceived stress among medical students using PSS-10. A PSS score of 29.58 was calculated in India[11] and 30.84 in CMHMC, Pakistan[16]. The stress level was significantly higher than that calculated in our study. A comparative research study was conducted in Bangladesh to assess differences in the mean perceived stress between public and private medical institutions. The overall prevalence of perceived stress was calculated to be 54% and there was a statistically significant difference in the level of stress between public and private medical schools[13]. The limitation of our study is that it only involves a single institution. The future studies should focus on assessing stress levels among multiple institutions in order to address this problem on a larger scale.

A number of other studies have been done on stress using different scales. Varying degrees of stress were reported because these researches were carried out using different instrument or it could be a real difference due to different socio-demographic backgrounds[9,10, 11,12].

We also calculated the PSS scores among individual classes and differences were assessed. Stress amongst 1st year medical students was significantly higher and different from other years. A plausible reason maybe that there is a sudden transition from pre-medical course to medical course and students find it very difficult to cope with the undue pressure of increased study load, changed learning environment and being away from home. The Teachers are not very helpful, supportive or facilitating like those in school days and there is lack of counselors in the university. An interesting result of the current study was that the degree of stress lessened by advancing year. Researches carried out in India and Canada showed similar results[11,18]. Opposite results were seen in Germany which might be due to different socio-demographic backgrounds[6].

In our study, academic factors were reported as most prevalent stressors with regards to severity and frequency. Thus our second hypothesis that majority of probable stressors affect the academic performance of the medical students was proved. Among them 'Poor Performance in Examination' and 'Frequency in Examination' are the most stressful events.

Various academic stressors were identified in researches conducted in India and Pakistan [9, 11, 20]. Both the researches showed that 'increased frequency of examination' is the most common academic stressor around the world. The medical educationists should work in this domain and try to overcome this major problem faced by students.

The most potential stressors related to psychosocial and health related stressors were 'Living Away From Home', 'Bad Nutrition', 'Lack of Sleep', 'Low Quality Food in Mess'. The studies reported in different countries show similar results. The social life of students is so much affected that they find it very

difficult to interact with people and mostly spend their time alone[2,3,12]. Sleeping disorders have significantly risen among students in the past couple of years. According to a research carried out in a medical college in Pakistan, stress badly affects the sleep quality of medical students and they end up taking sedative pills to overcome their sleep disorders.[20]

Our research only involves the female undergraduate medical students as FJMU is an all women institution. So a comparison of stress between both genders is unavailable. Other researches have assessed the differences in stress levels amongst female and male medical student. A research conducted in KSA showed that the prevalence of stress was higher ($p<0.5$) among females (75.7%) than among males (57%)[22]. Future studies should involve multiple institutions to make such comparisons.

It is suggested that the medical educators should guide the students in stressful times so as to direct them on right path. This can be done by more student teacher interactions in healthy activities like sports, conferences and seminars and co-curricular activities where students get time to express themselves and overcome their complex.

CONCLUSION

The study showed a high level of perceived stress among fresh enrolling MBBS students. Academic stressors were the most frequent stressors affecting the overall performance of medical students. It is important for medical educators to appreciate the level of stress and its various causes among medical undergraduates. We suggest early guidance and regular assessments of stressors which will help students to overcome academic derailments that may lead to dropout in medical education and prepare students for stressful career of a health professional.

Author's Contribution:

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

REFERENCES

1. Tempski P, Bellodi PL, Paro HB, Enns SC, Martins MA, Schraiber LB. What do medical students think about their quality of life? A qualitative study. BMC Med Educ 2012;12:106.
2. Pagnin D, de Queiroz V. Comparison of quality of life between medical students and young general populations. Educ Health (Abingdon) 2015;28(3): 209–12.
3. Hwang IC, Park KH, Kim JJ, Yim J, Ko KP, Bae SM, et al. Perceived Social Support as a Determinant of Quality of Life Among Medical Students: 6-Month Follow-up Study. Acad Psychiatr 2016.
4. Suñer-Soler R, Grau-Martín A, Font-Mayolas S, Gras ME, Bertran C, Sullman MJ. Burnout and quality of life among Spanish healthcare personnel. J Psychiatr Ment Health Nurs 2013;20:305-13.
5. Hurst CS, Baranik LE, Daniel F. College student stressors: A review of the qualitative research. Stress Health 2013;29(4):275–85.
6. Voltmer E, Kotter T, Spahn C. Perceived medical school stress and the development of behavior and experience patterns in German medical students. Med Teach 2012;34(10):840.
7. Dahlin M, Joneborg N, Runeson B. Stress and depression among medical students: a cross-sectional study. Med Educ 2005;39(6):594–604.
8. Chowdhury R, Mukherjee A. .Perceived psychological stress among undergraduate medical students: Role of academic factors. Indian J Public Health 2017;61(1):55-57.
9. Hurst CS, Baranik LE, Daniel F. College student stressors: A review of the qualitative research. Stress Health 2013;29(4):275–85.
10. Ross S, Cleland J, Macleod MJ. Stress, debt and undergraduate medical student performance. Med Educ 2006;40(6):584–9.
11. Chowdhury R, Mukherjee A. .Perceived psychological stress among undergraduate medical students: Role of academic factors. Indian J Public Health 2017;61(1):55-57.
12. Harikiran AG, Srinagesh J. Perceived sources of stress amongst final year dental under graduate students in a dental teaching institution at Bangalore, India: a cross sectional study. Indian J Dent Res 2012;23(3):331-6.
13. Eva EO, Islam Z. Prevalence of stress among medical students: a comparative study between public and private medical schools in Bangladesh. BMC Res Notes 2015;8:327.
14. Lins L, Carvalho FM, Menezes MS, Porto-Silva L, Damasceno H. Health-related quality of life of students from a private medical school in Brazil. Int J Med Educ 2015;6 :149–54.
15. Chan SF, La Greca AM. Perceived stress scale (PSS). In: Gellman MD, Turner JR, editors. Encyclopedia of behavioural medicine. Springer: New York; 2013.
16. Shah M, Hasan S. Perceived stress, sources and severity of stress among medical undergraduates in

a Pakistani Medical School. BMC Med Educ 2010; 10:2.

17. Eleni A, Evangelos A, Christos L, Liza V, Charalambos G, George C, et al. Perceived Stress Scale: Reliability and Validity Study in Greece. Int J Environmental Res Pub Health 2011;8:3287-98.
18. Coburn D, Jovaisas AV. Perceived sources of stress among first-year medical students. J Med Educ 1975;50:589-95.
19. Rotenstein LS, Ramos MA, Torre M, Segal JB, Peluso MJ, Guille C, et al. Prevalence of Depression, Depressive Symptoms, and Suicidal Ideation Among Medical StudentsA Systematic Review and Meta-Analysis. JAMA 2016;316 (21):2214–2236.
20. Waqas A, Spogmai Khan. Association of academic stress with sleeping difficulties in medical students of a Pakistani medical school: a cross sectional survey. Peer J 2015;3:e840.
21. Sreeramareddy CT, Shankar PR, Binu VS, Mukhopadhyay C, Ray B, Menezes RG. Psychological morbidity, sources of stress and coping strategies among undergraduate medical students of Nepal. BMC Med Educ 2007;7:26-10.
22. Hamza M. Abdulghani. Stress and Its Effects on Medical Students: A Cross-sectional Study at a College of Medicine in Saudi Arabia. J Health Popul Nutr 2011;29(5):516–522.

Original Article

Patient's Safety as Integrated Part of Medical Curricula: Perceptions of Postgraduate Medical Doctors from Two Selected Teaching Institutes Peshawar Pakistan

Sher Bahadur[1], Saminullah Khan[2] and Attaullah Jan[1]

ABSTRACT

Objective: To Perceptions of postgraduate medical doctors Patient's safety as integrated part of medical curricula in Peshawar Pakistan.

Study Design: Qualitative study

Place and Duration of Study: This study was conducted at the Department of Pediatrics, Khyber Institute of Child Health, Peshawar and Rehman Medical College Peshawar from April 2010 to May 2016.

Materials and Methods: This was a qualitative study based on exploratory design where data was gathered through focus group discussion (FGDs) from post graduate medical doctors (Trainee Medical Officers, TMO) from two selected teaching hospitals i.e. Hayatabad Medical Complex (HMC) and Rehman Medical Institute (RMI) Peshawar. Thematic data analysis was done manually for construction of results in terms of narrations

Results: The basic definition of the patient's safety to them was "health care provision in such that there is no harm to the patients" while incorrect diagnoses and treatment was considered as medical error. Other reported characteristics related medical error are; ignoring patients, lack of skills of procedure and any unethical conducts. One of the senior TMOs explained it in these words "major component of medical error is incorrect diagnose, doctors usually miss diagnose the patients and later realize their mistake". Based on these definition almost all of the respondents accepted that everybody (doctor) experienced some sort of these incidents or medical errors during the journey of their career, most likely during house job the error took placed. The human factors in this regards included; work burden, fatigue, dealing with complex cases and attitude of the individual doctors and poor hospital management supervision system. Incident reporting system in the hospitals are not implemented yet in the teaching hospital. The participants were of the view that patient's safety concerns are given due importance in medical curriculums of Pakistan.

Conclusion: Patients' safety was considered as core component of clinical practices. It was emphasized that Patients' safety module is needed to be formally incorporated in undergraduates and post graduate medical curriculum in Pakistan.

Key Words: Patient's Safety, Medical Curricula, Perceptions of Postgraduate Medical Doctors

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INTRODUCTION

The eventual goal of a curriculum in medical education is to address and solve the problems that affect the health of the public. Recently patient safety has come out to be a distinct discipline of heath care services and raised considerable public concerns.[1]

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In Pakistan the media have reported a significant number of patients being harmed and even killed due to medical errors, thus it emphasizes to plan for patient safety. However the area of patient safety care has been neglected specially in developing countries including Pakistan. It is apparent that a notable number of patients harmed/killed being admitted in the hospitals. In Pakistan in most of the health care setup, there is a lack of trans-disciplinary, evidence-based strategies for the patient safety. Furthermore there are also lacks of incident Reporting System and risk management strategies in our health care system especially at public hospitals.[2]

As result of mass media campaigns, the graph of awareness among general population is in its ascending fashion, hence they demand for safe and evidence based health care at any cost.[3] In this regards undergraduate education plays an important role in the broadcasting of

the correct concepts, skills, and knowledge about patient safety. However apart all these importance, health care professionals (students) are not been properly guided.[4]

Considering the significance of the problem many medical colleges in the world have added patient safety as formal teaching in their curricula.[5] The issue has not been given its due attention in our setup.[6] There is dire need that the medical students should be well versed in correct concepts, knowledge and skills about patient safety. Therefore it is very vital that medical students should be guided toward the principal of patient safety and should become a core of undergraduate curricula.[4]

MATERIALS AND METHODS

This study was conducted at the Department of Pediatrics, Khyber Institute of Child Health, Peshawar and Rehman Medical College Peshawar from April 2010 to May 2016.The exploratory design was used to address the through detailed focus group discussion gathering the data rich in context. The study was conducted on participants who were able to provide a wealth of information that led us to the reason of lake of patient safety measures in our health care setup or vice versa. It also explored the understanding of several other factors influencing the patients' safety measures in the curriculum and practical field. Study participants comprised of trainee medical officers from two selected tertiary care hospitals (RMI &HMC), Peshawar. Semi-structured pre-tested in-depth interviews guideline was conducted to explore perceptions of Trainee Medical Officers, having at least 3 years of clinical experience. A total of three FGDs were conducted which comprised of 6-8 participants. Data collected from different TMOs were fully transcribed accurately by independent expert transcriber and verified by the researcher. Data analysis of the transcripts was done by the researcher and external independent coder. The process of data analysis followed below steps. A list has been made of all the ideas and the similar ideas were clustered together. The final themes were formulated after reviewing the sub-nodes of respondents.

