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Editorial

COVID-19 In Children And Its Complication

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Corona Viruses (Covs) are enveloped, single stranded, Zoonotic, RNA Viruses of a large family. Corona Virus disease 2019 (Covid-19) is a contagious disease caused by severe acute respiratory syndrome corona virus 2 (SARS- COV- 2). The first known case was identified in Wuhan China in December 2019 [1]. The disease has spread worldwide, leading to an ongoing pandemic [2]. Till June 6, 2021, a total of more than 173913068 confirmed case and approximately 3740588 total deaths for COVID-19 had been reported globally by world meter. In Bangladesh the first three known case were reported on 8 March 2020. Transmission of COVID-19 occurs when people are exposed to virus containing respiratory droplets & airborne particles exhaled by an infected person [3, 4]. Those particles may be inhaled or may reach the mouth, nose, or eyes of a person through touching or direct deposition [3]. The risk of infection is highest when people are in close proximity for a long time, but particles can be inhaled over longer distances, particularly indoors in poorly ventilated & crowded spaces [3,5]. In those conditions small particles can remain suspended in the air for minutes to hours [3]. Touching a contaminated surface or object may lead to infection.

In humans corona viruses mostly cause respiratory & gastrointestinal symptoms. Clinical manifestations range from a common cold to severe diseases such as bronchiolitis, Pneumonia, ARDS multiorgan failure & even death. SARS- COV – 2 less commonly affect children & less severe disease compared with adults and are associated with lower fatality, Evidence suggests children are as likely as adults to become infected with SARS- COV- 2 but are less likely to be symptomatic. The majority of children infected by Novel COV-2 have documented household contact, In contrast adult more often have nosocomial exposure [6]. According to the national guidelines on clinical management of corona virus disease 2019 (COVID-19) in Bangladesh slows corona symptoms are mild illness (Influenza like illness-ILT), moderate case (pneumonia), severe case (severe pneumonia) & critical cases (sepsis, septic shock, ARDS, respiratory & any organ failure that requires ICU care).[7]

Most children with COVID-19 have mild symptoms or have no symptoms at all. The most common symptoms of COVID-19 in children are fever & caugh, but children may have any of these signs & symptoms of COVID-19. Such as fever or chills, cough, runny nose, sore throat, shortness of breath or difficulty breathing, Diarrhoea, nausea or vomiting, stomachache, Headache, myalgia poor feeding.[8]

Although child with COVID-19 have milder effects & better prognoses than adults however, children are susceptible to multisystem inflammatory syndrome in children (MIS-C) [9]. In this conditions child may present with acute abdominal pain, diarrhoea, vomiting, myalgia, low BP, rashes, pink eyes, swollen hands & feets, strawberry tongue. These clinical features are similar to Kawasaki disease in which blood vessels become inflamed throughout the body.[10] In MIS-C, othre's serious complications may occurs such as- Heart failure, acute kidney injury, increased blood coagulation, coronary artery aneurysms, macrophage activation syndrome & Toxic shock syndrome. [11]

Complications usually developed in certain risk group of children such as children with asthma or chronic lung disease, DM, congenital heart disease, sickle cell disease, genetic & metabolic conditions, Immune suppression due to any cause.

UK study says the majority of patients <18 years old experienced a mild disease & less than 1% of them died [12]. A study of European children with COVID-19 suggests deaths are extremely rare. Four out of 582 children studied died. Two of whom had known underlying health conditions.

Most children with SARS-COV- 2 infection will not require any specific therapy, only supportive care. But there are some recommendation to give specific therapy for children with risk groups. Remdesivir is recommended for hospitalized children aged 7-12 years

with risk factors for severe disease & increasing need for supplemental oxygen. Also recommended to all age groups of children who are hospitalized & increasing need for supplemental O_2. Dexamethasone for hospitalized children who required high flow O_2, Invasive mechanical ventilation extra corporeal membrane oxygenation. The panel recommends against the use of convalescent plasma for hospitalized children with COVID-19 who do not acquire mechanical ventilations except in a clinical trial. Multisystem inflammatory syndrome in children (MIS-C) are treated with anti-inflammatory medications, treatment of shock, prevention of thrombosis most children and treated with I/V immunoglobulin, with or without corticosteroids, Tocilizumab, Anakinra& infliximab have also been used. Inotropic or vasoactive agents are often used for children with cardiac dysfunction & Hypotension low dose aspirin has been used as an antiplatelet drug. Anticoagulants also have been used.[13,14,15]

It's important to remember that most people who have COVID-19 recover quickly but it even more important to reduce the spread of the disease by following precautions such as wearing mask, maintain social distancing, avoid crowds, keeping hands clear and vaccinate the child. Vaccination is the main stay of prevention & lessens the severity of covid disease.

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Original Article

Evaluation of Serum Zinc and Iron in Women Taking Oral Contraceptive

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Abstract

Background: *Oral contraceptives are most efficient, accessible and convenient method of contraception among the other available methods. The oral contraceptive pill fulfills the great human need for birth control with unrivalled effectiveness. The pill can effectively prevent pregnancy and alleviate menstrual disorder while used correctly. Many biochemical profiles of women taking oral contraceptives are disturbed due to metabolic alterations induced by its hormone content.*

Objectives: *To find out the relationship between serum zinc, serum iron and use of oral contraceptive.*

Materials and Methods: *The case control study was carried out in the Department of Biochemistry, Mymensingh Medical College, Mymensingh, during the period of July 2015 to June 2016 to evaluate the status of serum zinc and iron in women taking oral contraceptive. For this study, 100 age-matched women were selected and grouped as 50 oral contraceptive user and 50 non oral contraceptive user. Data were analyzed with the help of SPSS version 21.*

Results: *Mean ± SD level of serum zinc and iron were 59.58±6.58 µg/dl and 123.77±18.37 µg/dl in oral contraceptive user women, while in normal healthy women the levels were 97.84±8.70 µg/dl and 86.65±12.86 µg/dl respectively. Serum zinc was significantly decreased in oral contraceptive user group but serum iron was significantly increased when compared with that of normal healthy group ($p<0.001$).*

Conclusion: *The study showed decreased trend of serum zinc and increased serum iron in oral contraceptive users when compared with non-oral contraceptive users. Hence, it can be concluded that there may be significant association of serum zinc and iron level with oral contraceptives.*

Keywords*: Oral contraceptives, Serum zinc, Serum iron.*

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Introduction

Contraceptives are devices or techniques that permit sexual union without resultant pregnancy.[1] In Bangladesh among the available modern methods of contraceptives, about 30% couples use oral contraceptives.[2] Combined oral contraceptives are highly effective, reversible and popular one.[3] Available and heavily used contraceptive in Bangladesh has been the oral pill (Sukhi) containing estrogen and progestin.[4] Oral contraceptive pill stops ovulation by preventing the ovaries from releasing ovum. They also thicken cervical mucus making it harder for sperm to enter the uterus.[5] The major side effects were found to be dreaded conditions like malignancy and thromboembolic cardiovascular disease. Among the cardiovascular disorders, hypertension, myocardial infarction, hemorrhagic or ischemic strokes and venous thromboembolic conditions were mentionable[6]. There has been interest in recent years about alterations in various metabolic processes and trace elements profiles associated with the use of contraceptives. Changes in life style, environmental factors, dietary habits and active ingredients of hormonal agents have been known to affect status of micronutrients in humans.[7] Changes in tissue level or bioavailability of those elements could play a significant role in health risk and the pathogenesis of some disorders such as cardiovascular complications, the aging process at certain cancers have been associated with the use of contraceptives.[8]

Zinc is a component of more than 300 enzymes needed to repair wounds, maintain fertility in adults and growth in children, synthesize protein, reproduction of cells, preserve vision, boost immune function and protect against free radicals. Zinc may be regarded as an antioxidant since the enzyme superoxide dismutase protects the body against free radical damage. The storage and secretion of insulin from beta-cells of pancreas require Zn.[9] Zn deficiency is a serious problem in developing countries. Many studies have shown the adverse effects on growth and morbidity as well as the prevention of infection by Zn supplementation.[10]

Iron is an essential element for almost all living organisms. 65% of the iron in the body is bound up in hemoglobin molecules in red blood cells. About 4% is bound up in myoglobin molecules. Around 30% of the iron in the body stored as ferritin or hemosiderin in spleen, bone marrow and liver. Oral contraceptive pill attributed changes in iron level in body.[9] Disorders of iron metabolism are among the most common diseases of humans and encompass a broad spectrum of diseases with diverse clinical manifestations, ranging from anemia to iron overload, and possibly to neurodegenerative diseases.[11]

Materials and Methods

This cross sectional study was carried out in the Department of Biochemistry, Mymensingh Medical College, and the subjects were collected from the Model Family Planning Clinic of Mymensingh Medical College Hospital during the period of July 2015 to June 2016. For this 50 apparently healthy married women with age ranging from 20 to 35 years taking no hormonal contraceptives for at least one year selected as controls (Group-I) and age matched 50 married women taking oral contraceptive pill for at least six months were taken as cases (Group-II). Subjects having systemic illness like diabetes mellitus, hypertension, tuberculosis, kala-azar were excluded from the study. Apparently looking obese, taking other hormonal contraceptive pill other than combined estrogen progesterone preparation was excluded.

Informed written consent was taken from each study subject and ethical approval for the study was obtained from the Ethical Committee of Mymensingh Medical College and Hospital.

Height, Body weight and Blood pressure were measured and Body Mass Index (BMI) was calculated.

Serum zinc was estimated by colorimetric method with 2-(5-borm-2-pyridilazu)-5-[-N-propyl-N-(3-sulfopropy l) amino] –phenol (Makino 1982).

Serum iron was measured by colorimetric method using the test kit. Serum iron is liberated from its complex with transferrin by the action of surfactants atacid pH values;it is reduced to Fe^{2+} and reacts with batho-phenanthroline to produce a coloured complex which is photometrically determind.

Data were analyzed with the help of SPSS version 21. Quantitative data were expressed as mean and standard deviation and comparison between groups was done by Student's unpaired't' test.

Results

In this study, age range was from 20 to 35 years for both case and control group. It was observed that the mean age of Gr-I and Gr-II was 26.16±3.38 and 26.12±3.28 years respectively and the level of significance was 0.47 ($p>0.05$). Thus difference in mean age was not significant between OCP users case and apparently healthy control group.

In this study, mean ± SD age of controls (Gr-I) and cases (Gr-II) were 26.16±3.38 and 26.12±3.28 years respectively, which showed no significant difference ($p>0.05$). Mean ± SD BMI of controls and cases were 21.63±2.11 kg/m^2 and 21.67±2.11 kg/m^2 respectively, which showed no significant difference ($p>0.05$); as shown in **Table I:**

Table I: Demographic features of study subjects.

Demographic features	Group I (control) Mean± SD	Group II (case) Mean± SD	p value
Age (years)	26.16±3.38	26.12±3.28	0.47 ^{ns}
BMI (kg/m^2)	21.63 ±2.11	21.67±2.11	1.000 ^{ns}

Data were expressed as mean and standard deviation and comparison between groups were done by Student's unpaired't' test.

Table II shows the level of serum zinc and serum iron in study subjects. The study revealed that mean (± SD) of serum zinc level (mg/dl) were 97.84±8.70 and 59.58±6.68 in control and cases respectively which was significantly lower in cases ($p<0.001$). Mean± SD of serum iron (µg/dl) were 86.65±12.86 and 123.77±18.37 in controls and cases respectively which was significantly higher in cases ($p<0.001$).

Table II: Serum zinc and iron levels of the study subjects.

Demographic features	Group I (control) Mean± SD	Group II (case) Mean± SD	p value
Age (years)	26.16±3.38	26.12±3.28	0.47 ^{ns}
BMI (kg/m^2)	21.63 ±2.11	21.67±2.11	1.000 ^{ns}

Data were expressed as mean and standard deviation and comparison between groups were done by Student's unpaired't' test.

Discussion

The oral contraceptive pill fulfills the great human need for birth control with unrivalled effectiveness.[12] The pill can effectively prevent pregnancy and alleviate menstrual disorder while used correctly.[13] Many biochemical parameters of women taking oral contraceptives are disturbed due to metabolic alterations induced by its hormone content. Researches had been continuing for many decades to explore risk

versus benefits of different contraceptive methods. The present study was designed to observe some biochemical alterations in women taking combined oral contraceptives containing 30-µgm ethiny1 estradiol and 150-µgm levonorgestrel. Combined oral contraceptives (Sukhi) is the mostly used brand in rural community as it is distributed free of cost.[14] Therefore, metabolic alteration might be initiated earlier that go on silently without developing any overt clinical abnormality. On the contrary, long time use of hormones such as oral contraceptives can affect various metabolic pathways to such an extent that would cause detectable clinical abnormality.[15]

In the present study serum zinc was found to be significantly decreased in OCP user as compared to healthy woman. These findings were in agreement with the result of O Akinloye et al. 2011; Falah, Sani & Firoozrai 2009; Vir & Love (1981). Prasad et al. 1975 recorded lowering of serum zinc in oral contraceptives users.

The mechanism by which oral contraceptives reduce serum zinc level is not clearly understood. Fall in serum zinc occurred soon after administration of contraceptive steroids either progesterone alone or in combination with oestrogen. On the basis of the fact it was postulated that progestin and oestrogen might be equally effective to reduce serum zinc. It was further suggested that reduction of zinc level might be due to alteration of steroid induced binding affinities.[16] Reduced serum zinc level in plasma with simultaneous increase of erythrocytic zinc level, so redistribution of zinc between plasma and erythrocytes as an effect of contraceptive steroids would be another possible explanation in favour of this fact.[17] Still this aspect needs further elucidation. Increased use of oral contraceptives agents has stimulated wide interests in their effects on many aspects of human metabolism. Metabolic changes have been attributed to serum zinc and iron due to use of oral contraceptive.[18]

Iron is needed to make hemoglobin, the red colored substance in blood that carries oxygen. It has been argued that if less blood is lost each month, less blood needs to be manufactured. The combined oral contraceptive pills (COCPs) can increase the serum iron concentration by reducing the menstrual period to 3 to 4 days and reduce the amount of blood loss in each menstrual cycle. COCPs also reduces the endometrial thickness that shortens the menstrual period. Several studies showed that the estrogen can increase the hepatic synthesis of transferrin (iron transporter protein) that lead to increase in the serum iron level.[15] In many instances, it is not entirely clear whether the effects observed are due to progesterone or estrogen. The rise of serum iron and iron binding protein in women on COCPs is due to progestogenic rather than the estrogenic compound of the preparation.[19] It could be interesting to know whether the increase in serum iron concentration with oral contraceptive drugs is due to an increased efficiency of iron absorption or to increased mobilization of iron from tissue stores.

Conclusion

The present study showed significant alteration in serum zinc and iron levels. This study was done within the context of the facilities available to us. Our sample size was small due to limitation of time and fund. Considering the side effects, close biochemical monitoring and follow up must be emphasized for women on oral contraceptive.

It may be recommended to carry out a large scale prospective study with the application of modern sophisticated technology to elucidate alteration in biochemical parameters including other trace elements and organ function test which can give a conclusive decision.

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Original Article

Photo-Anthropometric Study of Medial Wall of Fully Ossified Dry Human Orbital Cavities

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Abstract

Background: *Orbital morphometry is important to provide useful baseline data for ophthalmologist, anthropologist, otolaryngologist, radiologist, maxilo-facial surgeon, reconstructive cosmetic surgeon and forensic medicine expert. The existing data suggest that the location of various foramina in the orbit vary in different ancestral population. An understanding of orbital disease demands a clear concept of normal orbital anatomy. Safe and effective orbital surgery requires an extensive knowledge of the anatomy of the bony orbit and the morphometric relationship that exist within it.*

Objectives: *This cross sectional analytic study was planned to collect data regarding morphometric measurements of the adult human orbital cavity to guide the anatomist, ophthalmologist, maxillofacial surgeon, neurosurgeon, radiologist, otolaryngologist, anesthesiologist, forensic experts to adopt appropriate plans for diagnosis and treatment.*

Methods: *The study was performed on 200 (Two hundred) fully ossified dry orbital cavities of 100 human skulls. Collected from Department of Anatomy of different Medical College of Dhaka city. Variation between different foramina in the walls of both orbital cavity at different landmarks were recorded in millimeter by photographic methods (Adobe photoshop version 10). Paired students 't' test was done for statistical analysis of the result.*

Results: *In the present study, The difference was significant between right and left side ($P<0.05$). Mean distances from the anterior lacrimal crest (ALC) to the anterior ethmoidal foramen (AEF) was higher on the right side in comparison to left side. The difference of the distance from anterior lacrimal crest (ALC) to the medial border of the optic canal (OC) was not significant ($P = 0.834$) between right and left orbital cavities.*

Conclusions: *There was significant difference between right and left orbital cavities from the anterior lacrimal crest (ALC) to the anterior ethmoidal foramen (AEF). Other parameters showed no significant difference between right and left orbital cavities.*

Key words- *Photo anthropometric parameters, Medial wall, Fully ossified.*

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Introduction

The two orbital cavities are situated on either side of the sagittal plane of the skull between the cranium and the skeleton of the face. Each orbital cavity essentially is intended as a socket for the eyeball but it also contains associated muscles, vessels, nerves, lacrimal apparatus, fascial strata, and soft pad of fat. In a nutshell it lodges the visual apparatus.

It is made up of seven bones namely maxilla, palatine, frontal, zygomatic, sphenoid, ethmoid & lacrimal. Bones are arranged to enclose a roughly quadrilateral pyramidal cavity with the apex located posteriorly forming the optic canal and the base located anteriorly forming the orbital margin.[1]. Each orbit presents a roof, floor or inferior wall, medial and lateral walls, a base or orbital opening and an apex. Orbital morphometry is important to provide useful baseline data for ophthalmology, anthropology, otolaryngology, radiology, maxilo-facial surgery, reconstructive cosmetic surgery and forensic medicine[2].

Several diseases such as trauma, inflammation, infections, and tumors can involve the orbital cavity. During performing surgeries in the orbit like orbital decompression, enucleation, exenteration, optic nerve decompression and vascular ligation to avoid injuries to the important structures in the orbit, mainly neurovascular bundles passing through various foramina and fissures, precise knowledge of the anatomy of these openings is important. The existing data suggest that the location of various foramina in the orbit vary in different ancestral population[3]. The inferior wall is formed by the orbital plate of maxilla, orbital surface of zygomatic bone and orbital process of palatine bone. In the inferior orbital wall, the inferior orbital approach is involved in several procedures, including exploration for fracture, decompression and maxillectomy[4,5]. The inferior orbital fissure is defined as a space between the lateral wall and floor of the orbit .This fissure runs in an anterolateral direction from the maxillary strut posteriorly to the zygomatic bone anteriorly. The inferior orbital fissure joins the orbit with the pterygopalatine fossa, infratemporal and temporal fossa. The morphometric anatomy of the inferior orbital fissure is classified into three segments relative to the infraorbital nerve and fossae. In the posteromedial segment, the foramen rotundum, superior orbital fissure and pterygopalatine fossa communicate with the orbit and cavernous sinus. The middle segment of the inferior orbital fissure communicates with the infratemporal fossa and anterolateral segment to the temporal fossa. The inferior orbital fissure is an important landmark for endonasal endoscopic surgery of the skull base. Knowledge of its anatomy can helps both neurosurgeons and otolarygologist who navigate in this region[6]. Photo-anthropometry is the process of obtaining measurements by means of photographs. The term Photo-anthropometry, when used by anthropometrists, has generally referred to measurement from photographs. Digital photographic techniques potentially offer a highly practical, convenient and cost effective method. The reliability of the photographic technique is satisfactory. 2D digitization method is accurate, and it can be applied to both clinical practice and research. Photographic method has several advantages over conventional measurement methods. The same landmarks used in several different measurements have to be located repeatedly when direct measurements are made. In digital photography, there is no need to locate landmarks prior the image taking. Another advantage of digital photography is the opportunity to preserve the material, which allows to repeat the measurements anytime and to add new parameters in latter measurements.

Materials and methods

This cross-sectional analytical study was carried out at Department of Anatomy, Dhaka Medical College, Dhaka from July 2014 to June 2015. The study was performed on both orbital cavities of one hundred fully ossified dry human skull. Damaged or broken orbital cavities in fully ossified dry human skull were excluded from the study**.** Different measurements of orbital cavities of one hundred fully ossified dry human skull was recorded by photographic methods and 10 dry human skull was measured by physical methods to

calculate the conversion factor. Before going to photographic measurement the human dry skull was placed on a wooden flat table at the same level of digital camera. The camera was fixed to a stand and the distance of the camera from the skull was fixed at 120 cm, with a fixed focus, zoom and illumination.The photograph of the orbital cavities were taken by the digital camera (Sony cyber shot 16.1 mega pixels).The photograph was uploaded in to the computer. The photographic measurements of the orbits was done by using a computer program Adobe Photoshop version 10. And measurements by physical methods was carried out on 10 dry human skull out of 100 to ascertain the conversion factor. Inferior wall and inferior orbital fissure were measured by digital slides caliper and the readings was noted in millimeter. These individual values of each photograph was converted into actual size by multiplying with the conversion factor. Calculation of conversion factor (CF) –

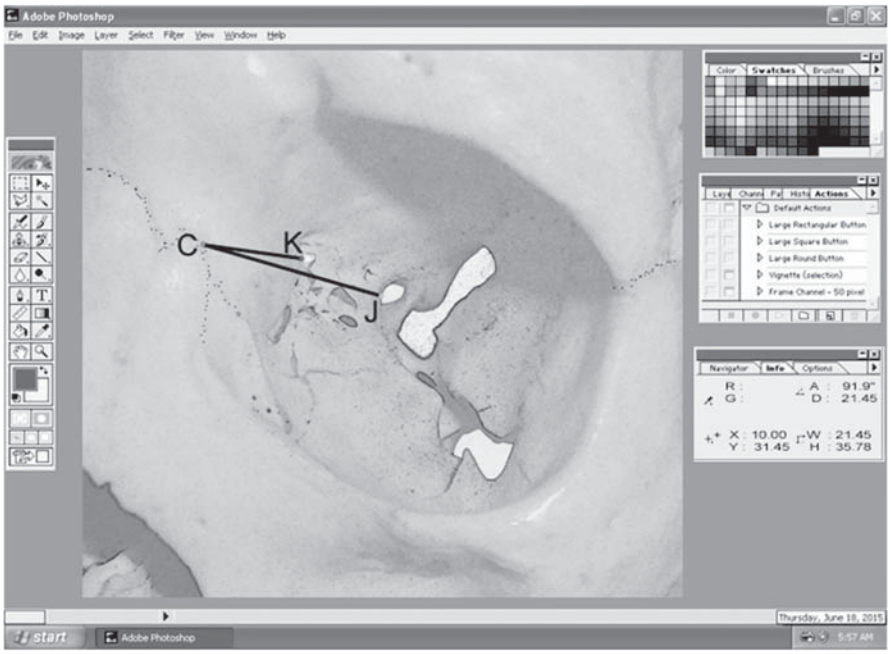
The conversion factor is a ratio, calculated by dividing a physically measured value of a variable, with a photographically measured value of the same variable of each orbital cavities to convert photographically measured values to actual measurements.

Formula for calculating conversion factor (CF):

Orbital height or width measured by physical method

CF = Orbital height or width measured by photographic method

All data were checked and edited after collection. Later the data were put into computer and were analyzed with the help of SPSS version 19.0 for windows. Statistical analyses were done by paired student's 't' test.



Photograph 1: showing distance of different foramen in the medial wall of the left orbital cavity. C– Midpoint of anterior lacrimal crest (ALC). J– Point in the medial border of the optic canal (OC). K – Point in the margin of the anterior ethmoidal foramen (AEF) which is closest to the midpoint of anterior lacrimal crest. C – J - Distance from the midpoint of the anterior lacrimal crest to the medial border of the optic canal. C - K – Distance from the midpoint of anterior lacrimal crest to the closest margin of the anterior ethmoidal foramen.

Comparison between the distance on the medial wall of the right and left orbital cavities from anterior lacrimal crest (ALC) to the medial border of the optic canal (OC) and anterior ethmoidal foramen (AEF)

Table 1 Shows

The mean (± SD) distances from the anterior lacrimal crest (ALC) to the medial border of the optic canal (OC) were 43.56 ± 3.44 mm on the right and 43.58 ±3.56 mm on the left orbital cavity.The range of the

distance from anterior lacrimal crest (ALC) to the medial border of the optic canal (OC) were 37.12 - 49.33 mm on the right side and 36.57 - 49.54 mm on the left side. The difference of the distance from anterior lacrimal crest (ALC) to the medial border of the optic canal (OC) was not significant (P = 0.834) between right and left orbital cavities.

The mean (± SD) distances from the anterior lacrimal crest (ALC) to the anterior ethmoidal foramen (AEF) was 24.11±2.74mm and 23.93±2.74mm on the right and left side respectively. The range of the distance from anterior lacrimal crest (ALC) to the anterior ethmoidal foramen (AEF) was 19.55- 29.40 mm and 20.10-29.44 mm on the right and left side respectively. The difference was significant between right and left side ((P<0.05). Mean distances from the anterior lacrimal crest (ALC) to the anterior ethmoidal foramen (AEF) was higher on the right side in comparison to left side

Table I: Comparison between the distance on the medial wall of the right and left orbital cavity from anterior lacrimal crest (ALC) to the medial border of the optic canal (OC) and anterior ethmoidal foramen (AEF)

Side	ALC to OC in mm Mean±SD	ALC to AEF in mm Mean±SD
Right(n=100)	43.56±3.44 (37.12-49.33)	24.11±2.74 (19.55-29.40)
Left(n=100)	43.58±3.56 (36.57-49.54)	23.93±2.62 (20.10-29.44)

P value 0.834^{ns} 0.046^{*}

Figures in parentheses indicate range. Comparison between right and left side done by paired Student's 't' test, ns = not significant, * = significant at P<0.05

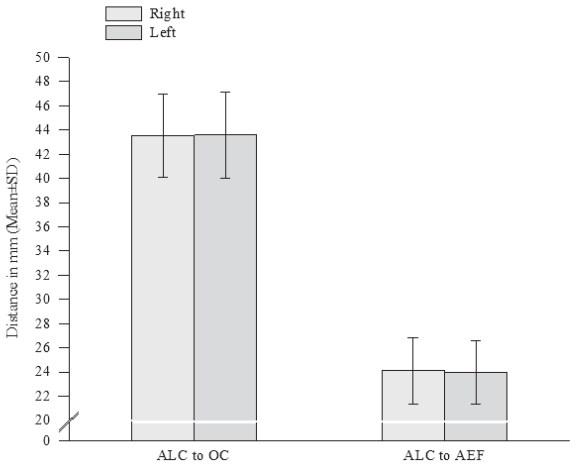


Fig. 4:2 Distance on the medial wall of the right and left orbital cavity from ALC to the medial border of the OC and to the AEF

ALC : Anterior lacrimal crest
OC : Optic canal
AEF : Anterior ethmoidal foramen

Discussion

The present work was undertaken to study various morphometric variables of both orbital cavities of one hundred fully ossified dry human skull. All the skulls were collected from the Anatomy Department of Dhaka medical college and other government and non-government medical colleges in Dhaka city. The main aim of the study is to find out that there is any difference exist between right and left orbital cavity. The study revealed some statistically important findings about morphometric variations of right and left orbital cavity.

The study revealed some statistically important findings about morphometric variations of right and left orbital cavity. But there is no published work on anthropometric measurements of orbital cavity from photographic image in our country. So, present study could not be compared with any previous similar study of Bangladesh. Hence a comparative discussion on the results of different variables of the measurement of orbital cavity of both sides were done with that of different authors and researchers of the other countries.

Observed results of morphological parameters showed some similarities as well as dissimilarities with the available publications. In the present study, the mean (±SD) distance from anterior lacrimal crest (ALC) to the medial border of the optic canal between right and left orbital cavity was not significant (P>0.05). On the other hand, the mean (±SD) distance from anterior lacrimal crest (ALC) to the anterior ethmoidal foramen between right and left orbital cavity was significant (P<0.05). This result is supported by Huanmanop T et al3. They conducted a study on 100 orbits in Thailand . They found non-significant difference (P>0.05) in the mean distance from anterior lacrimal crest (ALC) to the medial border of the optic canal. They also found that the mean (±SD) distance from anterior lacrimal crest (ALC) to the anterior ethmoidal foramen between right and left orbital cavity was significant (P<0.05). But in the mean distance from anterior lacrimal crest (ALC) to the medial border of the optic canal showed Similarity (P<0.05) & dissimilarity (P>P0.05) in the mean (±SD) distance from anterior lacrimal crest (ALC) to the anterior ethmoidal foramen of the findings of the present study with that of Huanmanop may be due to same racial and geographical traits.

Another study was conducted by Shilpa N et al on 136 orbits of unknown sex collected from Maharashtra, India[7]. According to their study, mean (±SD) distance from anterior lacrimal crest (ALC) to the medial border of the optic canal and anterior ethmoidal foramen between right and left orbital cavities were not significantly different (P>0.05). Significant differences were observed (P<0.0001) in the mean distance from anterior lacrimal crest (ALC) to the medial border of the optic canal and anterior ethmoidal foramen between right and left orbital cavities when the findings of present study were compared with Shilpa N et al [7].

Conclusion

The present study shows the significant difference between right and left orbital cavities from the anterior lacrimal crest (ALC) to the anterior ethmoidal foramen (AEF). Other parameters showed no significant difference between right and left orbital cavities.

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Original Article

Knowledge, Attitude & Practice of Salt Behavior Among Rural Married Women of Rupgonj, Bangladesh

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Abstract

Background: *Non-communicable disease like Cardiovascular diseases are the main cause of deaths in Bangladesh and reducing dietary salt intake is recommended to improve the population's health.*

Methods: *This was a cross sectional study based on rural married women. Respondents were selected based on purposive sampling technique according to the availability and consent. Face-to-face interviews were conducted using interviewer administered semi-structured pretested questionnaire which was developed by using WHO Modified Salt Module of STEPS Questionnaire.*

The study was aimed to asses knowledge, attitude and practice (KAP) towards salt utilization.