RESULTS

Regarding perception of patient safety most of them perceived patient safety "mean ho harm to the patients" which are included: Prevention of patient from other disease while treating the first one, preventing patients from any accident any hazards, ensuring of proper sterilization. One participants among TMOs mentioned, "Patient safety would mean that patient should not be harmed not porn to any accident, any hazard. He/she should be given proper treatment. He/she should be safe and should not get any disease while curing the first one".

Interpretation of medical error: Varying interpretation regarding medical error was given. The subsequent term was used for definition of medical error which included; incorrect investigations, wrong diagnosis or unnecessary long prescription. The important characteristics associated with medical error are: not giving appropriate time to the patients, skipping them not listening to them and lack of exposure and knowledge about medical surgical instruments. One of the senior TMOs explained it in these words "major component of medical error is incorrect diagnose, doctors usually miss diagnose the patients and later realize their mistake" another

Interpretation of adverse Events: Major proportion of the respondents perceived adverse Events as an outcome of medical error. One of the TMO narrated, "Adverse effect, happen when error is done". Again ignorance was linked with adverse events as defined by one of the participant "If patient safety is ignored this mean adverse Events".

Incidence of medical error encountered: Almost all of the respondents accepted that everybody (doctor) experienced some sort of these incidents or medical errors during the journey of their career, most likely during house job the error took placed. The frequent errors concerning patient safety were included; error during blood sample taking, medication and some sort of procedure performing. Mostly patients were not fully informed of guided regarding the procedure they went. One of the participants voiced, "Everybody experienced some sort of these incidents or medical errors….The doctors are not doing any errors it is just negligence"

Human factors of medical error: Factors influencing the patient's safety measures included; human, system and management related factors. The human factors included work burden, fatigue, dealing with complex cases and attitude of the individual doctors. Secondly, doctors mostly unfamiliar to the instruments like; surgical instruments, biomedical instrument and machines which in turn lead to the medical error. A senior participant narrated that "new doctors unusually not familiar to instruments due to lack of knowledge secondary to complexity and burden of work responsibility"

System related factors of medical error: About 3/4th of the participants also perceived that patient safety related incidence also occurs due to fault in the system which included; Lack of accountability , lack of proper protocols for the procedure (medical, surgical or others) hence no practices or follow-up (like accidents reports) observed.

Participant knowledge about accident report in the system: The importance of incident reporting system was admitted by most of participants, however, they added that such system is lacking in our organizations. A female TMO said that "Every hospital has an hierarchy of management and everyone should submitted incidence report if occurred….unfortunately

we yet not seen anyone who reported or asked for submission of incidence report"

Possible challenges for patient safety being part of curriculum in Pakistan: The main challenges reported are; poor attitude, lack of proper system, lack of interest of higher authority for the curriculum change. A comprehensive statement was given by one of the senior registrar "possible challenges in teaching patient safety to be part of our undergraduate and post graduate curriculum could be roughly, poor attitude, lack of interest of higher authority in this regards, lack of proper system (accountability) and most importantly the lack of welling to acceptance of change in curriculum"

DISCUSSION

Health Care organizations in the world are now continuously trying to improve health status of the clients by creating a health safety culture.[7] In this regards, World Health Organization (WHO) published and recommended "Patient Safety Curriculum Guide" for health care professionals especially for doctors. This Guide was developed after a series of meeting and tasks accomplishment by group of universities.[8]

The current study used a mixed methodology to assess the attitude and perception of trainee medical officers regarding patient's safety perspectives as part of undergraduate and postgraduate medical curriculum in Pakistan. Results indicates that majority of TMOs were of the view that medical errors usually occur, but could be preventable. One fourth of the students pointed that "after an error occurs, an effective strategy is to work harder to be more careful" a similar finding was also reported by Leung GK, Patil NG,[9] and about 1/2 of them were of the opinion that that medical error is common among incompetent doctor and on other hand competent doctor rarely commit medical errors, however this statement indicates an elementary misunderstanding about the nature and form of human error. [10]

Participants pointed out that doctor's especially senior physician should spare some of their time for patient's safety. This is also evident from literature where strategies regarding patient's safety and evidence based practices and was found effective in term of health outcomes. A "unit-based Patient Safety Leadership Walk-rounds (PSWR)"model was tested and good health impact was observed. [11]

Unfortunately Incidence reporting in selected hospitals the system was not formally functioning. This indicates that if proper incidence reporting system established in tertiary care hospitals, there will be a marked reduction in medical error in future as also evident from Shaw KN et al, observation. He found that error in medication among children has significantly reduced when quality health care was assured by implementing patient's safety measures. [12]

Knowledge about "patient's safety" among physician was also associated with medical error. Ghalandarpoorattar SM, et al,[13] found clear gaps between physician's knowledge and actual practices concerning patient safety. It was stated that "education in medical error management to professionally support error disclosure might help reduce the gap".[13]

Comparatively to other domains of patient safety, the key informants admitted that poor attitude among physicians were observed regarding reporting of medical errors. However they further added that a Physician is not always supposed to report medical errors on routine bases". Whereas routinely reporting of medical error was found very effective in reduction of error and improvement of patient safety.[14]

Keeping the importance of the patients' safety in the recent era 3/4th of TMO suggested that patient's safety curriculum should be the part of undergraduate and post graduate medical curriculum. Hence majority of them agreed that "Learning how to improve patient safety is an appropriate use of time in medical school". Learning of patient safety aspect as undergraduate level was supported by most of the literature and found significantly effective.[15-18] Although the actual knowledge is not presented in the current study but varying definitions of patient safety, medical error and adverse effects were reported by TMOs. Most of them reported basic indicators of patient's safety however; none of them have stated a concise definition. Almost all of them have experienced medical error during their journey of medical practices. They further reported that medical error have directly associated with; human, system and management factors. [19]These findings of present study are in consistence with other literatures where these factors were found directly associated with medical errors among these, human factorswere the main cause of medical errors.[20]

The core contributing factors in present study were; lack of appreciations, poor health infrastructure, lack of implementations, and medical complexity as potential causes of errors. The participants further added that patient's safety features not being part of medical curriculum in Pakistan, are due to; poor attitude of physicians and lake of patient safety culture. More or less similar statements were reported by World Health Organization.[2] WHO has categorized these challenges into; system related factors, new innovations in medical field, work load and poor attitude of physicians along with lack of accountabilities and responsibilities due to which things can often go wrong and unintentional, but serious harm comes to patients during routine clinical practice, or as a result of a clinical decision.[2]

Curriculum review in the present study indicates that patients safety curriculum proposed by WHO was not given due importance in Pakistan. The terms proposed by W.H.O was not found in both undergraduate and postgraduate medical curriculum in Pakistan. Ethical

consideration; however were given due importance in addition to principals of proper medications, diagnosis and appropriate treatment. It is also important to emphasize that there is no other sources or guidance on content of patients safety or consensus on what, and how much to include in the curriculum apart from W.H.O recommendation. There is also uncertainty on the level of effectiveness of these measures taken or the impact on patient safety in a particular country. Although patient safety is regarded as an issue of vital importance throughout the world as indicated in the literature but fewer Universities have made serious effort in making patient safety as part of their curriculum to a degree which can translate theory into practice.[21] There is also lack of consistency in the content of the curriculum which makes it difficult to include in a module with suitable content or deliverable changes in practice. There is evidence of brief, mixed and separate and extended module curricula but the formats vary. The teaching method of these modules may also vary from traditional lecture to video assisted simulation formats.[22]

CONCLUSION

Trainee Medical Officers of selected institute were aware of medical errors being inevitable aspects vary from situation to situation. There was however poor response in term of agreement regarding incidence reporting. The medical errors being inevitable aspects was broadly liked with three basic factors; the human factor, system and management factors which have further multi-facets linkages, contributing to medical error. The interpretation about patient safety was basically considered as proper diagnose, treatment and avoidance from hospital acquired infections

Author's Contribution:

Concept & Design of Study:	Sher Bahadur
Drafting:	Saminullah Khan
Data Analysis:	Attaullah Jan
Revisiting Critically:	Sher Bahadur, Saminullah Khan
Final Approval of version:	Sher Bahadur

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REFERENCES

1. Berdahl A. Institute of Medicine study puts the spotlight on patient safety issues. Hosp Outlook 2000;3(2):6.
2. Walton M, Woodward H, Van Staalduinen S, Lemer C, Greaves F, Noble D, et al. Republished paper: The WHO patient safety curriculum guide for medical schools. Postgrad Med J 2011;87 (1026):317-21.
3. Flanagan B, Nestel D, Joseph M. Making patient safety the focus: crisis resource management in the undergraduate curriculum. Med Educ 2004;38(1): 56-66.
4. Nie Y, Li L, Duan Y, Chen P, Barraclough BH, Zhang M, et al. Patient safety education for undergraduate medical students: a systematic review. BMC Med Educ 2011;11:33.
5. Kim CS, Lukela MP, Parekh VI, Mangrulkar RS, Del Valle J, Spahlinger DA, et al. Teaching internal medicine residents quality improvement and patient safety: a lean thinking approach. Am J Med Qual 2010;25(3):211-7.
6. Misbah S, Mahboob U. Strengths, weaknesses, opportunities, and threats analysis of integrating the World Health Organization patient safety curriculum into undergraduate medical education in Pakistan: a qualitative case study. J Educ Eval Health Prof 2017;14:35.
7. Jones KJ, Skinner A, Xu L, Sun J, Mueller K. The AHRQ Hospital Survey on Patient Safety Culture: A Tool to Plan and Evaluate Patient Safety Programs Culture and Redesign). 2008.
8. World Health Organization (WHO). Global patient safety research priorities [Internet]. c2009. Available from: http://www.who.int/patientsafety/ research/en/.
9. Leung GK, Patil NG. Patient safety in the undergraduate curriculum: medical students' perception. Hong Kong Med J 2010;16(2):101-5.
10. Norris B. Human factors and safe patient care. J Nurs Manag 2009;17(2):203-11.
11. Taylor AM, Chuo J, Figueroa-Altmann A, DiTaranto S, Shaw KN. Using four-phased unit-based patient safety walkrounds to uncover correctable system flaws. Jt Comm J Qual Patient Saf 2013;39(9):396-403.
12. Shaw KN, Lillis KA, Ruddy RM, Mahajan PV, Lichenstein R, Olsen CS, et al. Reported medication events in a paediatric emergency research network: sharing to improve patient safety. Emerg Med J 2012;30(10):815-9.
13. Ghalandarpoorattar SM, Kaviani A, Asghari F. Medical error disclosure: the gap between attitude and practice. Postgrad Med J 2012;88(1037):130-3.
14. Woolever DR. The Impact of a Patient Safety Program on Medical Error Reporting Findings) 2005.
15. Aggarwal R, Mytton OT, Derbrew M, Hananel D, Heydenburg M, Issenberg B, et al. Training and simulation for patient safety. Qual Saf Health Care 2010;19 Suppl 2:i34-43.
16. Kyrkjebo JM, Brattebo G, Smith-Strom H. Improving patient safety by using interprofessional simulation training in health professional education. J Interpr Care 2006;20(5):507-16.