Results: *This study was conducted among150 rural married women, among them 48% women were within the range of 20-30 yrs in which 30% completed their primary level, 70% were home maker and half of their husband were service holder and businessman, 57.3% were from nuclear family. Among 150 respondents 40% took just right amount of salt and 28.7% respondents took too much salt. In which 44% thought it's important to lowering the salt and 37.3% thought very important to lowering the salt. Almost 80% respondents knew about salt health problem relationship. Their knowledge regarding salt intake was high but their practice scenario was different. Among them 80% never read the salt packaging and 51.3% never used low salt during cooking and 61.3% respondents always used salt in meal. Its remarkable that they know extra salt is bad for them in spite of that 84% took extra salt with meal.*

Conclusion: *It was noticed gap between level of knowledge as well as attitude and level of salt and salty foods practices among the rural Bangladeshi population.*

Key word: *Knowledge, Attitude, Practice, Non-communicable Disease.*

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Introduction

The World Health Organization's (WHO) report on the global status of Non Communicable Diseases (NCDs) in 2014, reported that out of the 56 million deaths that occurred worldwide during 2012, around 38 million deaths were linked to NCDs[1]. Non-communicable diseases (NCDs) are considered one of the main health challenges of the 21st century as they represent a major risk to human health and economic growth especially in low-income and middle-income countries[2]. Among all the major NCDs, hypertension is considered as an independent as well as etiologically relevant risk factor for CVDs [3]. The course of hypertension is significantly contributed by high dietary salt intake and a causal relationship between them is globally established now[4]. Worldwide salt is the main dietary source of sodium and excess consumption of dietary sodium has been found associated to an increased risk of hypertension and CVDs [5].

The physiological need of dietary salt is 3.8 gm which is less than the recommendation of 5gm salt per day by WHO. Therefore it is considered that there is a realistic conciliation exists between the beneficial and attainable in terms of reducing salt consumption [6]. Evidence suggests that a reduction in salt intake from 9-12gm a day to a recommended level would project to prevent 2.5 million annual deaths from cardiovascular diseases worldwide[7].

Reducing salt intake has been identified as one of the most cost effective measures for improving population health. Clinical trials showed that lowering dietary sodium intake can reduce CVDs risk by reducing high blood pressure. A study in the United States intended to explore the potential impact of reducing dietary salt by 3 g per day estimated a decrease in annual healthcare costs by a range of $10 billion to $24 billion, and projected a significant decrease in the incidence of coronary heart disease, stroke, and myocardial infarction . Hence, the WHO recommends reducing salt intake to less than 5 g/day and sodium to less than 2 g/day in adults to help prevent high blood pressure, coronary heart disease, and stroke [8].

The mean of daily salt consumption was 5-16 gm in coastal areas[9] in rural areas and 9-11gm in different urban areas among Bangladeshi general population which is more than the WHO recommendation for total salt consumption[10]

But the salt intake pattern in term of knowledge, attitude and practice was not assessed yet in Bangladeshi rural population. In a survey of Nottingham University a high proportion of respondents (83.8%) believed salt to be detrimental to health but overall there was a poor level of knowledge of the salt content of a range of foods and 85% per cent of respondents had purchased reduced salt food product[11].

Considering these facts, highlighting the importance of assessing salt intake and determining salt related knowledge, attitudes, and practices to assist in the development of national salt reduction interventions.

Methods

The study was conducted by single time data collection procedure from rural area and this study was conducted at Ichapura village, Thana- Rupgonj, District- Narayangonj. This was a cross sectional study based on rural married women. In the urban area, the educational status is much better than the rural site. The availability of mass media, internet also make the people of urban site to know about the risk of taking high salt intake. Married women were taken because they make arrangement for cooking in the family. Respondents were selected based on purposive sampling technique according to the availability and consent. Face-to-face interviews were conducted using interviewer administered semi-structured pretested questionnaire which was developed by using WHO Modified Salt Module of STEPS Questionnaire.

The study was aimed to asses knowledge, attitude and practice (KAP) towards salt utilization.

Data collection instrument

A semi-structured questionnaire was used in which someone is asked some question related to socio-demographic characteristics and salt consumption behavior, among which some questions were directly adopted from core and expanded portion of dietary salt section of the STEPS instrument version 3.1. The STEPS Instrument covers three different levels of non-communicable disease risk factors assessment: Step 1 (questionnaire), Step 2 (physical measurements) and Step 3 (biochemical measurements). Only Step 1

was used in this study and some additional questions on added salt intake in meal were included in the questionnaire for the comprehensiveness and completeness of the information.

Statistical analysis

After data collection, all the completed questionnaires were checked for any error or inconsistency before coding and entering them into the database. The data were entered in a Microsoft Excel sheet first and then imported into SPSS for analysis. In SPSS, logical checking of data was done by sorting and frequency running. All the categorical data regarding knowledge and practice of salt intake were expressed as frequency and percentage.

Result

This study was conducted among 150 rural married women, among them 48% women age within the range of 20-30 yrs in which 30% completed their primary level, 70% were home maker and half of their husband were service holder and businessman, 57.3% were from nuclear family. Among 150 respondents 40% took just right amount of salt and 28.7% respondents took too much salt. In which 44% thought it's important to lowering the salt and 37.3% thought very important to lowering the salt. Almost 80% respondents knew about salt health problem relationship. Their knowledge regarding salt intake was high but their practice scenario was different. Among them 80% never read the salt packaging and 51.3% never used low salt during cooking and 61.3% respondents always used salt in meal. Its remarkable that they know extra salt is bad for them in spite of that 84% took extra salt with meal.

In a conclusion, it was noticed gap between level of knowledge as well as attitude and level of salt and salty foods practices among the rural Bangladeshi population.

Table I: Socio demographic Information, n=150

Variables	Frequency (N)	Percentage (%)
Age group		
20 -30	72	48
31 -40	44	29.3
41 -50	24	16
>50	10	6.7
Religion of the respondents		
Islam	145	96.7
Hindu	05	3.3
Types of Family		
Nuclear family	86	57.3
Joint family	64	42.7
Number of family member		
3 -5	69	63.9
6 -10	38	35.2
>6	01	0.9
Sex of the Respondent		
Male	66	61.1
Female	42	38.9
Monthly family income of the respondent		
Less than 15000	63	42.0
16000 - 30000	63	42.0
31000 - 45000	14	9.3
More than 45000	10	6.7

Table II: knowledge, attitude and practice (KAP) towards salt utilization, n=150

Variables	Frequency	Percentage (%)
Amount of salt consumption		
Too much	43	28.7
Just the right amount	61	40.7
Too little	26	17.3
Far too little	7	4.7
Don't	13	8.7
Important lowering the salt		
Very important	56	37
Some important	66	44.0
Not at all important	28	18.7
Salt can causes health problem		
Yes	120	80
No	30	20
Read the salt packaging		
Yes	29	19.3
No	121	80.7
Buy low salt		
Yes	9	6.0
No	141	94.0
Use low salt during cooking		
Yes	73	48.7
No	77	51.3
Add salt intake in meal		
Always	92	61.3
Often	10	6.7
Sometime	21	14.0
Rarely	12	8.0
Never	15	10.0
Extra salt per day		
> 1 spoon	118	78.7
≥ 1 spoon	8	5.2
Don't take extra salt	24	16

Discussion

This was a cross sectional study based on rural married women. Respondents were selected based on purposive sampling technique according to the availability and consent. Face-to-face interviews were conducted using interviewer administered semi-structured pretested questionnaire which was developed using WHO Modified Salt Module of STEPS Questionnaire.

The study was aimed to to asses knowledge, attitude and practice (KAP) towards salt utilization.

This study was conducted among150 rural married women, among them 48% women age within the range of 20-30yrs in which 30% completed their primary level, 70% were home maker and half of their husband were service holder and businessman, 57.3% were from nuclear family. Among 150 respondents 40% took just right amount of salt and 28.7% respondents took too much salt. In which 44% thought it's important to lowering the salt and 37.3% thought very important to lowering the salt. Almost 80% respondents knew about salt health problem relationship. Their knowledge regarding salt intake was high but their practice scenario was different. Among them 80% never read the salt packaging and 51.3% never used low salt during cooking and 61.3% respondents always used salt in meal. Its remarkable that they know extra salt is bad for them in spite of that 84% took extra salt with meal.

The knowledge regarding salt intake was high but little reflection in their habit of consuming added salt. Current study found comparatively higher proportions of perceptions towards salt intake as for both just right amount (40.4%) and too much (28.7%) than another domestic study conducted among the university faculty members and doctors whereas these proportions were 29.3% and 10.9% respectively[12]. The possible difference between the respondents answers could be, doctors and faculty members answer can be considered more accurate than the general population answer as overre presentation might be happened; whereas another unpublished study among the medical and nonmedical undergraduate students found less and higher proportions of perceptions for just right amount (55.8%) and too much (6.9%) respectively[13]. which is also shows clear difference that means it could be said that perception of different group is different regarding salt intake; again higher proportions for both of these perceptions than the Greek adults[14] and also higher for too much consumption than the American population (12.9%)[15], but less proportion for too much consumption than Chinese people[16].

Another Indian study on rural and urban adult shows that Twenty-four per cent of rural and 40·5 % of urban participants knew that a high-salt diet causes high blood pressure. Nearly one-fifth of both rural and urban participants knew that there should be a maximum daily limit for consumption of salt. In rural and urban areas, 46·6 and 45·1 %, respectively, perceived it important to reduce the salt content of their diet; however, only 3·7 and 10·2 %, respectively, reported taking some actions. Participants reported they were consuming 'too little salt', 'just the right amount of salt' or 'too much salt', but their corresponding mean (95 % CI) actual salt consumption (g/d; as measured by 24 h urinary Na excretion) was higher, especially among rural participants (rural: 9·2 (8·13, 10·22), 8·5 (8·19, 8·77) or 8·4 (7·72, 8·99); urban: 5·6 (4·67, 6·57), 5·7 (5·32, 6·01) or 4·6 (4·10, 5·14), respectively)[17].

Study found a noticeably that their knowledge regarding salt intake was high but they (84%) took extra salt per day and among them 118 respondents took <5 gm/day and 8 respondents took >5gm/day. It's alarming that maximum respondents took extra salt every day.

Finally it can be said that the findings of this study cannot be generalized .A large scale country wide study can solve this issue.

Conclusion

The knowledge, attitude and practice regarding added salt intake in the study population is appreciable. Though the participants were from rural but still the prevalence of added salt intake is higher. This study provided a scenario of salt intake behavior among rural reproductive age women which may differ from unban. So future policies can be formulated to ensure the practice of recommended salt intake, to reduce the burden of hypertension for this group of population.

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Original Article

Outcome of Unsafe Abortion in Rural Community

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Abstract

Background: *Unsafe abortion is one of the important causes of maternal morbidity and mortality globally. Globally more than half of the unintended pregnancies end in induced abortion. Approximately half of the admissions to gynaecology units in major hospitals of Bangladesh are for complications of abortion.*

Objective: *This study aimed to assess the outcome of unsafe abortion.*

Material and Methods: *It was a descriptive cross sectional study carried out in the department of Obstetrics & Gynaecology, Jahurul Islam Medical College Hospital, Kishoregonj from October 2013 to March 2014. Total 50 patients of unsafe abortion were included in this study. After collecting all the data of different test results analyses were done by SPSS version 15.0.*

Results: *This study showed maximum outcome (78%) were incomplete abortion and after proper management at hospital 82% cured, whereas 18% were improved and out of danger.*

Conclusion: *This study suggests that unsafe abortion can be devastating for a woman but outcome is good if managed properly.*

Key words*: Unsafe abortion, outcome*

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Introduction

Unsafe abortion is defined as a procedure for terminating an unwanted pregnancy, either by persons lacking the necessary skills, or in an environment lacking the minimal medical standards, or both (WHO).[1] Unsafe abortions are a major cause of injury and death among women worldwide. Worldwide, an estimated 68000 women die as a result of complications from unsafe induced abortions every year—about eight per hour.[2] Worldwide an estimated 5 million women are hospitalized every year for treatment of abortion related complications, such as hemorrhage and sepsis.[3] It is one of the most neglected problems of health care in developing countries.[4] This study is therefore aimed at determining the outcome of unsafe abortion cases in rural community.

Materials and Methods

It was a cross sectional study conducted in the department of Obstetrics and Gynaecology of Jahurul Islam Medical College Hospital, Kishoregonj, Bangladesh, from October 2013 to March 2014.Total 50 patients attending in the Department of Obstetrics and Gynaecology (both inpatient and outpatient), JIMCH, having history of termination of unwanted pregnancy by skilled personnel and/or carried out at unregistered private clinics or at home at a gestational less than or equal 22 weeks.

Results

This study was undertaken with the objective to assess the outcome of unsafe abortion and their contributing factors in rural community. A total of 50 unsafe abortion cases were included in this study.

Table I: Distribution of the cases by their age (n=50)

Age in years	Frequency	Percentage (%)
<20	8	16
21 -25	8	16
26 -30	16	32
31 -35	13	26
>35	5	10
Total	**50**	**100**

In table I, five age groups were plotted. Most of the patients belong to 26-30 years age group 16 (32%).

Table II: Distribution of the patients by their methods of abortion (n=50)

Method of abortion	Frequency	Percentage (%)
Allopathic	25	50
Homeopathic	1	2
Herbal	3	6
MR	20	40
Other	1	1

According to table II, half of the respondents 25(50%) took allopathic drug for termination of pregnancy followed by MR 20(40%), herbal 3(6%), homeopathic 1(2%) and other 1(2%).

Table III: Distribution of the patients according to their outcome of unsafe abortion (n=50)

Outcome	Frequency	Percentage (%)
Incomplete abortion	39	78
Septic abortion	7	14
Hypovolumic shock	12	24
Perforation of uterus	1	2
Cervical stenosis	3	6

Table III shows most common outcome of unsafe abortion was incomplete abortion 39(78%), followed by hypovolumic shock 12(24%), septic abortion 7(14%), cervical stenosis 3(06%) and perforation of uterus 1(2%).

Figure 1: Treatment outcome

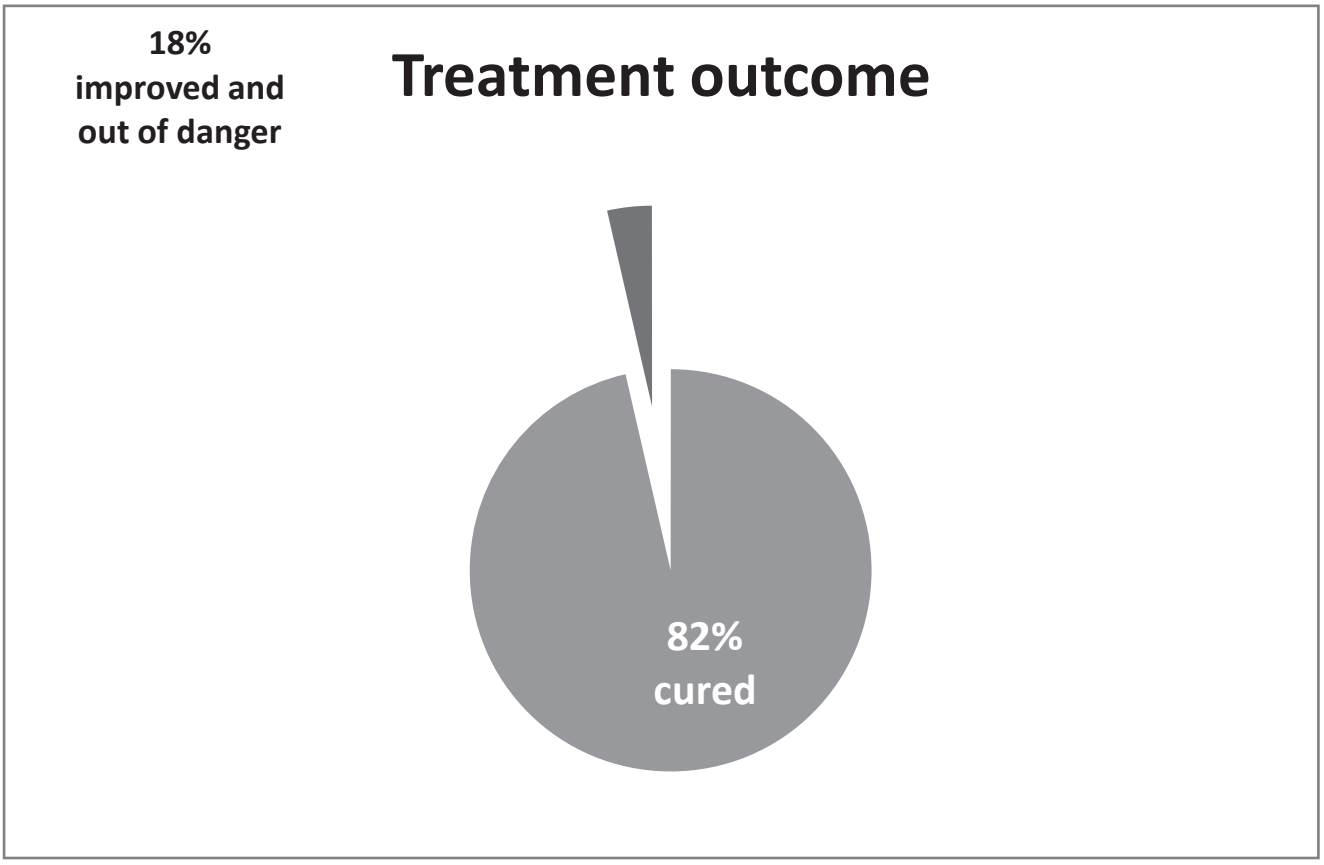

Figure 1: Distribution of patients by their treatment outcome (n=50)

Figure 1 shows that maximum patients 41(82%) were cured after treated at hospital and 9(18%) were improved and out of danger.