17. Salas E, Paige JT, Rosen MA. Creating new realities in healthcare: the status of simulation-based training as a patient safety improvement strategy. BMJ Qual Saf 2013;22(6):449-52.
18. Shavit I, Keidan I, Hoffmann Y, Mishuk L, Rubin O, Ziv A, et al. Enhancing patient safety during pediatric sedation: the impact of simulation-based training of nonanesthesiologists. Arch Pediatr Adolesc Med 2007;161(8):740-3.
19. Holden RJ, Karsh BT. A review of medical error reporting system design considerations and a proposed cross-level systems research framework. Hum Factors 2007;49(2):257-76.
20. Kawano R. [Patient safety and quality of medical care. Topics: III. Management of patient safety and quality of medical care: theory and practice; 2. Human factors in medical care]. Nihon Naika Gakkai Zasshi 2012;101(12):3463-9.
21. Wakefield A, Attree M, Braidman I, Carlisle C, Johnson M, Cooke H. Patient safety: do nursing and medical curricula address this theme? Nurse Educ Today 2005;25(4):333-40.
22. Flanagan B, Nestel D, Joseph M. Making patient safety the focus: crisis resource management in the undergraduate curriculum. Med Educ 2004;38: 56-66.

Original Article

Finger Surgeries

Safety and Efficacy of Lidocaine with Adrenaline for Ring Block Anesthesia in Finger Surgeries

Fahad Mirza[1], Moiz Sadiq[2], Batool Urooj Rajput[2] and Syed Sheeraz ur Rahman[3]

ABSTRACT

Objective: To determine the safety and efficacy of Lidocaine (Xylocaine) with adrenaline (1:100,000) for ring block anesthesia in finger surgeries.

Study Design: Descriptive case series study.

Place and Duration of Study: This study was conducted at the Plastic Surgery Unit, Liaquat National Hospital, Karachi from October 17, 2015 to April 16, 2016.

Materials and Methods: All 18- 60 years patients of either gender with post traumatic injuries to fingers with duration of trauma <1 week or elective surgeries of fingers with presence of pathology less than 1 year were enrolled. Patients received lidocaine 1% with 1:100,000 epinephrine on the finger/fingers to be operated. Efficacy and safety of anesthetic combination was noted.

Results: Mean age of the patients was 32.93±11.17 years. Mean time since trauma was 62.64±99.73 days. Male preponderance was found to be higher. Type of injury was RTA in 17 (26.2%) patients, door entrapment 11 (16.9%), machine 11 (16.9%) and other injuries in 26 (40%) of the patients. Safety was observed in all 65 (100%) patients whereas efficacy was observed in 60 (92.3%) fingers of the patients.

Conclusion: Safety and efficacy of Lidocaine with adrenaline was found satisfactory for ring block anesthesia in finger surgeries.

Key Words: Safety, Efficacy, Lidocaine with adrenaline, Ring block anesthesia, Finger Surgeries

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INTRODUCTION

Digital nerve block is a widely used method for hand surgeries which is typically less painful and provides a greater duration of consistent anesthesia in the operative field[1,2,3]. Different techniques have been studied and those with rapid onset of action were found to be more beneficial[4,5]. Studies have shown adrenaline when used in combination with lidocaine increases the duration of action of the anesthesia, enabling longer procedures to be undertaken, larger amount of Lidocaine that can be given and also ensuring post-operative pain relief[6]. Adrenaline due to its vasoconstrictive effect causes constriction of the digital arteries, ensuring a relatively bloodless field and obviating the need of finger tourniquets[7].

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Also adrenaline enables surgery with lower dosage of sedatives and also facilitates in certain other procedures like tenolysis and tenorraphy. Bashir et al has 80% effectiveness with lidocaine and epinephrine with dorsal approach however 100% effectiveness with volar blocks[8].

Chowdry et al in 2010 in a retrospective study has found 98% oxygen saturation in patients administered lidocaine with epinephrine compared to lidocaine group alone 96%[9]. Bashir M et al in 2015 in a prospective randomized study found that an interval of 25 minutes between injection of lidocaine with epinephrine and beginning off procedure provides vastly superior operative field visibility[10].

Conventionally surgeons in our local community and internationally were hesitant to use lidocaine with adrenaline due to the misconception that adrenaline being a vasoconstrictor of vessels would cause intense vasoconstriction of digital arteries leading to impaired blood flow and subsequent finger ischemia. However this misconception has been invalidated by recent clinical studies and trials and has now become a widely used method internationally. Epinephrine with local anesthetic had no increased risk of skin necrosis. Wide awake hand surgery is a new perspective employing the combined administration of lidocaine with adrenaline. It is a safe method and enables surgery to be undertaken without the use of tourniquets, sedation and regional anesthesia[11,12].

Since these misconceptions widely exist in our community, and due to scarcity of clinical data in our society including the center where this study was conducted, we have aimed our study to determine the safety and efficacy of lidocaine with epinephrine for finger block anesthesia and provide current and local statistics of efficacy of both drugs administered as a combination and to spread awareness of its effectiveness and safety, and if its efficacy and safety is found to be higher, than same modality would be advocated to surgeons for future finger procedures.

MATERIALS AND METHODS

Descriptive case series study was conducted in Department of Plastic Surgery Unit at Liaquat National Hospital, Karachi from October 17, 2015 to April 16, 2016.

Sample Size: Assuming proportion of adequate visual field 91%12, Confidence level 95%, absolute precision 7%, the sample size came out to be 65 fingers.

Sampling Technique: Non Probability Consecutive

Sample Selection:

Inclusion criteria: Age 18- 60 years

Either Gender: Post traumatic injuries to fingers with duration of trauma less than one week or elective surgeries of fingers with presence of pathology less than 1 year.

Exclusion criteria:

Patients with allergy to local anesthetics.

Patients with bleeding disorders, (confirmed on history.)

Previous vascular insufficiency, previous digital replantation or peripheral neuropathy. Confirmed on history and presence of surgical scars.

Patients with poor peripheral perfusion before the surgery, (capillary refill >2 secs)

Those who did not give written consent for inclusion in the study.

Data Collection Procedure:

Patients was selected on the basis of inclusion and exclusion criteria, the risks and benefits of the study was explained to them and after their consent to take part in the study, a detailed Porforma was filled. After all preoperative assessment, patients received lidocaine 1% with 1:100,000 epinephrine between the dorsal and palmar surfaces, at the base on both the radial and ulnar sides of the finger/fingers to be operated. The blocks were given by 3ml syringes with 1.5cms 27 gauge needles. Efficacy (bloodless field) was rated as adequate if the procedure was successfully finished without application of a finger tourniquet, or inadequate, if procedure needed application of a finger tourniquet to be successfully finished. 2.5 hours after application of lidocaine with epinephrine finger was assessed for presence/absence of capillary refill and colour (pink/pale-blue). The presence of capillary refill and a pink finger denotes good finger perfusion and proves safety of anesthetic combination.

Statistical Methods: The statistical analysis was performed by using SPSS.20. Mean and standard deviation was calculated from age and time since trauma. Frequencies and percentages were calculated for type of injury, gender, number of fingers involved, efficacy and safety. Effect modifiers like age, gender, number of fingers, duration since trauma and type of injury was stratified to see the effect of this on outcome. Chi square test was applied taking 'p' value less than or equal to 0.05 as significant.

RESULTS

Mean age of the patients was 32.93±11.17 years. Majority of the patients 35 (53.8%) were presented with ≤30 years of age.

Table No.1: Demographics

Factors	Mean with SD
Age (in years)	32.93 ± 11.17
≤ 30 years	35
> 30 years	30
Time since trauma (days)	62.64±99.73
≤ 60 days	47
> 60 days	18
Gender	
Male	41
Female	24

Table No.2: Type of injury, indication of surgery and safety and efficacy of anesthetic agent

Factors	No. of patients
No. of fingers involved	
1 finger	48
2 fingers	17
Type of Injury	
Machine	11
RTA	17
Door entrapment	11
Others	26
Indication for Surgery	
Emergency	39
Elective	26
Safety of local anesthetic agent	
Yes	65
No	0
Efficacy of anesthetics agent	
Yes	60
No	5

Mean time since trauma was 62.64±99.73 days. Majority of the patients 47 (72.3%) were presented with ≤60 days of duration since trauma. Male preponderance was found to be higher 41 (63.1%) as compared to females 24 (36.9%). (Table1)

Majority of the patients i.e. 48 (73.8%) presented with only 1 finger of injury. Cause of injury was RTA in 17

(26.2%) patients, door entrapment in 11 (16.9%), machine in 11 (16.9%) and other injuries in 26 (40%) of the patients. Indication of surgery was trauma in majority 39 (58.9%) patient whereas elective indication of surgery was found in 26 (42.1%) patients. Safety was observed in all 65 (100%) patients whereas efficacy was observed in 60 (92.3%) patients (Table 2).

Stratification was done to see the effect of age, gender, time since trauma, numbers of finger involved, type of injury and indication of surgery on the outcome. Results are shown in Table 3.

Table No.3: Results

Factors	Efficacy		P Value
	Yes	No	
Age in Years			0.112
≤ 30 years	31	4	
> 30 years	29	1	
Gender			0.644
Male	37	4	
Female	23	1	
Time since trauma			0.125
≤ 60 days	45	2	
> 60 days	15	3	
No. of fingers involved			0.745
1 finger	44	4	
2 fingers	16	1	
Injury type			0.253
Machine	11	0	
RTA	16	1	
Door Entrapment	11	0	
Others	22	2	
Indication			0.148
Trauma	38 (63.3)	1 (20.0)	
Elective	22 (36.7)	4 (80.0)	

DISCUSSION

The idea that epinephrine should never be injected into fingers originated sometime between 1920 and 1940, when procaine was used with and without epinephrine, with resulting reports of finger necrosis. Nearly all of the 48 reported cases of finger necrosis attributable to procaine local anesthesia occurred before 1950, with most implicating procaine injected without epinephrine[13].

Procaine is quite acidic, with a pH of 3.6, and it further acidifies to a pH as low as 1 with prolonged storage; this acidity, not the addition of epinephrine, is likely responsible for the historical reports of finger necrosis[14].

Lidocaine, by contrast, has been used safely both with and without epinephrine. An extensive review of the literature from 1880 to 2000 revealed no documented cases of finger necrosis resulting from local anesthesia with lidocaine plus epinephrine**Error! Bookmark not defined.Error! Bookmark not defined.**.

Clinical evidence demonstrating the safety of lidocaine mixed with epinephrine is extensive and was well-summarized by Mann and Hammert[15].

In 2001, Wilhelmi et al[16] reported that epinephrine plus lidocaine injection was safe in all 29 fingers injected with it. In 2010, Chowdhry et al[17] reported no epinephrine-induced complications in a clinical series of 1,111 consecutive cases of digital block anesthesia with lidocaine plus epinephrine. A multicenter trial known as the Dalhousie project prospectively reviewed 3,110 consecutive cases of lidocaine with epinephrine ≤1:100,000 injected electively into fingers and hands[18].

No cases of digital necrosis or need for phentolamine rescue were reported.

In our study it was found that oxygen saturation in patients administered lidocaine with epinephrine remains normal. It was also found that if time is given between injection of lidocaine with epinephrine and beginning off procedure, it provides clear operative field.

The Cochrane review 2014 has found monotherapy or even combination therapy of local anesthetics to be of benefit in terms of short term anesthesia and in reducing the complications related to post procedural anesthesia[19]. Lidocaine was superior in efficacy than bupivacaine in terms of shorter mean onset of anesthesia, less pain at the site of injection and less cardiotoxic potential in hand surgeries[20].

Studies have shown adrenaline not only increases the duration of action of lidocaine when used in combination but also provides clear operative field due to its vasocontrictive effect and it enables longer procedures to be undertaken due to larger amount of Lidocaine that can be safely given and it also ensures post-operative pain relief[21].