Discussion

Worldwide millions of women seek induced abortion. When it is successful and complete it remains secret and if complicated get highlighted due to their management at hospital level. The hospital data represents just tip of the ice berg. The problem at the community level is much bigger and graver.[5] A total number of 50 unsafe abortion were included in this study showing 32% patients were in the age group of 26-30 years. Among 50 cases in this study, half of them (50%) opted for allopathic (mostly misoprostol) drugs to induce abortion followed by MR (40%), insertion of stick (2%) and other methods (2%) Homeopathic and 6% by Herbal medication).

The patients had more than one outcome of unsafe abortion at time they were admitted into the hospital. In more than three fourth (78%) of the cases, outcome were incomplete abortion. Near about one fourth (24%) were in hypovolumic shock. In 14% cases outcome were septic abortion, 6% cases cervical stenosis and 2% cases perforation of uterus. At Ayub Medical College Hospital, twenty patients (38.4%) presented with heavy per vaginal bleeding due to incomplete nature of the procedure. Twelve patients (23%) presented in shock due to excessive per vaginal bleeding. Ten patients (19.2%) had uterine perforation and intra-peritoneal hemorrhage. Two patients (3.8%) had gut injury associated with uterine perforation. Three patients (5.7%) developed septicaemia due to uterine gangrene. Ten patients (19.2%) had acute pelvic infection presented with pelvic abscess and acute pelvic inflammatory disease.[6]

In this study it has been observed that in spite of various sufferings and diversified complications more than four fifth (82%) of the cases got cured with a short period and 18% were declared improvement of condition and out of danger.

Conclusion

Unsafe abortion is a common and serious gynaecological problem worldwide. Consistent and correct use of modern methods of contraception can prevent many unwanted pregnancies and thus reduce unsafe abortion.

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Original Article

Comparative Study of Serum Uric Acid in Hypertensive Adult Population of Bangladesh

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Abstract

Background: *Hypertension is recognized as the most common cardiovascular disorder and a leading cause of morbidity and mortality in both developed and developing countries. Several factors are responsible for development of hypertension. Among them increased level of serum uric acid may lead to develop hypertension.*

Objective: *The objective of the study was to evaluate the relationship between serum uric level & hypertension in adult population of Bangladesh.*

Methods: *A total of 100 subjects were enrolled by purposive and convenient sampling. Study populations were divided into case and control group based on presence or absence of hypertension respectively. Serum uric acid level was measured in both group and compared.*

Results: *Patients of case & control group were similar in terms of age and sex. Serum uric acid was significantly ($P < 0.001$) higher in case group than control group. A significant positive correlation between serum uric acid and Systolic blood pressure (SBP) & Diastolic blood pressure (DBP) was observed.*

Conclusion: *From this study it can be concluded that increased level of serum uric acid was associated with hypertension. Increased level of serum uric acid was found to be significantly and positively correlated with Systolic blood pressure (SBP) and Diastolic blood pressure (DBP).*

Key words: *Serum uric acid, Hypertension.*

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Introduction

Hypertension is the emerging public health problem of adult population across the world, affecting one in every four individuals.[1] It is the third leading killer disease in the globe and is responsible for one in every eight death.[2]Essential hypertension has been appropriately called the silent killer because it is usually asymptomatic and undetected.[3] Hypertension accounts for an estimated 54 percent of all strokes and 47 percent of all ischemic heart disease events globally.[4] Hypertension in adult is diagnosed when the average of two or more diastolic and systolic blood pressure measurements on at least two subsequent visits are more than 90 and 140 mmHg respectively.[5]The prevalence of hypertension is increasing day by day. The estimated total number of adults with hypertension in 2000 was 972 million. Of these, 333 million were estimated to be in economically developed countries and 639 million in economically developing countries. By 2025, the number of people with hypertension will increase by about 60% to a total of 1.56 billion as the proportion of elderly people will increase significantly. Since the proportion of hypertensive people will increase dramatically worldwide, the prevention, detection, treatment and control of this condition should be a top priority.[6]

The etiological factors associated with hypertension is difficult to predict because hypertension develops due to a complex interaction of genes and environmental factors. Various risk factors are responsible for development of hypertension. Among them elevated level of serum uric acid is thought to play a pathogenic role in hypertension. The mechanism of development of hypertension in hyperurecemia is mediated by inflammation, vascular smooth muscle cell proliferation in renal microcirculation, endothelial dysfunction and activation of renin-angiotensin system.[7,8,9,10]Refference value of serum uric acid is 4.4-7.7mg/dl in adult male and 2.3-6.6mg/dl in adult female.[11]Hence the present study was done to assess the role of increased serum uric acid level in development of hypertension.

Methods

This case control study was carried out in the Department of Biochemistry of BSMMU, Shahbag, Dhaka from March 2013 to March 2014. A group of clinically diagnosed hypertensive patients were selected as cases. Hypertensive cases were diagnosed according to JNC VII criteria. Equal number of apparently age & sex matched healthy normotensive adults were selected as control. History of diabetes mellitus, obesity, renal disease, alcohol abuse, preeclampsic toxemia, intake of drugs that known to cause hyperurecemia like thiazide diuretics were excluded from the study. 5 ml of fasting blood sample was collected from the study subjects. Serum was isolated and serum uric acid level was measured by sprectrophotometric principle in architect autoanalyser. Data was analyzed by SPSS 16.0 version and descriptive statistics were presented as frequencies and percentages.

Results

The study included 50 cases and 50 controls. The mean age of the case and control group were 44.72 ± 8.96 years and 42.30 ± 9.50 years respectively (Table I).

The mean age of the case group was higher than the control group but the difference was not statistically significant (P =0.193). Male Female ratio was 1:1.

Table I: Distribution of study subjects according to age and sex

	Group		p value
	Case (n=50)	**Control (n=50)**	
Age (years) (Mean ± SD)	44.72 ± 8.96	42.30 ± 9.50	0.193
Sex			
Male	25 (50.0)	25 (50.0)	
Female	25 (50.0)	25 (50.0)	

t test was done to measure the level of significance. Figure within parentheses indicates in percentage. Biochemical status of the study population was measured and analysed (Table II). Mean serum uric acid level was 9.79 ± 1.63mg/dl in case group and 5.33 ± 1.17mg/dl in control group. Regarding biochemical parameter there was statistical significant difference (P < 0.001).

Table II: Comparison of serum uric acid level between case and control

Parameter	Group		p value
	Case	Control	
Serum u ric a cid (mg/dl)	9.79 ± 1.63	5.33 ± 1.17	<0.001

t test was done to measure the level of significance.

The figure 1 showing, there was a positive correlation between serum uric acid and systolic blood pressure. It was observed that the correlation was statistically significant (r = +0.349, p= 0.013) by Pearson correlation test.

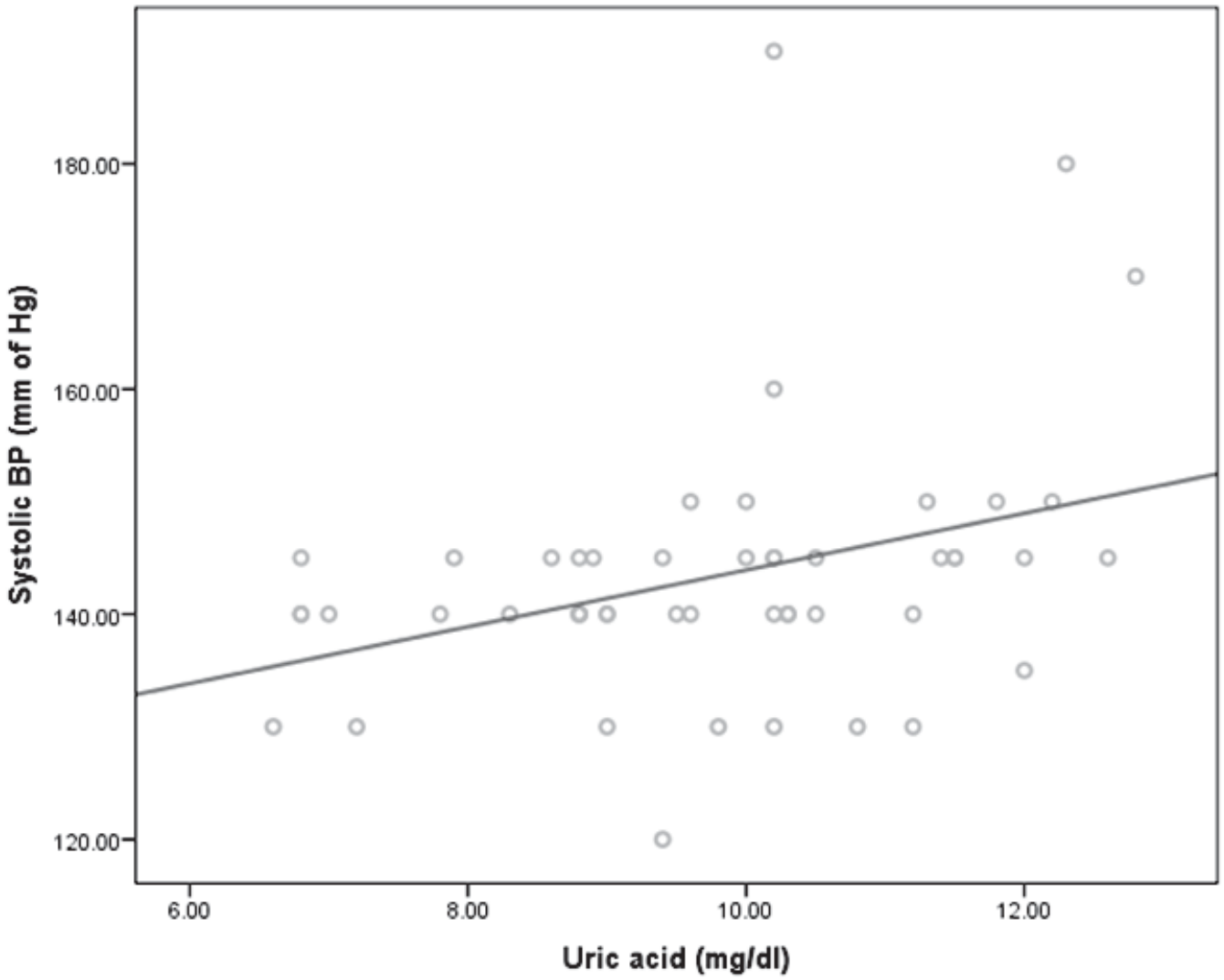

Figure 1: Correlation of uric acid with systolic BP in cases. Pearson correlation, r is 0.349 with a p value of 0.013.

The figure 2 showing, there was a positive correlation between serum uric acid and diastolic blood pressure. It was observed that the correlation is statistically significant (r = + 0.415, p = 0.003) by Pearson correlation test.

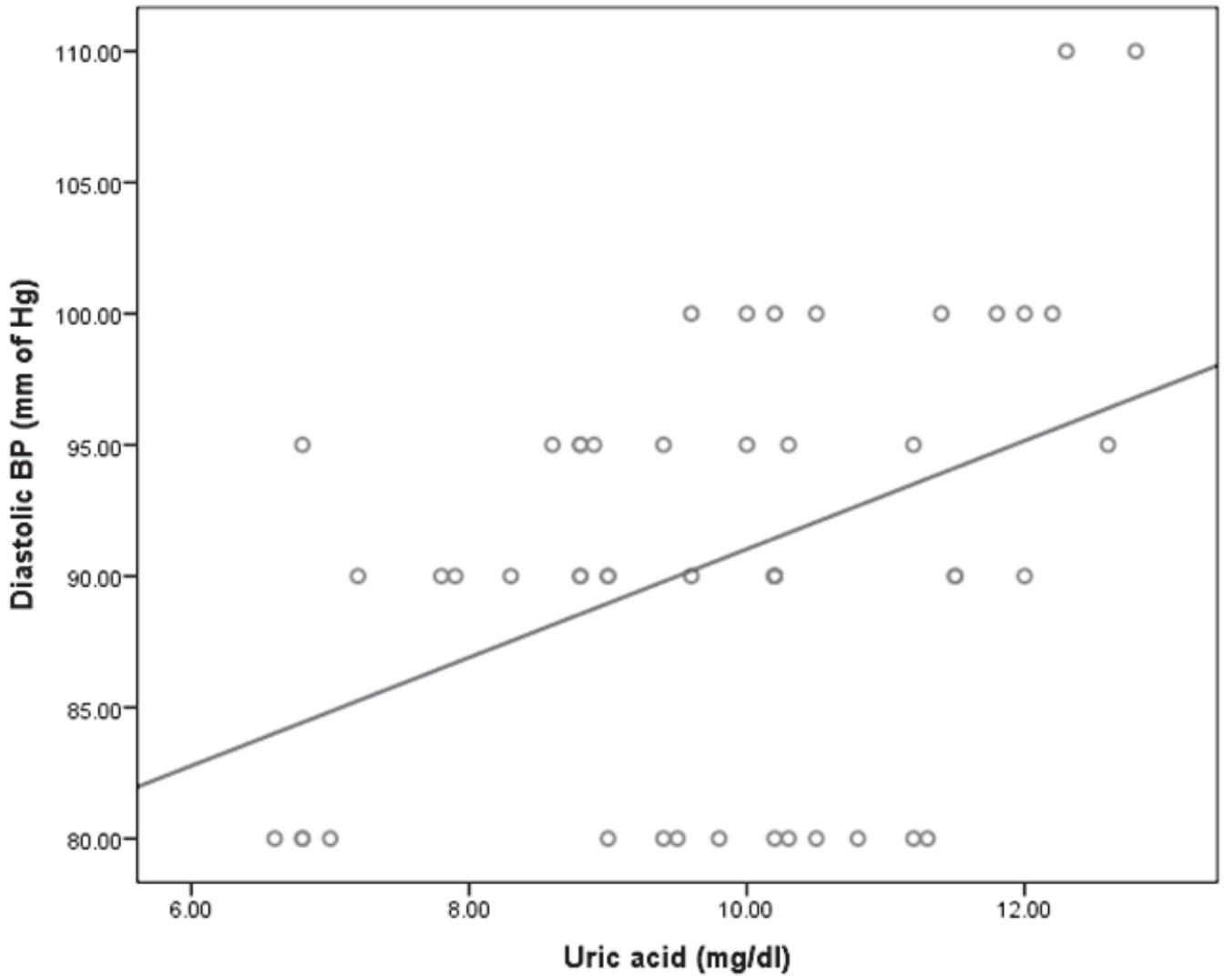

Figure 2: Correlation of uric acid with diastolic BP in cases. Pearson correlation, r is 0.415 with a p value of 0.003.

Discussion

This case control, analytical study was conducted to evaluate the relationship between serum uric acid& hypertension. A total of 100 subjects were included in the study based on predefined enrollment criteria. They were grouped into cases (hypertensive) and controls (normotensive) on the basis of presence or absence of hypertension. In this study male and female subjects were equal in number both in case and control group.

Present study showed that the mean age of the case and control group were 44.72 ± 8.96 years and 42.30 ± 9.50 years respectively ranging from 25-60 years. This study showed that mean serum uric acid level (9.79±1.63 mg/dl) was significantly higher (p< 0.001) in hypertensive subjects than controls (5.33 ± 1.17 mg/dl)

Similar observations were reported by other investigators of different countries. In an Indian study

conducted by Reddy RP, Monigari N and Hande M found that serum uric acid level was significantly elevated in hypertensive as compared to normotensive individuals. The range of serum uric acid in cases was 1.40-11.30 mg/dl where as in control was 1.50-6.50 mg/dl. The mean serum uric acid in cases was 5.32 mg/dl controls was 3.75 mg/dl. [12]

Another Indian study conducted by Kanwar G and Jain N also showed that mean serum uric acid level was significantly higher in patients with hypertension in comparison to normotensives. The mean serum uric acid was 6.94± 1.14 mg/dl in cases and 4.39±0.93 mg/dl in controls.[13]

Present study also showed significant positive correlation between serum uric acid level with systolic blood pressure ($p = 0.013$) and diastolic blood pressure ($p = 0.003$).This findings were supported by other studies. A cross sectional study conducted by Ali N et al. on Bangladeshi hypertensive adult population showed that hyperurecemia was significantly and positively correlated with systolic ($r= 0.191$, $p= 0.008$) and diastolic blood pressure ($r= 0.188$, $p= 0.009$).[14] Another study in Cameroon conducted by Assob JCN showed significant positive correlation between serum uric acid level with systolic ($p< 0.0001$) and diastolic blood pressure ($p<0.0001$).[15]

Limitation of the study

It was a single centre study and the number of study population was limited and the sample size was not reflecting the whole country scenario.

Conclusion

From this study it can be concluded that increased level of serum uric acid was associated with hypertension. Serum uric acid was found to be positively correlated with systolic & diastolic blood pressure.

Recommendation

The findings of our study will help the hypertensive individuals to build up their awareness & to modify their life style & dietary habit. Since hypertension is mostly a preventable problem, due care can be taken to deal this problem by implementation of multidimensional preventive strategies. Avoidance of food that raises serum uric acid may decrease hyperurecemia and chance of development of hypertension. We recommend a further population based and multicenter studies on this issue in our country, which will provide further information and will be beneficial for the large group of hypertensive patients for their preventive measures, diagnosis, management and treatment.

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Original Article

Serum Folic Acid Level in Vitiligo Patients: A Case Control Study

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Abstract

Background: *Vitiligo is a common dermatological problem and the prevalence is more than 8% worldwide. It causes cosmetic disfigurement and psychological problem, which has an impact on person's social & professional life .It also causes sun burn and skin cancer. Low level of folic acid may play a role in the pathogenesis of vitiligo.*

Objective: *The present study was carried out to assess serum folic acid level in subjects with vitiligo.*

Methods: *For this study, 50 subjects with vitiligo aged 20-50 years were considered as the study group (Group B) and 50 age matched healthy subjects were considered as control group (Group A) for comparison. Serum folic acid level was measured & compared in both group.*

Results: *In this study, serum folic acid (p= 0.016) was significantly lower in vitiligo patients as compared to healthy controls. Serum folic acid was significantly lower (p= 0.016) in progressive vitiligo patients than stable vitiligo patients. Serum folic acid was significantly (p=0.029) negatively correlated with duration of vitiligo.*

Conclusion: *From the study results, it was concluded that nutritional deficiency of folic acid may be a precipitating factor in the pathogenesis of vitiligo & indirectly support the free radical mediated damage of melanocytes. Therefore, estimation of serum folic acid level in vitiligo patients & in addition folic acid supplementation might be beneficial for the treatment of vitiligo.*

Key words: *Vitiligo, Folic acid.*

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Introduction

Vitiligo is an acquired, idiopathic disorder characterized by depigmented patches in skin due to destruction of melanocytes. People of all ages and both sexes are affected equally. Patients lose their skin color usually in a patchy and progressive manner.[1] Clinically the activity of vitiligo is of two types, progressive and stable. In progressive disease there is enlargement of already present lesion and or the appearance of new lesion within two months and in stable vitiligo there is no change in the lesion within two months.[2] The prevalence of vitiligo is around 1% in the United States & Europe. It ranges from < 0.1% to > 8% worldwide.[3] In India, the prevalence ranges from 0.09% to 8%. In China, Nepal & Srilanka the prevalence of vitiligo are 0.09%, 0.9% & 1.2 % respectively.[4]

Although vitiligo can affect any part of the body but the common sites are the exposed areas (face, neck, eyelids, nostrils, finger tips & toes), body folds (armpits, groin), nipple, lips and genitalia. It starts as multiple pigmented mole that develops a peripheral pigmented zone then gradually become fade & disappear in time. The white patches gradually enlarge over weeks to months. Vitiligo extends rapidly for a few months then stabilizes.[5]

People with vitiligo may be at increased risk of developing social & psychological stress. The main impact of vitiligo is the psychological effect. Vitiligo patients have lower self-esteem, higher levels of perceived stigma and disability, anger, poorer Quality Of Life (QOL) overall and negative impact on sexual relationships.[6] Beside this patients may develop skin cancer & sun burn.[7]

The exact cause of vitiligo is unknown but the most probable mechanisms are free radicals induced & immune mediated damage of melanocytes.[8] Free radicals like superoxide anion (O_2^-), hydroxyl radical (OH^-) cause lipid peroxidation & produce lipid peroxides & lipoxides. These oxides yield malondialdehyde that causes destruction of melanocytes.[9]

Folic acid deficiency is one of the important determinant of serum homocysteine level because it is involved in homocysteine and methionine metabolism. Serum homocysteine level may increases in folic acid deficiency. Excess homocysteine induce oxidative stress which causes destruction of melanocytes.[10] Homocysteine has also an inhibitory action on the tyrosinase activity of skin. So, decreased folic acid may increase in serum homocysteine level that may interfere with normal melanogenesis & play a role in pathogenesis of vitiligo.[11]

Methods

The present study was a case control study and conducted in the Department of Physiology, Dhaka Medical College, Dhaka from July 2014 to June 2015. A total of 100 subjects were selected with age ranging from 20 to 50 years. Among them, 50 subjects with vitiligo were considered as the study group (Group B) and 50 age matched healthy subjects were considered as control group (Group A) for comparison. The subjects were selected from outpatient department of Dermatology & Venereology, BSMMU, Dhaka & from personal contact from different areas of Dhaka city. Subjects with hypertension, diabetes mellitus, renal failure, hypothyroidism, pregnancy, vitamin B_{12} and folic acid supplementation were excluded from the study. After selection, the aim and benefit of the study was explained to each patient. An informed written consent was taken from all the participants. Study protocol was approved by Institutional Ethics Committee of Dhaka Medical College. A detail medical

and family history of all subjects were recorded in a preformed questionnaire. Anthropometric measurement of the subjects was done and blood pressure was measured. With all aseptic precautions 5 ml blood from each study subject was collected after an overnight fast (at least 12 hours) to measure serum folic acid level. This parameter was estimated in the Department of Biochemistry, BSMMU, Dhaka by Chemiluminescent Microparticle Immunoassay Method. Data were analyzed by Student's 't' test and Pearson's correlation coefficient (r) test using SPSS for windows version 22.0.

Results

The general characteristics of study subjects and control group are presented in Table I. Both the groups were matched for age and BMI. Serum folic acid level was significantly lower in group B (p =0.016) in comparison to those of group A (Table II a). Again, serum folic acid level was significantly lower in group B_2 in comparison to those of group B_1 (Table II b).

Distribution of the subjects by different parameter in the study group are shown in Table III. Correlation of serum folic acid with duration of the disease is shown in Table III. Serum folic acid level showed significant ($p< 0.05$) negative correlation ($r = - 0.310$) with duration of vitiligo (Figure 1).

Table I :General characteristics of the subjects in both groups (n=100)

Parameters	Group		p value
	Group -A Healthy subjects (n =50)	Group -B Vitiligo patients (n =50)	(A vs B)
Age	35.00 ± 8.34 (20 -50)	33.08 ± 6.53 (20 - 50)	0.203 ns
Sex			
Male	25 (50.0)	25 (50.0)	
Female	25 (50.0)	25 (50.0)	
Height (m)	1.62 ± 0.07 (1.52 – 1.73)	1.62 ± 0.06 (1.55 – 1.73)	
Weight (kg)	61.66 ± 6.09 (50 - 70)	60.52 ± 6.36 (52 - 70)	
BMI (kg/m ^{2})	23.3 ± 1.5 (20.7 – 27.4)	22.8 ± 1.0 (21.0 – 25.8)	0.095 ns
Systolic BP (mmHg)	117.80 ± 12.46 (100 - 180)	114.1 ± 7.6 (100 - 125)	
Diastolic BP (mmHg)	75.7 ± 7.0 (60 - 85)	75.8 ± 7.9 (60 - 85)	

Results are expressed as mean ± SD. Figure in parentheses indicate range. Unpaired Student's 't' test was performed to compare between groups. The test of significance was calculated & p value < 0.05 was accepted as level of significance. n = number of subjects

Table II (a) : Study parameter of the subjects in both groups (n=100)

Parameter	Group		p value
	Group -A Healthy subjects (n =50)	Group -B Vitiligo patients (n =50)	(A vs B)
Serum folic acid (ng/ml)	6.1 ± 4.0	4.4 ± 2.3	0.016 *

Results are expressed as mean ± SD. Figure in parentheses indicate range. Unpaired Student's 't' test was performed to compare between groups. The test of significance was calculated & p value < 0.05 was accepted as level of significance. n = number of subjects, ns = not significant, */**/*** = significant

Table II (b) : **Study parameter in stable & progressive vitiligo patients in study group (n=50)**

Parameter	Activity of disease		p value
	Group -B_1 Stable vitiligo (n = 26)	Group -B_2 Progressive vitiligo (n = 24)	B_1 vs B_2
Serum folic acid (ng/ml)	5.2 ± 2.7	3.6 ± 1.4	0.014*

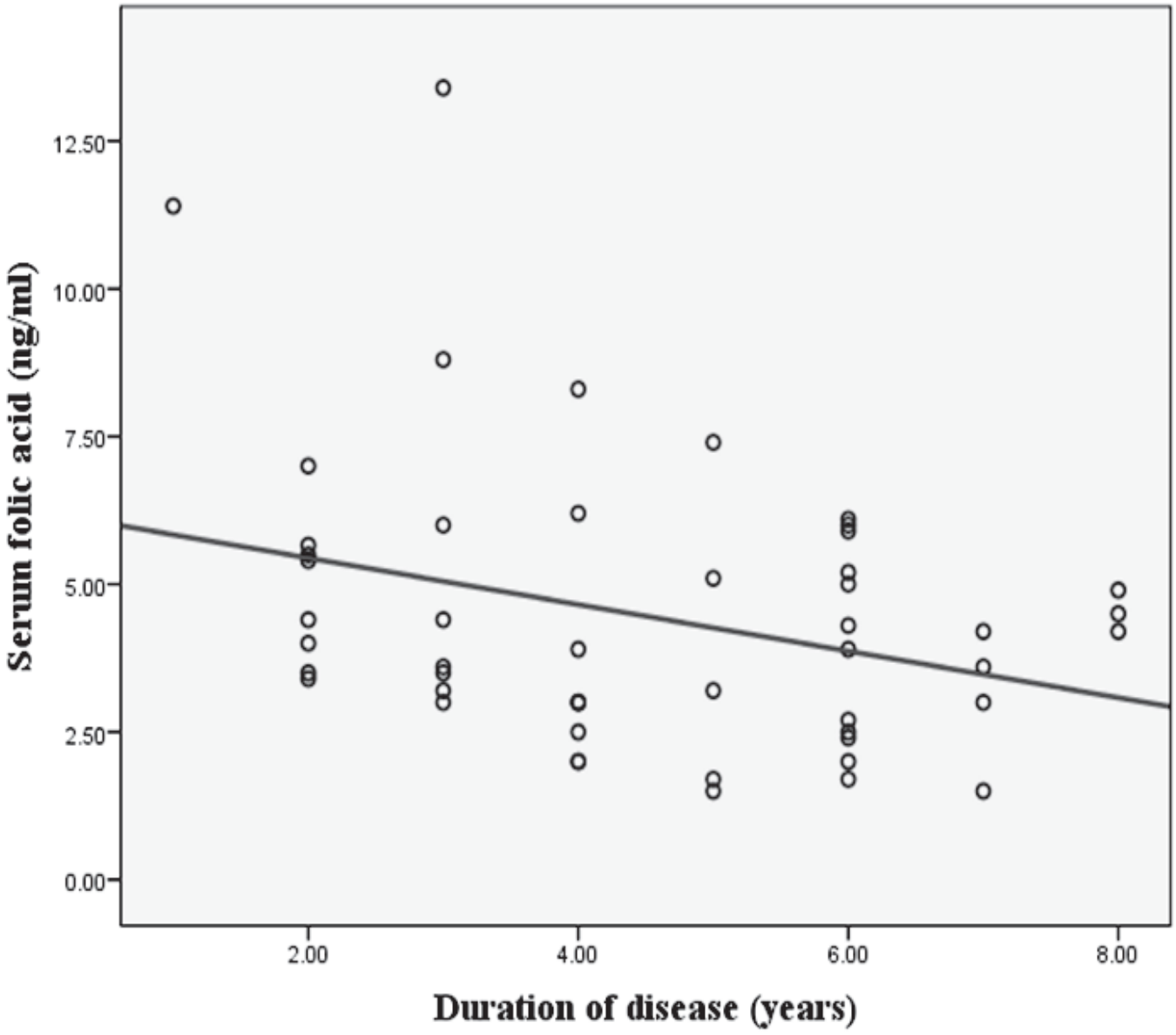
Results are expressed as mean ± SD. Figure in parentheses indicate range. Unpaired Student's 't' test was performed to compare between groups. The test of significance was calculated & p value < 0.05 was accepted as level of significance. n = number of subjects, ns = not significant, */**/*** = significant

Table III: Correlation of study parameter with duration of disease in study group (n=50)

Study parameter	Group B Vitiligo patients (n = 50)	
	r value	p value
Serum folic Acid	-0.310	0.029*

Pearson correlation coefficient (r) test was performed to compare relationship between parameters. The test of significance was calculated and p value < 0.05 was accepted as level of significance. n = number of subjects, ns = not significant, */**/*** = significant

Figure 1 : Correlation of serum folic acid level with duration of disease in study subjects (n= 50)



Group B: Study group (vitiligo patients)

r = -0.310, p < 0.05*

n = Number of subject, * = Significant

Discussion

This case control, analytical study was conducted to assess the relationship between serum folic acid & vitiligo. A total of 100 subjects were included in the study based on predefined enrollment criteria. They were grouped into cases (vitiligo patients) and controls (healthy subjects). In this study male and female subjects were equal in number both in case and control group.