During early days, adrenaline was not used in areas having end arteries as it was a common misconception worldwide that when lidocaine was used with adrenaline it could lead to impaired blood flow and eventually to finger ischemia as fingers have end arteries and adrenaline being vasoconstrictor can cause intense vasoconstriction of digital vessels. However recent clinical studies and trials has proved that indeed using lidocaine with adrenaline is useful in terms of longer duration of action, clear field, increases maximum dose and has now become a widely used method internationally.

This has led to the concept of wide awake anesthesia for surgeries which help in those patients who cannot undergo general anesthesia due to different medical conditions as well as those in which patients reflexes needs to be checked. This approach now a days is used for multiple procedures including tendon repair, tendon transfer, carpal tunnel release, trigger finger release, ganglion excision, de Quervain release, and soft-tissue

mass excision. Among hand surgeons, the wide awake approach is frequently referred to as the wide-awake local anesthesia technique (WALANT). In addition to the aforementioned indications, WALANT has also been used in conjunction with hand fractures, trapeziectomy, Dupuytren contracture, and wrist arthroscopy/ triangulofibro cartilage complex repair.

One must also know the contraindications for performing these anesthetic blockades. These are as follows: absolute, such as patient's refusal to undergo the procedure, peripheral vascular disease in the region, and infection next to the injection site. Relative, when it is absolutely necessary to test nerve function early in the postoperative period due to blockade establishment of sensory and motor conduction whenever this condition can mask the establishment of a postoperative compartment syndrome. And in a patient already with nerve damage or paresthesia, due to the always present possibility of causing nerve injury[22].There are several techniques with minor modifications that vary from author to author[23,24].

CONCLUSION

Safety and efficacy of Lidocaine with adrenaline was found satisfactory for ring block anesthesia in finger surgeries. No difference was observed in safety and efficacy with respect to age, gender, number of fingers, and duration since trauma and type of injury.

Author's Contribution:

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

REFERENCES

1. Sonohata M, Nagamine S, Maeda K, Ogawa K, Ishii H, Tsunoda K, et al. Subcutaneous single injection digital block with epinephrine. Anesthesiol Res Pract 2012;4.
2. Mann T, Hammert WC. Epinephrine and hand surgery: evidence based medicine. J Hand Surg Am 2012;37(6):1254-6.
3. Antevy PM, Zuckerbraun NS, Saladino RA, Pitetti RD. Evaluation of a transthecal digital nerve block in the injured pediatric patient. PediatrEmerg Care 2010;26:177.
4. Alhelail M, Al-Salamah M, Al-Mulhim M, Al-Hamid S. Comparison of bupivacaine and lidocaine with epinephrine for digital nerve blocks. Emerg Med J 2009 May;26(5):347-50.
5. Cuvillon P, Nouvellon E, Ripart J, Boyer JC, Dehour L, Mahamat A, et al. A comparison of the pharmacodynamics and pharmacokinetics of bupivacaine, ropivacaine (with epinephrine) and their equal volume mixtures with lidocaine used for femoral and sciatic nerve blocks: a double-blind randomized study. Anesth Analg 2009;108(2): 641-9.
6. Sönmez A, Yaman M, Ersoy B, Numanodlu A. Digital blocks with and without adrenalin: a randomised-controlled study of capillary blood parameters. J Hand Surg Eur 2008;33(4):515-8.
7. Oragui E, Parsons A, White T, Longo UG, Khan WS. Tourniquet use in upper limb surgery. Hand (N Y) 2011;6(2):165-73.
8. Bashir MM, Khan FA, Afzal S, Khan BA. Comparison of traditional two injections dorsal digital block with volar block. J Coll Physicians Surg Pak 2008;18(12):768-70.
9. Chowdhry S, Seidenstricker L, Cooney D, Hazani R, Wilhelmi B. Do Not use epinephrine in digital Blocks: Myth or Truth? Part II. A Retrospective Review of 1111 Cases. Plast & Reconstruc Surg 2010;126(6):2031-2034.
10. Bashir M, Qayyum R, Saleem M, Siddique K, Khan F. Effect of Time Interval Between Tumescent Local Anesthesia Infiltration and Start of Surgery on Operative Field Visibility in Hand Surgery Without Tourniquet. J Hand Surg Am 2015;40(8):1606-9.
11. Lalonde D. Minimally invasive anesthesia in wide awake hand surgery. Hand Clin 2014;30(1):1-6.
12. Lalonde D, Martin A. Epinephrine in local anesthesia in finger and hand surgery: the case for wide-awake anesthesia. J Am AcadOrthop Surg 2013;21(8):443-7.
13. Denkler KA. A comprehensive review of epinephrine in the finger: To do or not to do. Plast Reconstr Surg 2001;108(1): 114-124.
14. Thomson CJ, Lalonde DH, Denkler KA, Feicht AJ. A critical look at the evidence for and against elective epinephrine use in the finger. Plast Reconstr Surg 2007; 119(1):260-266.
15. Mann T, Hammert WC: Epinephrine and hand surgery. J Hand Surg Am 2012;37(6):1254-1256, quiz 1257.
16. Wilhelmi BJ, Blackwell SJ, Miller JH, et al: Do not use epinephrine in digital blocks: Myth or truth? Plast Reconstr Surg 2001;107(2):393-397.
17. Chowdhry S, Seidenstricker L, Cooney DS, Hazani R, Wilhelmi BJ. Do not use epinephrine in digital blocks: Myth or truth? Part II. A retrospective review of 1111 cases. Plast Reconstr Surg 2010; 126(6):2031-2034.
18. Lalonde DH, Bell M, Benoit P, Sparkes G, Denkler K, Chang P. A multicenter prospective study of 3,110 consecutive cases of elective epinephrine use

in the fingers and hand: The Dalhousie Project clinical phase. J Hand Surg Am 2005;30(5): 1061-1067.
19. Vinycomb TI, Sahhar LJ. Comparison of local anesthetics for digital nerve blocks: a systematic review. J Hand Surg Am 2014;39(4):744-751.
20. Krikava I1, Jarkovský J, Stourac P, Nováková M, Sevcík P. The effects of lidocaine on bupivacaine-induced cardiotoxicity in the isolated rat heart. Physiol Res 2010;59 Suppl 1:S65-9.
21. Sönmez A, Yaman M, Ersoy B, Numanodlu A. Digital blocks with and without adrenalin: A randomised- controlled study of capillary blood parameters. J Hand Surg Eur 2008; 33(4):515-518.
22. Fisher L, Gordon M. Anesthesia for hand surgery. In: Wolfe SW, Hotchkiss RN, Pederson WC, Kozin SH, editors. Green's operative hand surgery, 6th ed. Philadelphia: Elsevier/Churchill Livingstone;2011. p.32-4.
23. Cummings AJ, Tisol W, Meyer LE. Modified transthecal digital block versus traditional digital block for anesthesia of the finger. J Hand Surg 2004;29:44-8.
24. Sonohata A, Asami K, Ogawa S, et al. Single injection digital block: is a transthecal injection necessary? J Hand Surg 2009;34:94-8.

Original Article

Diagnostic Upper GI-Endoscopy Procedure

Spectrum of Clinical Complications, Observed During Diagnostic Upper GI-Endoscopy Procedure in Khyber Teaching Hospital Peshawar

Jamaluddin[1], Nizamuddin[2], Bughdad Khan[1] and Waheed Iqbal[2]

ABSTRACT

Objective: To evaluate the occurrence of different clinical complication in all patients during diagnostic upper gastrointestinal endoscopy procedure.

Study Design: Descriptive / cross sectional / single center study

Place and Duration of Study: This study was conducted at the Department of Medicine, Khyber Teaching Hospital, Peshawar from July 2017 to June 2018.

Materials and Methods: Total 500 patients, with mean age of 45±1 years, were enrolled in the study by non–probability consecutive sampling. From all these patients, who were advised diagnostic upper GI-endoscopy, informed consent was taken and all the demographic profile of the patients was recorded. Upper GI-endoscopy was performed and clinical adverse events like bleeding, perforation, aspiration, respiratory arrest, tachycardia, cardiac arrest, myocardial infarction and death were recorded. Data were analyzed using SPSS version 20 and graph pad prism version 6.0 while graph were constructed using Microsoft Excel 2013.

Results: Among 500 patients, 350 (70%) were male and 150 (30%) were female. Upper GI endoscopy was performed in all patients. Different clinical complications were observed in 25(5%) patients, while in 475(95%) patients, no major or minor clinical complications were observed. Out of 25 patients with observed clinical complications, 18 were male and 07 were female. No major complication like perforation, cardiac arrest, respiratory arrest and death was observed in any patients. Tachycardia, bleeding, aspiration and myocardial infarction was observed in 13, 09, 02 and 01 patients respectively. Increasing age and gender does not make any statistical significant difference of developing complications with p-value 1.0 though patient with age group of 46-55 and 56-65 are prone to develop complications as compared to other age groups (OR (95%CI 1.18 and 2.08) respectively.

Conclusion: These results clearly suggest, "That upper GI endoscopy is a very safe procedure in all indicated patients, if performed either directly or in the supervision of a senior and experienced endoscopist in a well prepared and properly investigated patients".

Key Words: Endoscopy, GI tract, complications and experienced endoscopist.

Citation of articles: Jamaluddin, Nizamuddin, Khan B, Iqbal W. Spectrum of Clinical Complications, Observed During Diagnostic Upper GI-Endoscopy Procedure in Khyber Teaching Hospital Peshawar. Med Forum 2018;29(8):69-72.

INTRODUCTION

Upper GI endoscopy is a common procedure that is performed nowadays in different clinical settings including gastroenterology, general medicine and surgery[1]. It is performed both in indoor patients and in all those patients who present to outdoor department on daily basis. Upper GI endoscopy is indicated for a number of diagnostic and therapeutic purposes[2].

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The most common diagnostic indications for upper GI endoscopy are long standing dyspepsia, hematemesis, dysphagia, melena, and weight loss with dyspepsia, loss of appetite with dyspepsia, anemia with dyspepsia, endoscopic ultrasound and follow up cases of treated case with carcinoma of the esophagus, stomach and duodenum. The most common therapeutic indications are band ligations or sclerotherapy of bleeding esophageal varices, dilatation of esophageal sphincter or achalasia and removal of foreign bodies[3].

Upper GI endoscopy can be considered a safe procedure, if performed by an experienced person in well-prepared patients. Most of the time, complications are usually seen in those cases where indication is weak, patient is not properly evaluated or prepared before the procedure and a non-experienced poorly skilled endoscopist performs the procedure. The minor complications usually observed during endoscopy like phobia, tachycardia, minor bleeding, slight aspiration

and mucosal injury could occur commonly without any threat to life[4]. Major complication like respiratory arrest, cardiac arrest, myocardial infarction, perforation, major bleeding and death less common and are rarely seen[5]. These complications can also be observed in those patients who have major concomitant disease, non-cooperative and emotionally labile[6]. Because of this safety, it is now a day considered as one of the most commonly performed invasive procedure in Pakistan and around the world.

There are many studies at international level. In all these studies, no major complications were observed which is an encouraging sign regarding the safety of this procedure. In most of the studies published at international level, minor complication like phobia, tachycardia, minor bleeding and mucosal injury were reported. In spite of such a significant clinical complications related procedure, there is very limited research data available at national level, especially conducted in exclusively physician settings. To fill this gape, this study was conducted in the department of medicine, Khyber teaching hospital Peshawar KPK to document all the possible complications and present it in systematic manner.