The results of this study showed significantly (p= 0.016) lower serum folic acid level in vitiligo patients (4.4±2.3 ng/ml) than control (6.1±4.0 ng/ml). Similar observations were reported by other investigators of different countries. In an Egyptian study conducted by Singh S, Singh U and Pandey SS in 2012 showed that serum folic acid level was significantly ($p < 0.05$) lower in vitilgo patients than healthy controls. The mean serum folic acid was 4.88±1.52 ng/ml in cases and 6.25±0.69 ng/ml in controls.[12]

But interestingly in a Turkish study conducted by Yasar A et al. in 2012 found significantly low serum folic acid in control (5.39±2.41ng/ml) than vitiligo patients (6.59±2.78 ng/ml).[13] In another study conducted in India in 2015 by Agarwal et al. showed that serum folic acid was significantly low in vitiligo patients than healthy controls. The mean serum folic acid was 4.18±3.55 ng/ml in cases and 7.3±3.67 ng/ml in controls.[14] On the other hand, some authors found low serum folic acid in vitiligo patients compared to control but it was not statistically significant. Park HH and Lee MH in a Korean study in 2004 did not found any difference regarding serum folic acid level between vitiligo patients and normal healthy control.[15] In a Egyptian study Sabry HH, Sabry JH and Hashim MM in 2014 found that serum folic acid level was 8.42±2.06 ng/ml in vitiligo patients and 9.39±2.38 ng/ml in normal healthy control. Here serum folic acid was low in vitiligo patients than healthy controls but it was not significant.[16]

This study also showed that the mean serum folic acid was significantly (p= 0.014) lower in progressive vitiligo patients than stable vitiligo patients. Again in this study serum folic acid level showed negative correlation with duration of disease and the relationship was statistically significant ($p = 0.029$).

Conclusion

After analyzing the results of the study, it may be concluded that nutritional deficiency of folic acid may lead to develop hyperhomocysteinemia. Increased level of serum homocysteine may be a precipitating factor in the pathogenesis of vitiligo & indirectly support the free radical mediated damage of melanocytes.

Limitations:

The limitations of this study are:

- Sample size was small & time duration was short. Sample was collected only from Dhaka city, which does not represent the whole country.
- Serum homocysteine and different markers of oxidative stress such as serum malondialdehyde, superoxide dismutase & for autoimmunity melanocyte specific T cell could not be measured due to financial constrains.

Recommendation

To make more conclusive result the following recommendations are proposed for further studies:

- Similar type of study can be done with large sample size.
- Sample can be collected from different parts of the country.
- Measurement of serum homocysteine, serum malondialdehyde & superoxide dismutase & detection of melanocyte specific T cell can be done with this study to evaluate the pathogenesis of vitiligo.
- Homocysteine lowering agents such as folic acid supplementation can be added in the vitiligo

treatment protocol. Moreover, the therapeutic role of supplementation with folic acid in vitiligo needs to be studied further.

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Original Article

Correlation of Follicle Stimulating Hormone, Anti-Müllerian Hormone And Antral Follicle Count Between Two Age Groups

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Abstract

Background: *Reduced ovarian reserve predicts poor ovarian response and poor success rates in infertile women who undergo assisted reproductive technology (ART). Ovarian reserve decreases with age but the rate of decline varies from one woman to another. Follicle stimulating hormone (FSH), anti-Müllerian hormone (AMH) and antral follicle count (AFC) represent the three most frequently utilized laboratory tests in determining ovarian reserve (OR).*

Objective: *To determine correlation between FSH, AMH and AFC in infertile female.*

Study design: *Observational (Cross sectional) study.*

Study setting and period: *This study was done in the Department of Reproductive Endocrinology and Infertility, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, between January 2019 to December 2019.*

Study population: *The study population consisted of all the diagnosed female infertility patients of reproductive age attending infertility OPD of the Department of Reproductive Endocrinology and Infertility at Bangabandhu Sheikh Mujib Medical University, during study period.*

Methods: I*n this prospective study 74 women were assessed. Subjects were divided into two age groups: ≤35 years group and >35 years group. FSH, and AFC were determined on 2nd /3rd day of their menstrual cycle and serum AMH on same day of cycle.*

Main outcome measure (s): *FSH and AFC (cycle $D_{2/3}$), random AMH*

Result: *Out of 74 infertile women, almost two third 47(63.5%) patients belonged to age group ≤35 years. The mean age was found 32.6±5.5 years. Serum FSH, AMH and AFC were significantly associated with different age group. A negative correlation was found between serum FSH and serum AMH in age group ≤35 years (r= -0.745; p=0.001) and > 35 years (r= -0.819; p=0.001) respectively. A negative correlation was found between serum FSH and total AFC in age group ≤35 years (r= -0.671; p=0.001) and >35 years (r= -0.733; p=0.001) respectively. A positive correlation was found between serum AMH and total AFC in age group ≤35 years (r= 0.778; p=0.001) and >35 years (r= 0.634; p=0.001) respectively. In multivariate logistic regression analysis serum AMH (<1.0 ng/ml) and total AFC (<5 number) were found to be significantly (p<0.05) associated with age group >35 years patients.*

Conclusion: *In both age group, FSH, AMH and AFC correlates but it is more pronounced in advanced age that means >35 years age group.*

Key words*: Infertility, Antimullerian Hormone, Antral Follicle Count, Follicle Stimulating Hormone, Ovarian Reserve.*

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Introduction

The term "ovarian reserve" has traditionally been used to describe a woman's reproductive potential, specifically the number and quality of oocytes she possesses.[1]

A woman is born with about 2 million primordial follicles, yet by the onset of menarche only about 400,000 follicles are left due to natural follicular atresia. As a woman reaches her mid-30s, the pace of oocyte depletion begins to increase and by the time she reaches her late 30s, the number of follicles declines to approximately 25,000, concomitant with a significant increase in miscarriage rate.[2]

Ovarian reserve is a complex clinical phenomenon influenced by age, genetics, and environmental variables.[2] The decline in a woman's ovarian reserve with time is irreversible and the rate at which women lose primordial follicles varies considerably, with wide variation regarding the onset of sterility and timing of the menopausal transition.[2]

Ovarian reserve tests started to emerge during the rise of ART in the late 1980s to predict both responsiveness to super ovulation drugs and the odds of pregnancy with treatment. They include both biochemical basal and provocative tests and ultrasound imaging of the ovaries. The first test to be introduced was day-3 follicle-stimulating hormone (FSH) (1988), followed by clomiphene citrate challenge test (CCCT) (1989), gonadotropin releasing-hormone (GnRH) agonist (1989), inhibin B (1997), antral follicular count (AFC) (1997), and antimüllerian hormone (AMH).[2]

Early follicular phase (basal) FSH as a marker of ovarian reserve was proposed almost 30 years ago, as a tool to predict ovarian response to in vitro fertilization (IVF).[3] This test is an indirect assessment of ovarian reserve and is based on the feedback inhibition of FSH pituitary secretion by ovarian factors.

Women with normal ovarian reserve have sufficient production of ovarian hormones at this early stage of the menstrual cycle to maintain FSH levels within normal range.[2]

However, basal FSH testing has several major limitations including significant intercycle and intracycle variability that limits its reliability.[4] it requires a functional hypothalamus-pituitary-ovarian axis, and it is not adequately sensitive for clinical utility–only elevations carrying significance.[5]

A single abnormal FSH value in a woman <40 years of age may not predict a poor response to stimulation or failure to achieve pregnancy and should prompt repeat testing.[6]

The ovary begins producing AMH in utero at about 36 weeks of gestation.[7] Its levels rise in young women beginning in adolescence and peak at about 25 years of age, then gradually decline until reaching undetectable levels a few years prior to menopause.

Since AMH is expressed during normal early folliculogenesis (secreted by early follicles up to 6 mm), it is relatively independent of gonadotropins circulating at physiologic levels and allows for testing anytime throughout the cycle.[2]

AFC is the sum of follicles in both ovaries as observed on ultrasound in the early follicular phase (day 2-4) of the menstrual cycle. Antral follicles are defined as those measuring 2-10 mm in largest mean diameter on 2-dimensional plane. AFC is easy to carry out, provides an immediate result, and has good intercycle reliability and good interobserver reliability when measured in experienced centers using a minimal number of sonographers. Its precision is compromised with overweight and obese individuals or when using multiple sonographers.[8]

Materials and methods

It was an observational (Cross sectional) study. This study was done in the Department of Reproductive Endocrinology and Infertility, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, between January 2019 to December 2019. The study population consisted of all the diagnosed female infertility patients of reproductive age. The women attending the study center during study period having primary or secondary infertility was considered as study population. They were divided in 2 groups ≤35 years and >35 years. Data was collected using a structured questionnaire following physical & lab examination. For D_2 FSH level fasting blood was collected on D2/3 of menstrual cycle, serum FSH level was measured by ADVIA Centraur$^{(R)}$ XP immunoassay system. For S. AMH level

blood sample was collected on any day of cycle and measured by BECKMAN COULTER machine using Chemiluminescent Immunoassay method. For AFC count TVS was done on D_{2-5} of cycle using KONTRON medical USG machine. Statistical analysis was carried out by using the Statistical Package for Social Sciences version 16.0 for Windows (SPSS Inc., Chicago, Illinois, USA). The mean values were calculated by frequencies and percentages. The quantitative observations were indicated by frequencies and percentages. Chi square test was used for categorical variables. Unpaired t-test was used for continuous variables. Pearson's correlation coefficient was used to test the relationship between the groups. Multivariate logistic regression analysis was used for risk factors of infertile women. P values <0.05 was considered as statistically significant.

Results

This is a observational (Cross sectional) study was carried out in the infertility outdoor, department of Reproductive Endocrinology and Infertility, Bangabandhu Sheikh Mujib Medical University, Dhaka, between January 2019 to December 2019. A total of 74 infertile women's were included in this study with maintaining inclusion & exclusion criteria. They were divided in 2 age groups ≤35 years and >35 years.

Table I: Distribution of the study patients by age (n=74)

Age (years)	Number of patients	Percentage
≤35	47	63.5
>35	27	36.5
Mean±SD	32.6±5.5	
Range (min -max)	22.0 - 40.0	

Table II: Distribution of the study patients according to serum FSH (n=74)

Serum FSH (IU/L)	Age ≤35 years (n=47)		Age >35 years (n=27)		P value
	N	%	n	%	
≤10.0 (Normal)	37	78.7	12	44.4	
>10.0 (Abnormal)	10	21.3	15	55.6	
Mean±SD	7.9±4.7		10.2±3.1		0.026 S
Range (min -max)	3.02 - 27.0		5.0 -16.0		

s= significant

P value reached from unpaired t-test

Table III: Distribution of the study patients according to serum AMH (n=74)

Serum AMH (ng/ml)	Age ≤35 years (n=47)		Age >35 years (n=27)		P value
	N	%	n	%	
<1.0 (Low)	6	12.8	13	48.1	
1.0 -3.5 (Normal)	41	87.2	14	51.9	
Mean±SD	2.24± 0.98		1.37±1.06		0.001 S
Range (min -max)	0.18 - 3.50		0.02 - 3.48		

s= significant
P value reached from unpaired t-test

Table IV: Distribution of the study patients according to total AFC (n=74)

Total AFC (Number)	Age ≤35 years (n=47)		Age >35 years (n=27)		P value
	N	%	n	%	
<5 (Low)	2	4.3	6	22.2	
5-15 (Normal)	42	89.4	20	74.1	
>15 (High)	3	6.4	1	3.7	
Mean±SD	12.0±3.4		8.5±3.3		0.001 s
Range (min -max)	4.0 - 18.0		4.0 - 16.0		

s= significant

P value reached from unpaired t-test

Table V: Multi variable logistic regression analysis for age >35 years

Risk factors	Regression coefficient (β)	Odds Ratio (OR)	95% CI for OR	P value
Serum FSH (>10.0 IU/L)	0.934	2.544	0.901 -7.182	0.078 ns
Serum AMH (<1.0 ng/ml)	1.531	4.626	1.649 -12.976	0.004 s
Total AFC (<5 number)	2.242	9.412	2.543 -34.838	0.001 s

s= significant, ns= not significant

P-value reached from multivariate analysis by binary logistic regression analysis

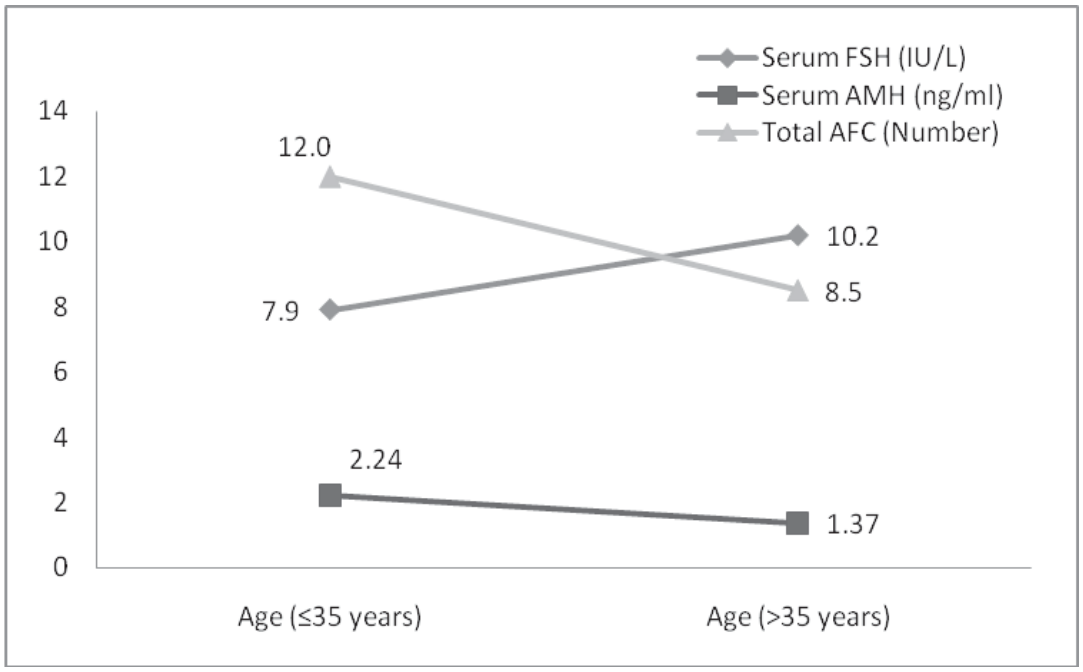

Figure 1: Line diagram showing mean serum FSH, serum AMH and total AFC in different age years.

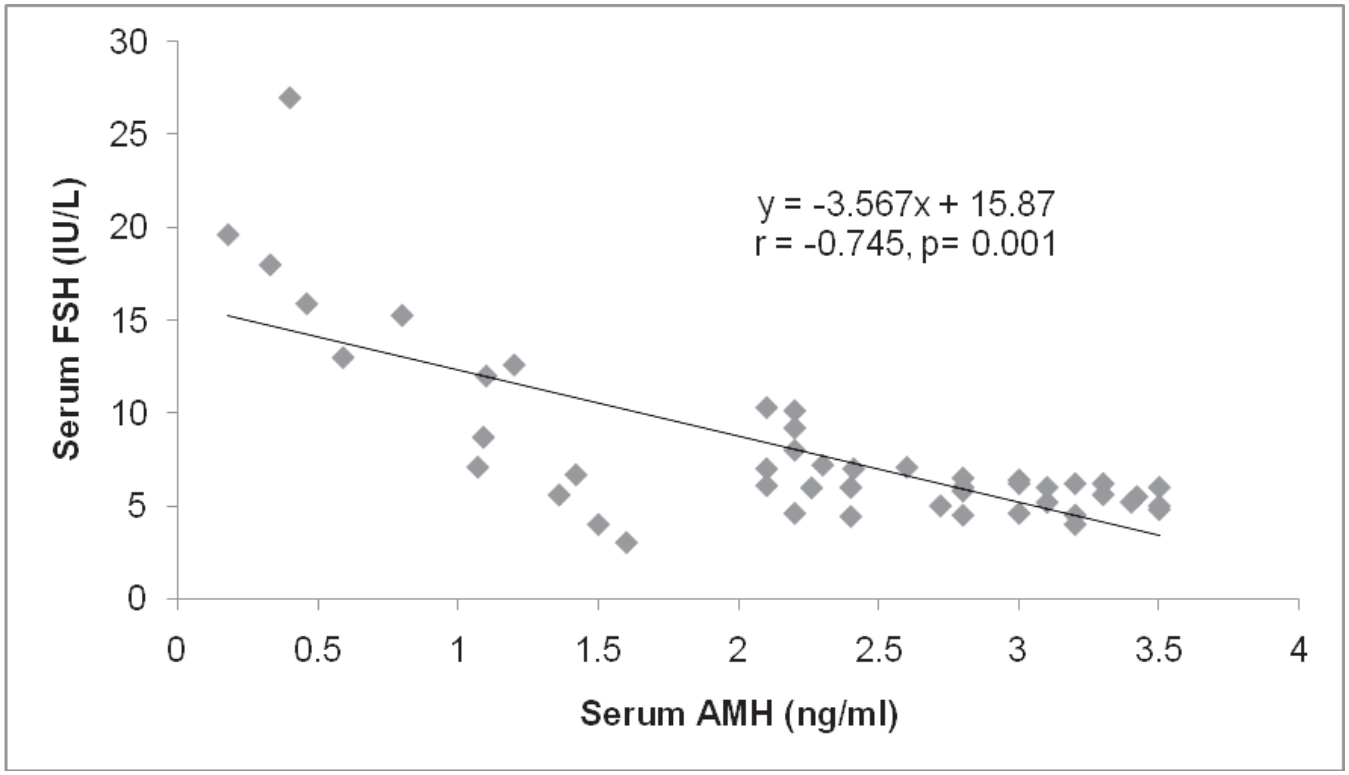

Figure 2: The scatter diagram showing negative correlation (r= -0.745; p=0.001) between serum FSH and serum AMH in age group ≤35 years.

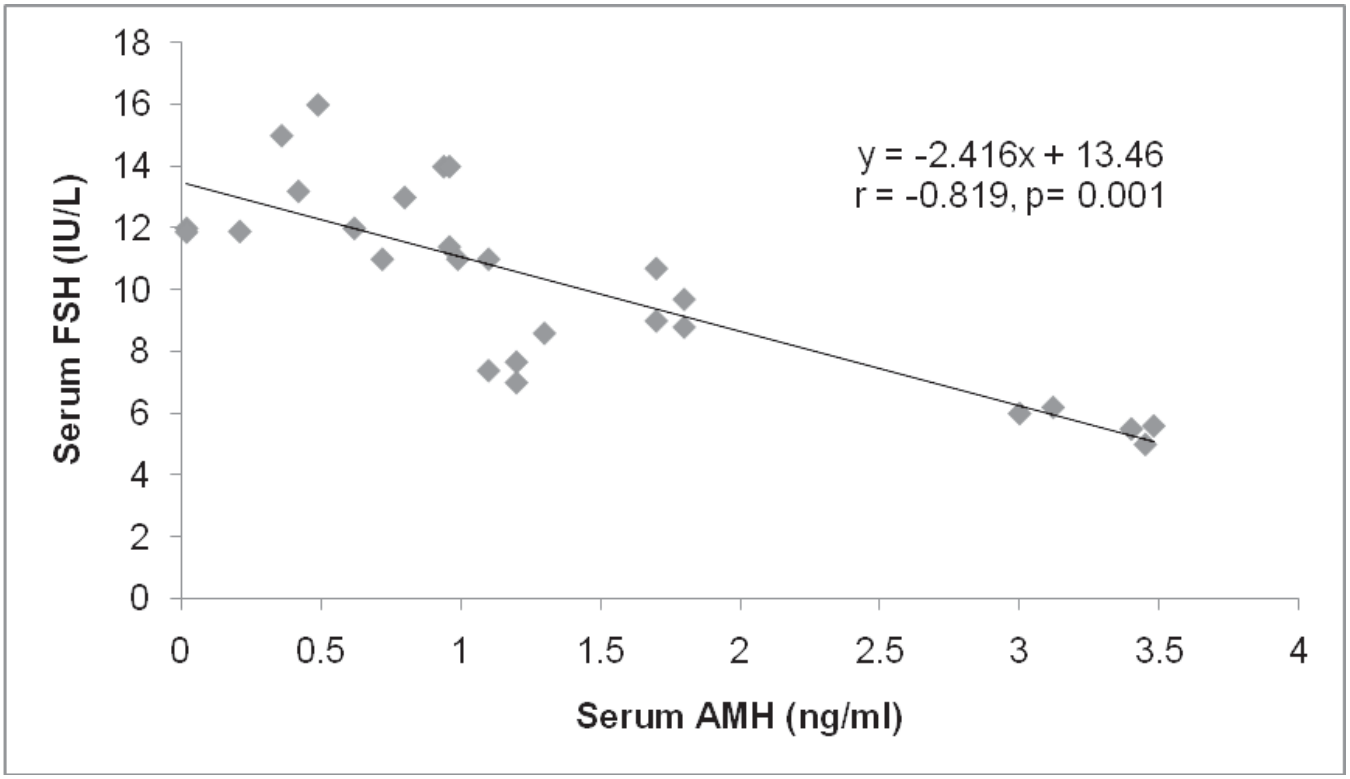

Figure 3: The scatter diagram showing negative correlation (r= -0.819; p=0.001) between serum FSH and serum AMH in age group >35 years.

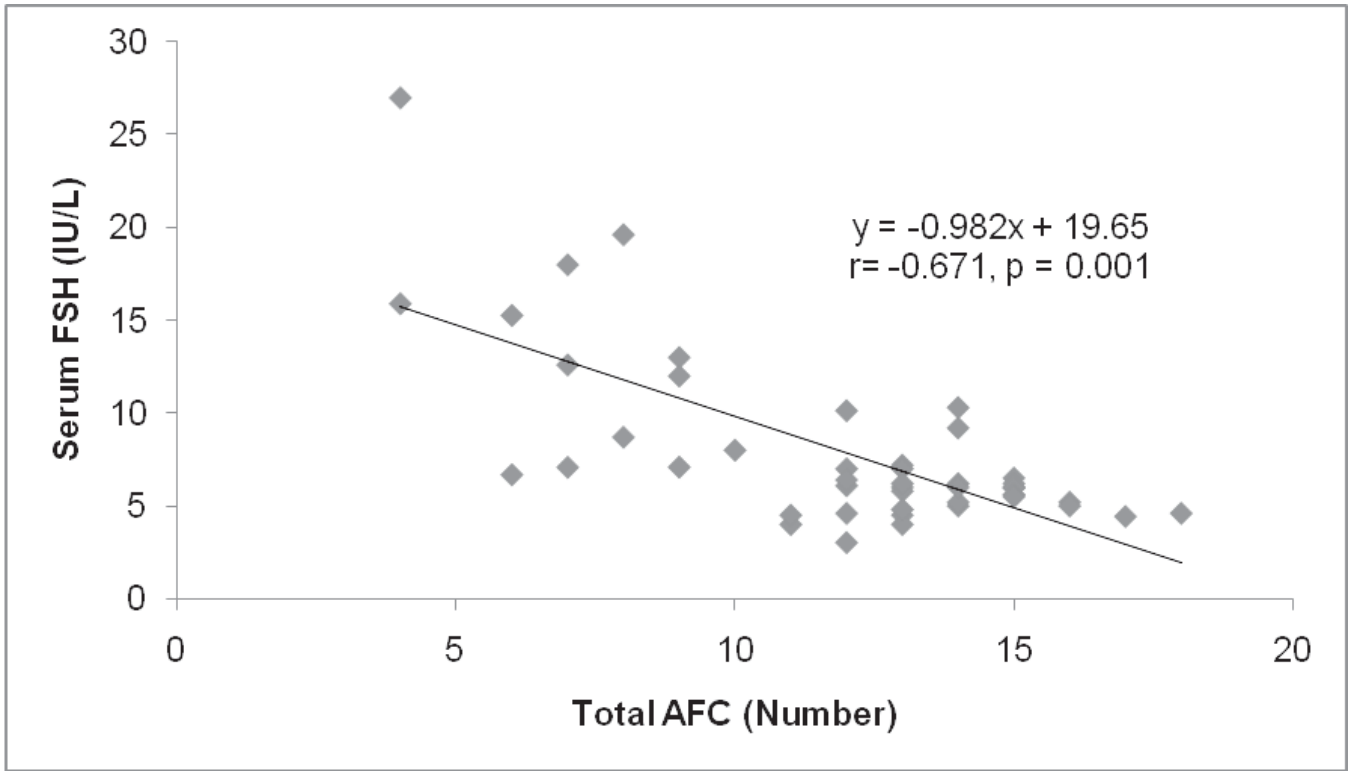

Figure 4: The scatter diagram showing negative correlation (r= -0.671; p=0.001) between serum FSH and total AFC in age group ≤35 years.

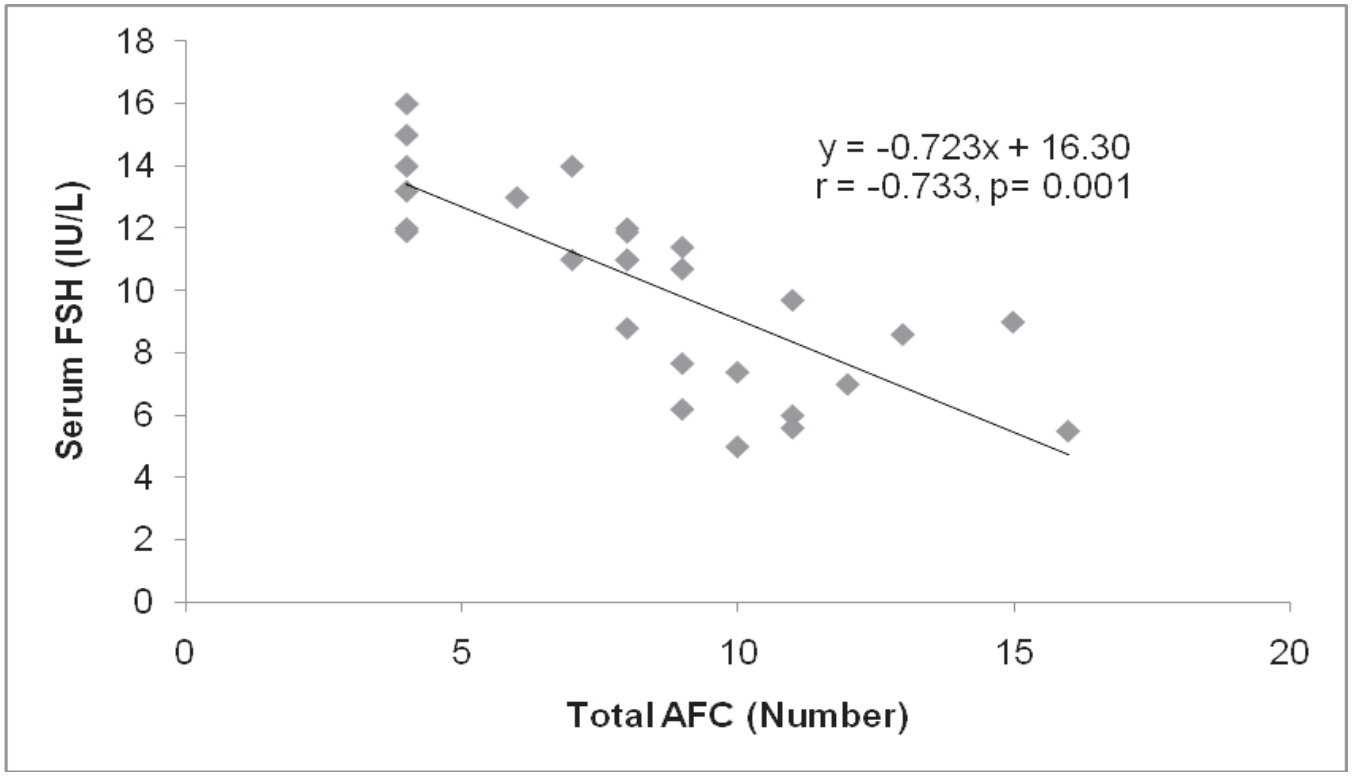

Figure 5: The scatter diagram showing negative correlation (r= -0.733; p=0.001) between serum FSH and total AFC in age group >35 years.

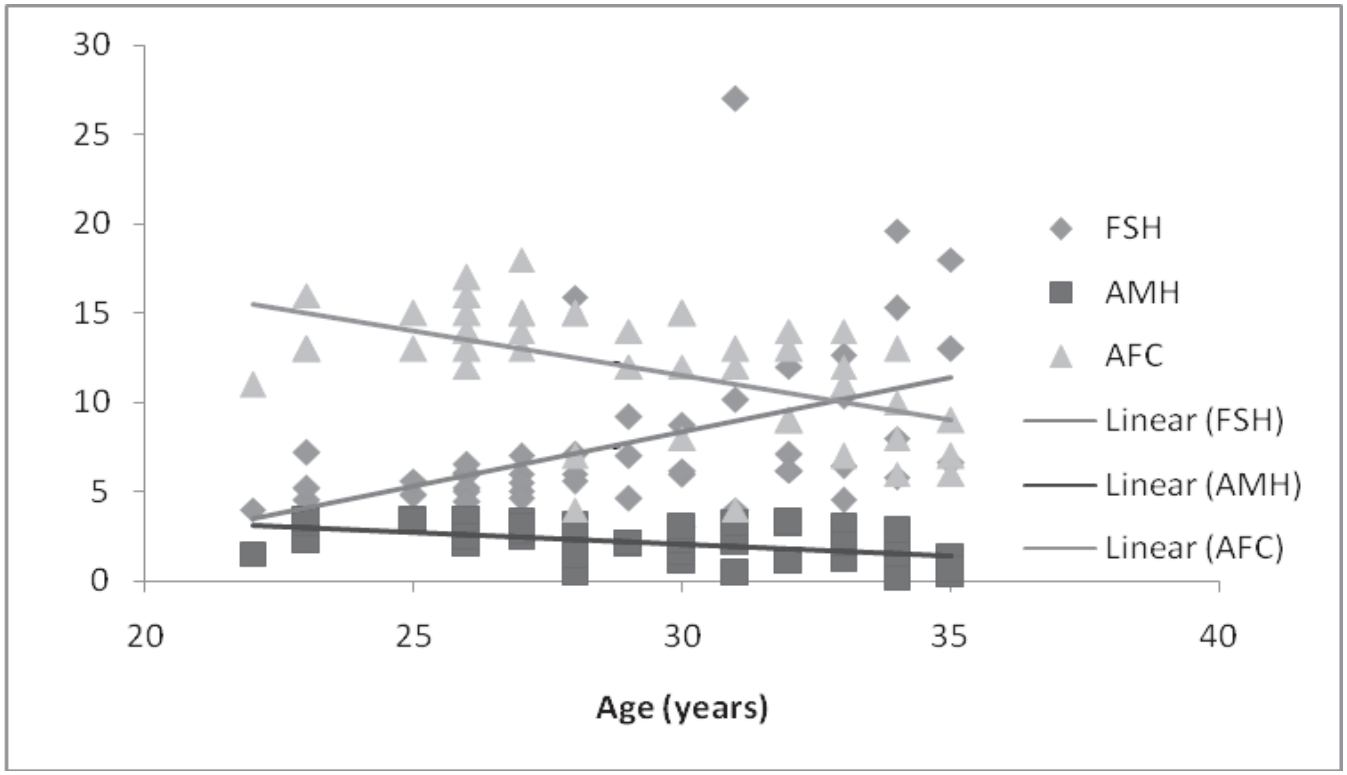

Figure 6: The scatter diagram showing correlation between serum FSH, serum AMH and total AFC with age group ≤35 years.