MATERIALS AND METHODS

This descriptive- cross sectional study was conducted in the department of Medicine, KMC/KTH Peshawar, from July 2017 to June 2018. Total 500 patients, whom endoscopy was performed, were enrolled for this study. Patients were selected by non-probability consecutive sampling. The group age were 25 and plus years, comprising 70% males and 30% females patients. To avoid confounders, all patients with known bleeding disorders, known ischemic heart diseases and known major respiratory diseases were excluded from the study.

Data Collection: After getting proper informed consent, total 500 patients who were advised upper GI endoscopy in outdoor and indoor department of KTH Peshawar were enrolled in the study in a consecutive manner. A strict inclusion and exclusion criterion was applied. The study was approved by the ethical board of the hospital. Demographic information like name, gender and age were recorded and all information regarding patients were kept confidential. All the possible complications, observed in these patients were recorded separately.

Data Analysis: All the information were presented in frequency and percentages. Data were analyze using SPSS version 20. Chi-Square test was done to determine any possible association between age groups, gender and complications. Odds ratio (OR) with 95% confidence interval was determine to find risk using graph pad prism version 6.0. Graph was constructed using Microsoft Excel 2013.

RESULTS

In these 500 participants, there was 350 (70%) male and 150 (30%) female, having mean age of 45±1.26 years with minimum age of 25 years. Out of these 500 patients, n=50 (10%) patients were 25-35 years old, n=150 (30%) patients were 36-45 years old, n=150 (30%) patients were 46-55 years old, n=100 (20%) patients were 56-65 years and n=50 (10%) patients were above 65 years of age. All this is shown in shown in Table 1 and graphically shown in figure 1.

Endoscopy related complications were observed in 25 (5%) patients. Out of these 25 patients, major complication like perforation, cardiac arrest, respiratory arrest and death was not observed in any patients. Tachycardia, bleeding, aspiration and myocardial infarction were observed in 13, 09, 02 and 01 patients respectively as shown in table 2 and graphically shown in figure 2.

Table 3 shows associations of complications in endoscopy with different age group. In all 25 patients , 02 were in age group of 25-35 years range, 06 were in age group of 36-45 years range, 07 were in age group of 46-55 years range, 08 were in age group of 55-56 years range and 02 were in age group of >65 years range. Although we did not find any possible statistical association between different age groups and complications but the age group between 46-55 and 56-65 were prone to developed complications as compared to other groups with OR (95% CI) 1.18 and 2.08 respectively.

Chi-square test was also done to determine the pattern of complications based on gender, reveals no statistical significant association with p-value 1.0 (95% CI 0.4526-2.711).

Table No.1: Distribution of the patients on the basis of age

Age (years)	Frequency	Percentage (%)
25-35	50	10
36-45	150	30
46-55	150	30
56-65	100	20
> 65	50	10
Total	**500**	**100**

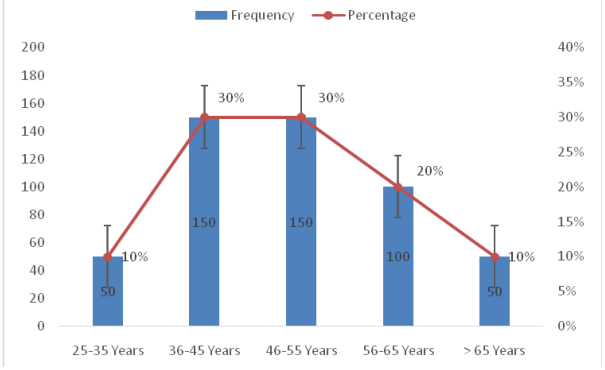

Figure No.1: Frequency of patients between different age groups

Table No. 2: Distribution of patients on the basis of complications

Type of complications	Numbers	Percentage
Bleeding	09	1.8%
Perforation	00	00%
Aspiration	02	0.4%
Cardiac Arrest	00	00%
Tachycardia	13	2.6%
Respiratory Arrest	00	00%
Myocardial infarction	01	.2%
Death	00	00%
No Complications	475	95%
Total	**500**	**100%**

Table No.3: Association of Endoscopy related complications in different Age groups

Age (Years)	Complications		p-value	95% CI	Odds Ratio
	Present	Absent			
23-35	02	48	Refer-ence	-	-
36-45	06	143	1.0	0.1966-5.159	1.007
46-55	07	142	1.0	0.237-5.893	**1.18**
56-65	08	92	0.49	0.426-10.22	**2.08**
>65	02	48	1.0	0.1352-7.396	1.0
Total	25	475			

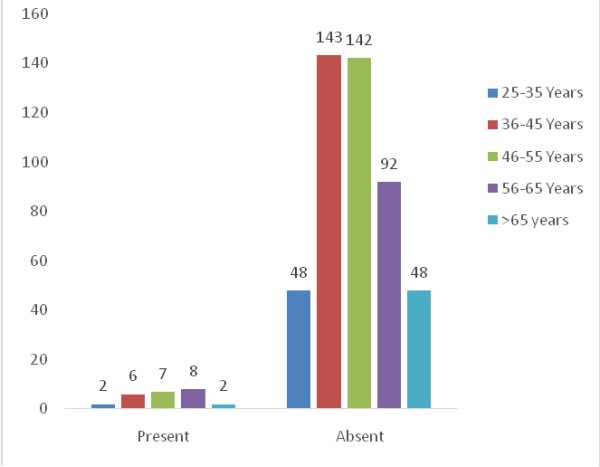

Figure No.2: Complications between age group

Table No.4: Endoscopy related complications based on gender

Compli-cations	Male	Female	p-value	95% CI	Odds ratio
Present	18	07	1.0	0.4526-2.711	1.1
Absent	332	143			
Total	350	150			

DISCUSSION

Upper GI endoscopy is a common procedure that is performed on routine basis, both in indoors and out door department. Gastroenterologist usually performs it, but a number of trained physicians and surgeon can perform it for clinical diagnosis. The prevalence of major complications related to upper GI endoscopy is very low that is 1 in 200 and mortality rate is even lower 1 in 2000[7] and it can be considered as safe procedure for diagnosis rather than therapeutics in which minimal adverse events may occurs[8].

Though there are many complications associated with GI endoscopy[9]. In our study, only minor complication like phobia, tachycardia, minor bleeding and mucosal injury were observed in a few patients and is considered non-significant. Similarly, major complication like respiratory arrest, cardiac arrest, myocardial infarction, perforation, major bleeding and death are rarely seen. These finding in our study regarding the major complications are close to the finding of two years audit conducted in 2012 by Bashiru Ismaila et al in Nigeria, where only two cases out 190 have developed major complication like respiratory arrest and esophageal tear[10].

Our study supports that major complications which can be life threatening rarely occur during upper GI endoscopy. The frequency of minor complications is also not significant and can be easily managed with timely intervention and proper counseling on the tableside. Our study is consistent with a study conducted 3770 elderly patient (above 70 years) which finds no major complications even in elderly patients[11-13]. Similarly, no major complications are reported in pregnant patients[14] and/or patient taking antithrombotic medications[15]. This risk of complications in GI endoscopy greatly decreases if proper guidelines are followed[16].

CONCLUSION

These finding show "that upper GI endoscopy is a safe procedure and the frequency of both major and minor complications is rare, if performed by experienced hands". However, future study on a very large scale from different centers is recommended to get complete picture.

Author's Contribution:

Concept & Design of Study:	Jamaluddin
Drafting:	Nizamuddin
Data Analysis:	Bughdad Khan, Waheed Iqbal
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Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Bisschops R, Areia M, Coron E, Dobru D, Kaskas B, Kuvaev R, et al. Performance measures for

upper gastrointestinal endoscopy: a European Society of Gastrointestinal Endoscopy (ESGE) quality improvement initiative. Endoscop 2016;48(09):843-64.
2. Birk M, Bauerfeind P, Deprez PH, Häfner M, Hartmann D, Hassan C, et al. Removal of foreign bodies in the upper gastrointestinal tract in adults: European Society of Gastrointestinal Endoscopy (ESGE) Clinical Guideline. Endoscop 2016;48(05):489-96.
3. Rizk MK, Sawhney MS, Cohen J, Pike IM, Adler DG, Dominitz JA, et al. Quality indicators common to all GI endoscopic procedures. Am J Gastroenterol 2015;110(1):48.
4. Bisschops R, Areia M, Coron E, Dobru D, Kaskas B, Kuvaev R, et al. Performance measures for upper gastrointestinal endoscopy: a european Society of gastrointestinal endoscopy quality improvement initiative. United Eur Gastroenterol J 2016;4(5):629-56.
5. Basavana Goudra AN, Singh PM, Gouda GB, Carlin A, Manjunath AK. Cardiac arrests in patients undergoing gastrointestinal endoscopy: a retrospective analysis of 73,029 procedures. Saudi J Gastroenterol: official J Saudi Gastroenterol Assoc 2015;21(6):400.
6. Levy I, Gralnek IM. Complications of diagnostic colonoscopy, upper endoscopy, and enteroscopy. Best Practice & Research Clinical Gastroenterol 2016;30(5):705-18.
7. Ben-Menachem T, Decker GA, Early DS, Evans J, Fanelli RD, Fisher DA, et al. Adverse events of upper GI endoscopy. Gastrointestinal Endoscop 2012;76(4):707-18.
8. Espino A, Garcia X, Mac-Namara M, Richter H, Pimentel F, Biel F, et al. 805 Complications of Gastrointestinal Endoscopy in 85,391 Procedures. Gastrointestinal Endoscop 2012;75(4):AB170.
9. Green J. Complications of gastrointestinal endoscopy. BSG Guidelines in Gastroenterol 2006:1-30.
10. Ismaila BO, Misauno MA. Gastrointestinal endoscopy in Nigeria-a prospective two year audit. Pan Afri Med J 2013;14(1).
11. Lippert E, Herfarth HH, Grunert N, Endlicher E, Klebl F. Gastrointestinal endoscopy in patients aged 75 years and older: risks, complications, and findings—a retrospective study. Int J Colorectal Dis 2015;30(3):363-6.
12. Loperfido S, Angelini G, Benedetti G, Chilovi F, Costan F, De Berardinis F, et al. Major early complications from diagnostic and therapeutic ERCP: a prospective multicenter study. Gastrointestinal Endoscop 1998;48(1):1-10.
13. Clarke G, Jacobson B, Hammett R, Carr-Locke D. The indications, utilization and safety of gastrointestinal endoscopy in an extremely elderly patient cohort. Endoscop 2001;33(07):580-4.
14. de Lima A, Zelinkova Z, van der Woude C. A prospective study of the safety of lower gastrointestinal endoscopy during pregnancy in patients with inflammatory bowel disease. J Crohn's and Colitis 2015;9(7):519-24.
15. Fujita M, Shiotani A, Murao T, Ishii M, Yamanaka Y, Nakato R, et al. Safety of gastrointestinal endoscopic biopsy in patients taking antithrombotics. Digestive Endoscop 2015;27(1): 25-9.
16. Beg S, Ragunath K, Wyman A, Banks M, Trudgill N, Pritchard DM, et al. Quality standards in upper gastrointestinal endoscopy: a position statement of the British Society of Gastroenterology (BSG) and Association of Upper Gastrointestinal Surgeons of Great Britain and Ireland (AUGIS). Gut 2017;gutj nl-2017-314109.

Original Article

Prevalence of Risk Factors in Patients Presents with Unstable Angina

Babar Bashir[1], Arshad Ali[1], Syed Shayan Ali[2] and Munir Hussain Siddiqui[2]

ABSTRACT

Objective: The main objective of this study was to determine the prevalence of risk factors in patients presenting with unstable angina, presented at DUHS and BBSUL.

Study Design: Observational / cross-sectional study.

Place and Duration of Study: This study was conducted at the General Medicine and Cardiology Department of DUHS from March 2016 to March 2017.

Materials and Methods: 81 patients with unstable angina in General Medicine and Cardiology ward that fulfilled the inclusion and exclusion criteria and gave informed consent were enrolled for the study. Patients were evaluated for obesity, diabetes, hypertension and dyslipidemia.

Results: Total 81 patients with unstable angina were included in this study Out of them 43 (53.1%) were male and 38 (46.9%) were female. Mean age was 60.23 ± 8.7. Majority of patients (49.4%) were lying in 51 to 60 years age group. Raised blood sugar in 51(63%) patients, raised blood pressure in 46(56.8%) & low HDL in 43(53.1%) were more prevalent with other risk factors.

Conclusion: This study provides a quantitative estimate of the prevalence of risk factors like Diabetes, low HDL, hypertension, hypertriglyceridaemia and obesity strongly correlates with unstable angina.

Key Words: Unstable Angina, Obesity, Dyslipidemia

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INTRODUCTION

Coronary artery disease or atherosclerotic (CAD) is the number one killer in USA and world wide[1,2]. Acute coronary artery syndrome comprises the spectrum of unstable angina to aute myocardial infarction. In south asian countries mortality to CAD is high and angina is common manifestation of coronary artery disease[3,4]. Most of the peoples have identifiable risk factors for CAD. These include family history, male sex, dyslipidemia, DM, hypertension, obesity, cigarette smoking and too much alcohol[5]. Pakistan being as under developed country the population spend their most of the income for the treatment of coronary artery disease because of lack of knowledge and lack of awareness about these identifiable risk factors[6]. With this we gather the data how much prevalent of these risk factors in patients of unstable angina which is one of the variety of CAD.

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MATERIALS AND METHODS

This study was conducted at DUHS and BBSU, Karachi from March 2016 to March 2017.This was a cross sectional study 81patients were included in this study and sample size is calculated scientifically with confidence interval 95% and sample technique were Non-probability purposive sampling. The patients were included in this study who were diagnosed cases of unstable angina with age more than 15years. Patients were labeled unstable angina positive if ECG showed no ST segment elevation and cardiac enzymes levels were not raised and the patients were excluded frome the study who were already had type 1 diabetes, renal failure, Cushing syndrome, known Hypertension, patients were taking lipid lowering drugs & ECG changes not consistent with unstable angina.

Data Collection Procedure: Data was collected on a pretested self administered Performa after taking permission from ethical committee of the hospital. The purpose, procedure risks and benefits of the study were explained to the patients and informed consent was taken. 81 patients admitted with unstable angina fulfilling inclusion criteria were included in the study. Patient were interviewed and screened for risk factors like HTN, DM, Hyperlipidemia, and Obesity.

The socio-demographic data including age and sex was recorded as well. All data was collected by the researcher on structured Performa.

Blood Pressure was measured at the time of admission by taking 2 readings after 5 minutes interval by the same doctor (to reduce observer bias) and mean of both the readings was calculated, making patient sit comfortably back straight and arm at heart level, no coffee, tea, cigarette smoking half hour before.

Waist circumference was measured by measuring the smaller circumference of the waist, usually just above the belly button, and dividing by the hip circumference at its widest part of the hip i.e. waist circumference >102 cm in men and> 88 cm in women was taken as central obesity.

Blood was taken at the time of admission for lipid profile and rechecked after 14 hrs fast along with fasting glucose level. Strict aseptic measures were taken to reduce systematic bias.

Data Analysis: The data was entered by two people to control the bias and analyzed with the help of SPSS Program version 18.1. Mean and standard deviation of numerical variables like age, waist circumference, systolic and diastolic blood pressure, triglyceride level, High-density lipoprotein levels and fasting blood sugar was taken. Frequency and percentage was computed for categorical variables like Age group, sex, and presence of metabolic syndrome. Confounding effect was controlled through stratification of age and gender. Results were described and also presented in form of tables and graphs.

RESULTS

Total 81 patients with unstable angina were included in this study. Out of them 43 (53.1%) were male and 38 (46.9%) were female (table 1). Mean age was 60.23 ± 8.7. Majority of patients (49.4%) were lying in 51 to 60 years age group (figure 1).

Mean triglycerides level of the study population was 148.95+- 26.47(95-223). Thirty one (38.5%) patients with unstable angina had hypertriglyceridemia among them 18(58.1%)were males and 13(41.1%)were females this difference was not statistically significant(p value- 0.480). Among 31 patients 15(48.4%) were in age group between 51- 60 years and that shows statistically significant(p value- 0.007) table no: 3. Mean HDL level was 45.16±10.37(26- 68).

Table No.1: Frequency of Gender: Total no: 81

Sex	Frequency	P- value
Male	43(53.1%)	0.018
Female	38(46.9%)	

Forty three patients had low HDL among them 26(60.5%) were males and 17(39.5%) were females that show stastically in significant (p value- 0.157). Mean FBS was 137.42+- 65.078 (61-334). Fifty one (63%) were had hyperglycemia among them 30(58.8%) were males and 21(41.2%) were females and that shows statistically insignificant p value- 0.177 and out 51 patients 18(35.3%) patients were in age group of 51- 60 years and that shoes statistically significant p value- 0.019. (table 3). Mean Systolic blood pressure of the study population was 139.20±24.3(100-200) and mean diastolic blood pressure was 87.47±13.1(60-115). Forty six patients had high blood pressure among them 23(50%) were males and 23(50%) were females with insignificant p value- 0.523. Out of 43 patients 14(30.4%) were in age group of 51-60 years and that shows significant p value- 0.001. table 3. Mean Waist was 92+- 11.24(71-113). Twenty seven patients were obese 16(59.3%) were males and 11(40.7%) were females that show insignificant p value- 0.431. Eleven patients(40.7%) out of 27 obese patients were in age group of 51-60 years and that shows statistically significant p value- 0.001. table 3.

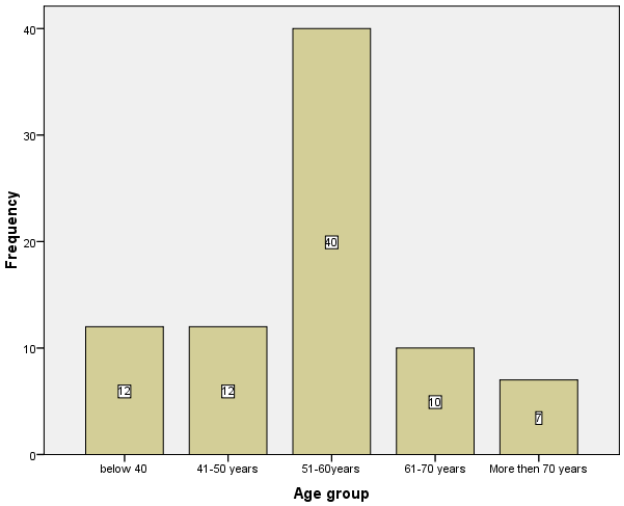

Figure No.1: Age Distribution In Different Age Groups

Table No. 2: Frequency of risk factors in patients with unstable angina

Variables	Mean	Male	Female	P-value
Trigly-cerides	148.95± 26.47	18 (58.1%)	13 (41.9%)	0.480
HDL	45.16± 10.37	26 (60.5%)	17 (44.7%)	0.157
FBS	137.42 ±65.078	30 (58.8%)	21 (41.2%)	0.177
HTN	SBP 139.20 ±24.3% DBP 87.47 ±13.1	23 (50%)	23 (50%)	0.523
Obesity		16 (59.3%)	11 (40%)	0.431

Table No. 3: Frequency of Different risk factors in patients with unstable angina in age group of 51-60 years.

Variable	Total no:	Patients of age group 51-60 years	P- value
Hypertrigly-ceridaemia	31 (38.5%)	15(48.4%)	0.007
Low HDL	43 (53.1%)	24(55.8%)	0.010
Raised fasting blood sugar	51 (63%)	18(35.3%)	0.019
HTN	46 (56.8%)	14(30.4%)	0.001
Obesity	27 (33.3%)	11 (40.7%)	0.001

DISCUSSION

South Asians undergo higher coronary heart disease mortality contrast with native majority[7,8]. It was earlier reported inside the whole cohort that South Asian subjects had an increased prevalence of hypertension, diabetes and a high-risk lipid profile despite of adjusting for socioeconomic class. South Asians have been reported as having atypical features when presenting with chest pain.

The variable association between cardiovascular risk factors and the presence/absence of chest pain remind clinicians that at the initial stage of disease, risk factors in populations studied may not be a substitute for true angina. The presence of diabetes mellitus has similarly been reported to not be a strong predictor for serious coronary outcomes (e.g. nonfatal myocardial infarction and cardiac death) in patients at an initial stage of the natural history of the disease (e.g. asymptomatic diabetes)[9]. Thus, the chest pain history should be emphasis by the clinicians, over risk factor profile for assessment of prognosis at this initial stage of cardiovascular disease[10,11].

Evidence for altered perception of angina in diabetes is mixed, with not all studies showing associations with silent ischaemia[12]. The majority of patients with diabetes experience angina in the same way as those without diabetes[13,14].This study not go for serum cholesterol including low density lipoprotein along with evaluation of type A personality.

Our study specifically focus on age group & it shows that incidence of ischemic heart disease is more common in age group 51 to 60 figure 1, moreover among risk factors low high density lipoptotein is independent most important risk factor responsible for unstable angina in same age group table no 3 (p value 0.010).

CONCLUSION

This study provides a quantitative estimate of the prevalence of risk factors like Diabetes, low HDL, hypertension, hypertriglyceridaemia and obesity strongly correlates with unstable angina.

Author's Contribution:

Concept & Design of Study:	Babar Bashir
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Revisiting Critically:	Babar Bashir, Arshad Ali
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Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Thomas M, Christopher B, Kevin J, Manish R. Coronary artery disease. Current medical diagnosis & management 2015;349.
2. Payak A, Kozela M. Cardiovascular disease in central & east Europe. Public health Review 2012; 33: 416-35.
3. Harding S, Risato M, Jeyhan A. Trends of CAD & Stroke mortality among immigrants in England & Wales. Heart 2008; 44(4) 463-70.
4. Zaman MJS, Shipky MJ. Incidence & prognosis of angina prctoris in south asian & white. J Public health 2011;33(3):430-38.
5. Stone, et al. Guideline on the treatment of blood cholesterol to reduce the sclerotic cardiovascular risk in adults. American heart association task force on practice guidelines. Circulation 2013;12.
6. Kalimuddin A, Azhar MA, Najma patel, Hafeez J. Prevalence & awareness of CVD including in a lower middle class urban community in an asian country. PHJ 2008;41(3-4).
7. Kurz DJ, Bernstein A, Hunt K. Simple point of care risk stratification in acute coronary syndromes: The AMIS model. Heart 2008.
8. Yan AT, Yan RT, Tan M. Risk scores for risk stratification in acute coronary syndromes: useful but simpler is not necessarily better. Eur Heart J 2007;28(9):1072–1078.
9. Bradshaw PJ, Ko DT, Newman AM. Validity of the GRACE (Global Registry of Acute Coronary Events) acute coronary syndrome prediction model for six month post-discharge death in an independent data set. Heart 2006;92(7):905–909.
10. Bassand JP, Hamm CW, Ardissino D. Guidelines for the diagnosis and treatment of non-ST-segment elevation acute coronary syndromes. The Task Force for the Diagnosis and Treatment of Non-ST-Segment Elevation Acute Coronary Syndromes of

the European Society of Cardiology. Eur Heart J 2007;28(13):1598–1660.

11. Henriksson M, Epstein D, Palmer S, Sculpher M, Clayton T, Pocock S, et al. The cost-effectiveness of an early interventional strategy in non-ST-elevation acute coronary syndrome based on the RITA 3 trial - technical report. Center for Medical Technology Assessment; 2008.
12. Bradshaw PJ, Ko DT, Newman AM. Validation of the Thrombolysis. Myocardial Infarction (TIMI) risk index for predicting early mortality in a population-based cohort of STEMI and non-STEMI patients. Canadian J Cardiol 2007;23(1): 51–56.
13. Zaman MJ, Junghans C, Sekhri N, et al. Presentation of stable angina pectoris among women and South Asian people. CMAJ 2008;179(7):659–67.
14. Young LH, Wackers FJT, Chyun DA, et al. Cardiac outcomes after screening for asymptomatic coronary artery disease in patients with Type 2 diabetes: the DIAD study: a randomized controlled trial. JAMA 2009;301(15):1547–55.

Original Article

Anti-Oxidant Status Following Treatment with Ciprofloxacin Toxic Effects on Chondrogenic Cells in Immature Rat Liters

Haji Muhammad Aslam Channa[1], Bhojo Mal Tanwani[2], Naheed Gohar[3] and Roohi Kanwal[4]

ABSTRACT

Objective: To investigate that in reverse, supplementation of zinc chloride if given simultaneously, can diminish the typical ciprofloxacin-induced chondrotoxicity in immature rat liters.
Study Design: A prospective experimental animal study
Place and Duration of Study: This study was conducted at the Department of Anatomy. Pir Abdul Qadir Shah Jeelani Institute of Medical Sciences Gambat District Khairpur Mir`S from Jan 2014 Dec 2014.
Materials and Methods: Ciprofloxacin & ZnCl2 was administrated to immature rat liters. 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.) Their mean chondrocyte count, chondrocyte size and their nucleus size per field was measured and were compared with similar value of control animals. The results were statistically analyzed to find out the significance.
Results: It was concluded after experimentation that ciprofloxacin administered in immature rat liters decreased mean chondrocyte count, chondrocyte size and their nucleus size per field, decreased by 213.7 ± 0.41, 11.12 ± 0.06 µm and 4.37 ± 0.12 µm respectively. That ciprofloxacin & ZnCl2 administration maintained the mean chondrocyte count, chondrocyte size and their nucleus size per field maintained by 274.4 ± 0.47, 10.47 ± 0.04 µm and 5.36 ± 0.03 µm respectively. That ZnCl2 administration increased the mean chondrocyte count, chondrocyte size and their nucleus size per field by 316.0 ± 0.40 , 10.82 ± 0.10 5 µm and 5.69 ± 0.04 µm respectively.
Conclusion: Application of ciprofloxacin and ZnCl2 post-natal in immature rat liters affected the mean chondrocyte count, chondrocyte size, and their nucleus size per field. ZnCl2 maintained mean chondrocyte count, chondrocyte size and their nucleus size per field leading to growth in immature rat liters.
Key Words: Ciprofloxacin, ZnCl2, chondrocyte count per field, chondrocyte size, chondrocyte nucleus, immature rat liters

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INTRODUCTION

Ciprofloxacin antibiotic belongs to the class fluoroquinolone which is a broad spectrum antibiotic and plays an active role for the control of both Gram Positive and Gram Negative bacteria[1]. Fluoroquinones functions by the inhibition of DNA Gyrase which is an enzyme belongs the class Topoisomerase and required by bacteria to complete their metabolic activities.[2]

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Quinilones are the components, which are bactericidal in nature, which denature the replication and transcription process results in the death of bacterial cells.

Large number of bacterial infections has been cured by Ciprofloxacin but many side effects have been evident from variable doses of this drug including tendon rupture, deterioration in bones, joints and disintegration to the cartilage of growing youngs[3].

Generally Physicians prescribes the quinolones to newborns, adults and even to pregnant/ nursing females without considering their side effects including the abrasions and injuries in cartilage of joints and instead of the fact that this drug is not recommended for their usage[4].

Nam et al., studied the adverse effect of continuous dosages of Quinolones and suggested that frequent dosages of this drug leads to the deterioration in bones and cartilage due to over concentration of fluoride contents in the body which results in impede growth and fragile bones.[5]

One of the essential trace element which play important role in maintenance of immune responses and initiation

of normal developmental patterns of body is Zinc, It is also responsible for the development of fetal systems, production of DNA, RNA as involved in proteins synthesis in the body.[6]

Two types of Skeletogenic cell produced during the developmental patterns of fetus, firstly Chondrocytes which are the cartilaginous cells and Osteoblasts that are bony in nature. Firstly the whole skeleton is composed of cartilaginous structure and gradually it transformed into bony skeleton in post natal period by ossification.[7]

MATERIALS AND METHODS

Effects of the different doses of Ciprofloxacin were examined in Albino rats. Through random sampling, Forty ovulating females were selected and they were mated with twenty males having age of 16 to 18 weeks. All animals were collected from Pir Abdul Qadir Shah Jeelani Institute of Medical Sciences Gambat. According to the Luck[8], the methodology of mating the members of similar strain was adopted. One male rat was mated with two different females in different cages. The signs of mating such as blood stained vagina with mucoid greenish/whitish material observed after twelve hours of mating which indicates the zero day of pregnancy.[9]

Four different groups A. B.C and D were formed by dividing 40 immature albino rats which were spontaneously selected from the whole lot. Ten members included in each group. Group A was considered as a control group, the members of which were given normal saline (0.1 ml) two time a day. The doses of normal saline were administrated intra-peritoneal for twenty days.

Group B was treated with injections of Ciprofloxacin (20mg/kg). All the doses were given intra peritoneally twice daily for twenty days.

Group C was treated with a little modification, they have given the injections of Ciprofloxacin along with the Zinc chloride (120 microgram.100 gram) prepared in distil water (7.4 µg in 0.1 ml).The injection of Zinc chloride was given thirty minutes before Ciprofloxacin administration. This whole dose was given two times a day for twenty days.

The members of Group D were treated with only Zinc chloride (120 microgram. 100 gram) for twenty days. At twenty first day immature rats were dissected for further examination. Anesthesia treatment was done before dissection. Bones were obtained from the limbs, Firstly fixation was done by putting them into 19% buffered formalin. After fixation, removal of calcium was required, the decalcification process was done by putting them in 10% Nitric acid and 10% Formic acid[10]. Pparplast was used for embedding purpose. Then sectional cutting was done by cutting the bones through rotary microtome into 4 micrometer thick longitudinal sections.

The staining was done by using Haemotoxylin and Eosin stain[11]. Measurement of forms and sizes of Tissues as well as quantitative analysis of bones were done by Histomorphometry. Statistical analysis of the results was also done by applying the 't' test mechanism on the data collected. Level of significance was also calculated[12].

RESULTS

Mean chondrocyte count per field in two weeks post-natal treated immature rat liters: Mean chondrocytes count were estimated by observing the fields in the samples from all four groups.

In group A, the mean of post natal chondocytes was estimated at 276.5 ± 1.05. Statistical analysis reveals that Group A show the high significant increase as compared to B, C and D. While B shows the non significant increase, As far as C and D are concerned, both shows the highly significant decrease (Table1).

In group B, the mean of post natal chondrocytes count was estimated as 213.7 ± 0.41. The results shows the highly significant decrease in number while observing the data from group A, C and D (Table 1).

In group C, the similar count of chondrocytes were made. It was estimated that mean count of post natal chondrocytes were 274.4 ± 0.47. Current calculation also shows a highly significant decrease by observing the data from group D ($P < 0.001$) and a non significant change ($P > 0.032$) was also observed during a comparison of present data of group C with group A (Table 1).

The results of group D shows the mean of post-natal chondrocyte count per field 316 ± 0.40 which declares a high significant increase as compared to the data from group A, B and C (Table 1).

Table No.1: Comparison of chondrocyte count per field in immature rat liters between post-natal control and treated groups

	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
Postnatal (Day-20)	276.5 ± 1.05^{øø}	213.7 ± 0.41	274.4 ± 0.47^{øø}	316.0 ± 0.40$^{**,øø,◊◊}$

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

Mean chondrocyte size per field in two weeks post-natal treated in immature rat liters: Sizes of the chondrocytes were also observed after the treatment with normal saline, ciprofloxacin and zinc chloride.

Mean sizes of all chondrocytes per field were estimated from the samples of animals of group A, B, C and D.

In group A, the mean chondrocyte size was estimated as 10.28 ± 0.02 µm. In histological examination of samples from group B, a highly significant increase has been seen, while in the samples from group C, a non-significant change been observed. In the members of group D statistical analysis described the high significant decrease in sizes of chondrocytes (Table 2).

In the histological examination of samples from group B and their statistical analysis, the mean size of chondrocytes was estimated as 8.40± 0.06 µm. Comparative analysis showed the highly significant decrease in sizes in B from group A, C and D (Table 2).

The mean size of chondrocytes in group C was calculated as 10.47 ±0.04 µm. The comparison of mean size of group C with group D showed the highly significant decrease i.e (P<0.001), When the result has been compared with the control group A, it showed the non significant change i.e. P>0.05 (Table 2).

In group D, the mean size of chondrocytes calculated as 10.82 ± 0.10 µm. Statistic analysis showed the highly significant increase in this group i.e. (P<0.001) as compared to THE groups A, B and C (Table 2).

Mean nuclear size of chondrocyte per field in two weeks post-natal treated immature rat liters: The sizes of nucleus of chondrocytes were also estimated from the microtome cut sections of cells. In the samples of group A, the mean size of nucleus of chondrocytes was estimated at 5.46 ± 0.09 µm.. The result has been contrasted with B, C and D. The data collected from B, showed the highly significant increase, while data evaluated from C reveals the non-significant change. The data analyzed from D suggested the highly significant decrease in sizes of nucleus of chondrocytes (Table 2).

Table No.2: Comparison of chondrocyte cell size (µM) and their nucleus size (µM) in immature rat liters between postnatal control & treated groups

	Group A Control (n=10)	Group B Cipro-floxacin (n=10)	Group C Cipro-floxacin + Zinc Chloride (n=10)	Group D Zinc Chloride (n=10)
	Mean ± SEM	Mean ± SEM	Mean ± SEM	Mean ± SEM
Chondrocyte Size - Cell (µm)	10.28 ± 0.02	11.12 ± 0.06 **	10.47 ± 0.04	10.82 ± 0.10$^{**,◊◊}$
Chondrocyte Size - Nucleus (µm)	5.46 ± 0.09^{øø}	4.37 ± 0.12	5.36 ± 0.03	5.69 ± 0.04$^{øø,◊◊}$

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

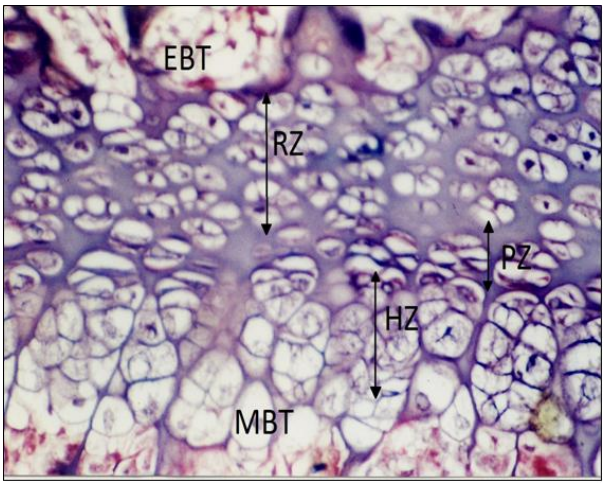

Figure No.1: H & E X 400: Photomicrograph of 5 µm thick longitudinal section of epiphyseal growth plate at proximal end of humerus from a 20th post-natal day control Group-A immature rat liters showing Metaphyseal bone trabeculae (MBT), Epiphyseal bone trabeculae (EBT),Reserve cell zone (RZ), Proliferative zone (PZ) and Hypertrophy zone (HZ)

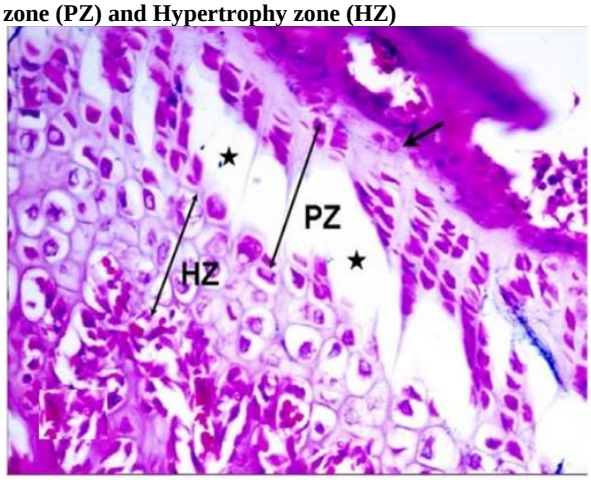

Figure No.2: H & E X 400: A photomicrograph of 5 µm thick longitudinal section in the femoral epiphyseal growth plate cartilage from a 20th post-natal day of ciprofloxacin-treated Group B immature rat liters showing few cells in the reserve zone ↑ wide clefts * with marked loss of chondrocyte columns of the proliferative zone (PZ) and diminished size of the hypertrophic zone (HZ).

The mean sizes of nucleus of chondrocytes from Group B were calculated as 4.37 ±0.12 µm. Statistic analysis revealed the high significant decrease in size of nucleus as the results were compared from the data from groups A, C and D (Table 2).

Samples from group C were also histological examined. It was found that the size of nucleus ranged as 5.36 ± 0.03 µm. Data calculated statistically and estimated that high significant decrease was found while comparing the data with group D i.e. (P< 0.001) and when it compared with the control group A, it showed the (P>0.05) i.e. a non significant change (Table 2).

In the samples from group D, mean nucleus size estimated as 5.69± 0.04 µm. The comparison of result

with other three groups i.e. A, B and C stated that high significant increase has been shown i.e. P<0.001 (Table 2).

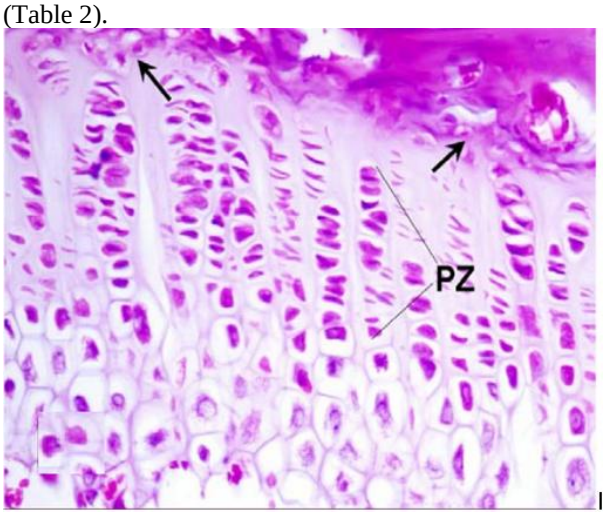

Figure No.3: H & E X 400: A photomicrograph of 5 µm thick longitudinal section of epiphyseal growth plate at proximal end of humerus from a 20th post-natal day Ciprofloxacin + Zncl2 treated Group-C immature rat liters showing preserved cellularity of reserve zone (↑) and regular cellular organization of chondrocyte columns of the proliferative zone (PZ).

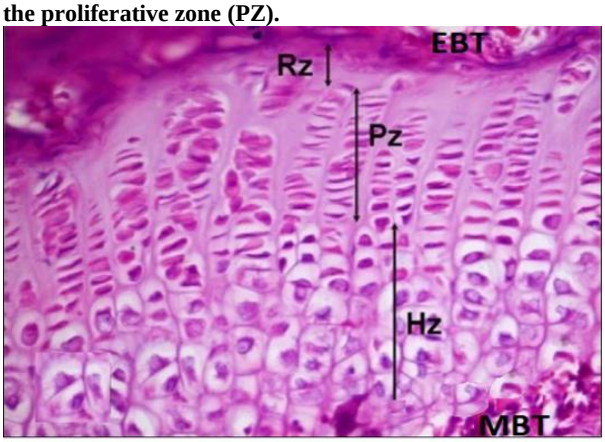

Figure No.4: H & E X 400: A photomicrograph of 5 µm thick longitudinal section of epiphyseal growth plate cartilage of humerus from a 20th post-natal day Zncl2 treated Group D immature rat liters showing junction of epiphyseal bone trabeculae (EBT),Reserve cell zone (RZ), thick Proliferative zone (PZ), Hypertrophy zone (HZ) and Metaphyseal bone trabeculae (MBT).

DISCUSSION

The effects of Ciprofloxacin in a single dose of 20mg/kg of body weight were examined in the cartilaginous cells i.e. chondrocytes of immature albino rats. The control group was treated with normal saline while zinc chloride was also added as a supplement along with ciprofloxacin to check its support during developmental period. Ciprofloxacin affected the newly developing cartilage cells and demonstrated highly significant decrease in different parameters of measurement i.e. chondrocytes count, chondrocytes sizes and the sizes of nucleus in those cells.

In group A, it was observed through microscopic histological evaluation of epiphyseal growth plate showed the abnormalities in the chondrocytes count, sizes as well as deformities in the nuclear membranes of those cartilaginous cells. During the fetal development, the main process of formation of rudimentary long bones is endochondral ossification[13].

The epiphyseal plate of the samples from group B revealed that highly significant decrease in count, sizes of cells and nuclei was found. This may be resulted in the higher ratio of cell necrosis in inner layers of epiphyseal plate.

According to Masadeh, Ciprofloxacin drugs have adverse effects on ossification, This drug accelerate the necrotic mechanism in calcification zone IV, as well as in other zones of cartilage formation. It also leads to the condensation of nuclear material in chondrocytes which results in abnormalities in morphological and cellular functions. Results of the current study line up with the results obtained by Masadeh[14].

The histological evaluation of the samples from group C resulted in the significant changes in their chondrocytes count, sizes and nuclei. The cells were normomorphic. No degradation in cellular lining or nuclear lining were showed. Addition of Zinc chloride with the doses of ciprofloxacin provided the stability to cellular development and played a supportive role during the mechanism of drug reaction. According to Nishada, Zinc provides support to the protein formation and act as a stabilizer and key integration factor during cell production. The results of current study line up with results of Nishada[15].

In the last group D, which were only treated with zinc chloride, no adverse effects has been seen in the cellular structure of chondrocytes. High significant increase has been observed. The cellular structure were normomorphic and stable.

According to Jou, Zinc components support good growth of cells and involved in quicker process of protein synthesis. Current study line up with the findings of Jou[16]

CONCLUSION

It is concluded that the application of ciprofloxacin and ZnCl2 in immature rat liters affected the mean chondrocyte count, chondrocyte size and their nucleus size per field. This study clearly shows the ability of zinc chloride to maintained the all parameters leading to growth of the immature rat liters. It is recommended that some more aspects of Ciprofloxacin and zinc chloride bonding effects should be investigated.

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Author's Contribution:

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Final Approval of version:	Haji Muhammad Aslam Channa

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

REFERENCES

1. Masadeh MM, Alzoubi KH, Al-Azzam SI, Khabour OF, Al-Buhairan AM. Ciprofloxacin-Induced Antibacterial Activity is Attenuated by Pretreatment with Antioxidant Agents. Pathogens 2016; 5(1): 239-245.
2. Channa MA, Ashfaq M, Jokhio AL, Khan MZ, Sahito MM. Effects of ciprofloxacin and zinc chloride in adult albino rat and pre-natal conceptus J Ayub Med Coll Abbottabad 2012;24(1):55-8.
3. Pfister K, Manzur D, Vorman J, Stahlman R. Diminshed ciprofloxacin Induced chondrotoxicity by supplementation with magnisium & vitamin E on immature rats. Anti Microbe agent chemother 2007; 51(3): 1022-1027.
4. Mont MA, Mathur SK, Frondoza CG, Hungerford DS, The Effects of Ciprofloxacin on Human Chondrocytes in Cell Culture. Curr Ther Res Clin Exp 2015; 77: 14–17.
5. Nam YS, Cho SY, Yang HY, Park KS, Jang JH, Kim YT, et al. Investigation of mutation distribution in DNA gyrase and topoisomerase IV genes in ciprofloxacin-non-susceptible Enterobacteriaceae isolated from blood cultures in a tertiary care university hospital in South Korea, 2005-2010. Int J Antimicrob Agents 2013;41:126–129.
6. Salvaggio A, Marino F, Albano M, Pecoraro R, Camiolo G,Tibullo D, et al. Toxic Effects of Zinc Chloride on the Bone Development in Danio rerio (Hamilton, 1822.). Front Physiol 2016;7: 153-160.
7. Küçükoğlu M., Binokay US, Boğa PA. The effects of zinc chloride during early embryonic development in zebrafish (Brachydanio rerio). Turk J Biol 2013; 37: 158–164.
8. Luck MR, Ye J, Almislimani H, Hibberd S. Follicular fluid rheology and the duration of the ovulatory process. J Reprod Fertil 2000; 120(2):411-21.
9. Chang HH, Schwartz Z, Kaufman MH. Limb and other Postcranial skeletal defects induced by amniotic sac puncture in the mouse. J Anatl 2011; 189:37-49.
10. Channa HMA, Ashfaque M, Mastoi SM, Qureshi MA. Effects of ciprofloxacin on growing cartilage in Albino rat pups. J Ayub Med Coll Abbottabad 2006;18(3):50–4.
11. Bancroft J D; Stevens A. Theory and Practice of Histological Techniques. 3rd ed. Edinburgh: Churchill Livingston;2010.p. 88,112, 232, 503.
12. Bland M. Introduction of medical statistics. 1st ed. Oxford:Oxford University press;2013.p.165–87.
13. Wang X, Jaffer G, Fosmire, Gay CV, Leach RM . Short term zinc deficiency inhibits chondrocyte proliferation and induces cell apoptosis in epiphyseal growth plate of young chickens. The Am soc Nutr Sci J Nutr 2002;123:665-673.
14. Masadeh M, Alzoubi K, Al-Azzam S. Flouroquinolones-induced antibacterial activity atteneuation by pretreatment with vitamin b12. Int J Pharmacol 2015; 11: 67–71.
15. Nishida K, Hasegawa A, Nakae S, Oboki K, Saito H, Yamasaki S, et al. Zinc transporter Znt5/ Slc30a5 is required for the mast cell mediated delayed-type allergic reaction but not the immediate type reaction. J Exp Med 2009;206(6): 1351-1364.
16. Jou MY, Philips AF, Lonnerdal BO. Maternal zinc deficiency in rat effect growth & glucose metabolism in the offspring by inducing insulin resistance post nataly 1,2. Am society Nutr 2010; 157:172-184.

Guidelines & Instructions

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When appropriate, may be included.

ACKNOWLEDGMENTS

List of all contributors who do not meet the criteria for Authorship, such as a person who provided purely technical help, writing assistance or department chair who provided only general support. Financial & Material support should be acknowledged.

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