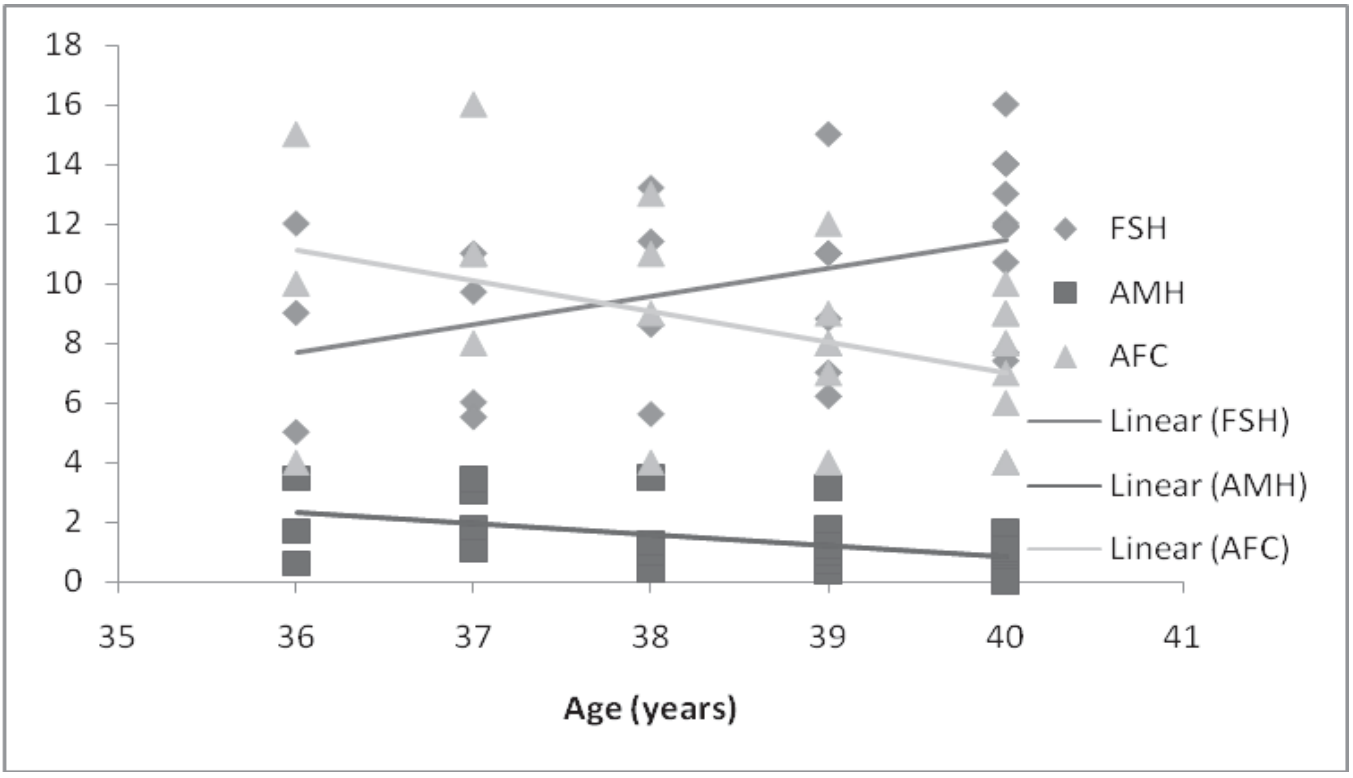

Figure 7: The scatter diagram showing correlation between serum FSH, serum AMH and total AFC with age group >35 years.

Discussion

This observational (Cross sectional) study was carried out at Reproductive Endocrinology and Infertility department of Bangabandhu Sheikh Mujib Medical University, Dhaka, between January 2019 to December 2019. Patients were selected according to exclusion and inclusion criteria. Patients were divided in two age groups ≤35 years and >35 years. For D_2 serum FSH blood was collected on 2nd day of menstrual cycle. TVS was done on 2nd-5th day of cycle for AFC. Serum AMH was done on any day of cycle. Then all the data were assessed and compared with age.

In present study , in age group ≤35 years, 37(78.7%) patients had serum FSH level ≤10.0 IU/L and >35 years age group 12(44.4%) patients had serum FSH level ≤ 10.0 IU/L. The mean serum FSH was found 7.9±4.7 IU/L in age group ≤35 years and 10.2±3.1 IU/L in age group >35 years. The mean difference was statistically significant (p<0.05) between two groups. Barbakadze et al.[9] found significant association between serum FSH with different age group.

They divided their subject into 3 age groups; <35 years, 35-40 years and 41-46 years. In their study serum FSH level showed a significantly higher result only in age group 41-46 years compared to age group <35 years.

Ozcan et al.[10] revealed that the AMH concentration declined significantly with increasing age. This decline began at the age of 30, and it became dramatically evident from the age of 35.

In the largest study analyzing age-specific medians for serum AMH by Seifer et al.[11] reported that both median and mean AMH values were inversely associated with age. The average yearly decrease in the median serum AMH value was 0.2 ng/ml/year upto age 35 then diminished to 0.1 ng/mL/year after the age of 35. The most striking study on means of AMH in general population is the study of Tremellen and Kolo.[12]

Barbakadze et al.[9] found significant negative correlation of serum AMH with advancing age group. This difference might be caused by several factors, including different populations with different genetic and environmental backgrounds, which could lead to a different ovarian biological age compared to chronological age.

The mechanism of follicle loss has not yet been well described. Many genetic and environmental factors that influence follicle loss have also not yet been identified. Barbakadze et al.[9] concluded that AMH was a more reliable biomarker of ovarian reserve compared to FSH and in addition the combination of AMH and AFC was superior with advancing age. Barbakadze et al.[9] also found significant association between serum AFC with different age group. In this current study in age group ≤ 35 years 42(89.4%) patients had normal (5-15 number) AFC and in age group ≤35 years and 20(74.1%) patients had normal (5-15 number) AFC. The mean total AFC was 12.0±3.4 number in age group ≤35 years and 8.5±3.3 number in age group >35 years. The mean difference was statistically significant (p<0.05) between two groups.

Barbakadze et al.[9] consisted that AMH showed a negative correlation with FSH (rs=-0.48, p<0.0001). Gada et al.[13] found that there was a negative correlation between AMH and FSH (R= -0.41). Okunola et al.[14] showed in their study the Pearson's coefficient for the correlation between FSH and AMH after controlling for age was -0.311 (P=0.012). Scheffer et al.[15] documented that AMH was significantly correlated with FSH (r=-0.32, *p*<.01).

In present study it was evident that there is a discordance between AMH and FSH, 40% patients ≤ 35 years age group had FSH level >10IU/L but AMH level >1 ng/ml. In >35 years of age group this discordance between FSH and AMH was 13.3%. Leader et al.[16] showed in a large study of 5354 women that discordance between FSH and AMH was 20% in age group ≤ 35 years.

Gleicher et al.[17] reported that women with normal AMH and FSH produced high number of oocytes, whereas women with normal FSH but decreasing AMH produced a significantly lower number of oocytes. This also indicates that serum AMH levels are more

important predictors of ovarian aging than FSH levels. This is similar with previous studies by Barad et al.[18] that shows that AMH levels are better predictors of response to ovarian stimulation and clinical pregnancy than baseline FSH.

The relatively lower slopes of increasing FSH in older age have made FSH a late predictor of ovarian reserves.[19]

In this study it was observed that moderately significant negative correlation (r= -0.671; p=0.001) between serum FSH and total AFC in age group ≤35 years and strong negative correlation (r= -0.733; p=0.001) between serum FSH and total AFC in age group >35 years. Similar study reported by Barbakadze et al.[9] where they found there was a moderate significant negative correlation between FSH and (r=-0.41, p<0.0001) <35 years age group.

In my study it was documented that strong positive correlation (r=0.778; p=0.001) between serum AMH and total AFC in age group ≤35 years. Moderate positive correlation (r= 0.634; p=0.001) between serum AMH and total AFC in age group >35 years. Similar study conducted by Barbakadze et al.[9] where they found AMH showed a strong positive correlation with AFC (r=0.71, p<0.0001) in lower age group. A different study assessing discordance between AMH and AFC in patients undergoing IVF found that 32.3%.[20]

Scheffer et al.[15] reported that AMH was significantly correlated with AFC (r=0.81, *p*<.00001). Gada et al. (2010) showed that there was a strong correlation between AMH and AFC (correlation coefficient; R= 0.72). Another study documented by Alebic et al.[21] where they found AMH was strongly correlated to AFC in the entire study population (regression equation: AMH = −4.4 + 1.5 × AFC; r = 0.732, P < 0.001).

Barbakadze et al.[9] reported that according to regression analysis, age only explained the variation of AMH in 22%, the variation of FSH in 14% and the variation of AFC in 27% of changes. Tehraninezhad et al. (2016) showed that among AFC and age, AFC was the independent predictor (beta=0.6, p=0.001). Among FSH and age, age was the only independent predicting variable (beta=-0.4, p=0.001). In this study it was found that in multivariate logistic regression analysis, patients having serum AMH (<1.0 ng/ml) was 4.626 (95% CI 1.649 to 12.976) times in age group >35 years. Patients having total AFC (<5 number) was 9.412 (95% CI 2.543 to 34.838) times in age group >35 years. Serum AMH and total AFC were found to be significantly (p<0.05) associated with age group >35 years patients.

Conclusion

In both age group, FSH, AMH and AFC correlates but it is more pronounced in advanced age that means >35 years age group.

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Original Article

Assessment of the Glycemic and Thyroid Status of Patients with Premenstrual Syndrome

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Abstract

Objectives: *In this study, our main aim is to evaluate the glycemic and thyroid status of PMS patients.*

Methods: *This cross-sectional observational study was done in the Department of Physiology, Chittagong Medical College, from January 2017 to December 2017. A total of 100 subjects between 18-22 years were selected by purposive sampling according to inclusion and exclusion criteria from the 1st year female medical students. They were divided into anaemic (Group A) and non anaemic (Group B) based on hemoglobin concentration.*

Result: *During the study, most of them belong to poor economic conditions.In group-A mean concentration of glucose was 70±12 whereas in group-B it was 72±11. Mean (±SD) TSH of the subjects was 0.95 ± 0.52 mIU/L and 0.93 ± 0.38 mIU/L in group A and group B respectively. No statistically significant differences were observed.*

Conclusion: *From our study, we can say that the lower level of blood glucose and insulin opposition in the PMS group during the follicular and luteal periods of the monthly cycle contrasted with those of healthy women. The lower blood glucose and thyroid brokenness in the PMS bunch contrasted with controls was perceptible. In like manner, as per the information from this investigation, hypoglycemia is an invigorating element of PMS manifestations.*

Keywords: *Glycemic, Anaemia, Premenstrual syndrome, Hemoglobin.*

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Introduction

Premenstrual syndrome (PMS) is a common clinical and psychological problem in adolescent girls. It reduces the quality of life of a girl. The severity varies in different subjects. Medical students have an increased risk of developing different symptoms for their stressful lifestyles. PMS involves several emotional and physical symptoms that arise between several days and weeks before menstrual flow starts. While many women experience some premenstrual discomfort, these premenstrual changes are not considered serious by most women and do not disrupt the life of a woman. In the week preceding menstruation, PMS is characterized by debilitating mood and behavioral changes that interfere with normal functioning.

There is a different etiology of PMS. Postpartum psychosis, lactational failure of mothers and emotional impairment, cognitive skill, language impairment of children are some complications of PMS. Anaemia is a common problem in adolescent girls in our country. [1,2,3]

The most common physical symptoms are headache, insomnia, breast tenderness, joint pain, abdominal bloating, and pelvic pain[1,4]. Common emotional symptoms are irritability, anxiety, depression, mood swing, confusion, and poor concentration.[5,6,7]

These symptoms start usually from the teen years and worsen with aging[9,10]. PMS can complicate the process of puberty. Social and educational performance is also affected. It results in poor self-esteem and dissatisfactionwhich affects the daily life of the patients.

Objective

General objective

To evaluate the glycemic and thyroid status of PMS patients.

Specific objective

- To detect the thyroid status of the study group
- To identify the socioeconomic factors of the study group.

Methodology

Type of study	Cross-sectional observational study
Place of study	Department of Physiology, Chittagong Medical College, Chittagong
Study period	January 2017 to December 2017
Study population	A total of 100 were chosen deliberately on the basis of symptoms mimicking PMS during the period from 8.00 a.m. to 2.30 p.m. every day during class hours for at least three consecutive months.
Sampling technique	Purposive

Method

During the study, the total sample size was 100. Subjects were divided into two groups: Group A and GroupB. Group A (Anaemic group), included 50 subjects having PMS symptoms with anaemia and Group B (Non anaemic group), included 50 subjects having PMS symptoms without anaemia. 1st year female medical students of Chittagong Medical College, Chittagong were included in this study. The study was done in the class periods with the consent of the Head of the Department. After completion of the daily topic, female students were separated in the same class, and study procedures were carried out.

Data analysis

Data analysis was done using SPSS software (Statistical Package for Social Sciences) for windows version 22. Pearson's correlation was done to see the relationship between anaemia and PMS, BMI, and PMS. Variables were expressed as range and mean ± SD. p-value < 0.05 was taken significant.

Result

Table-1 shows the demographic characteristics of the patients. Here no statistically significant differences of age were observed between the two groups. The mean (±SD) weight of the subjects was 50 ± 10.4 Kg and 55 ± 10.3 Kg in group A and group B respectively. The following table is given below in detail:

Table-1: Demographic characteristics of the patients

Variable	Group A(n=50)	Group B(n=50)
Age (years)	20 ± 0.5 (18 - 21)	20.1 ± 0.9 (18 - 21)
Height (cm)	63 ± 2.0 (55 - 67)	60 ± 1.9 (55 - 67)
Weight (kg)	50 ± 10.4 (32 - 92)	55 ± 10.3 (32 - 92)
BMI (kg/m^2)	22 ± 4.1 (15.6 -28.8)	20 ± 3.9 (15.6 -28.8)
Systolic BP (mm of Hg)	109.49 ± 7.0 (100 - 120)	110.82 ± 5.7 (100 - 120)
Diastolic BP (mm of Hg)	76.85 ± 4.9 (70 -80)	74.57 ± 3.5 (70 -80)
Pulse (beats/min)	78 ± 4.1 (70 - 88)	74 ± 3.4 (70 - 88)

Figure-1 shows the distribution of the patients according to socioeconomic factors where most of them belong to poor economic conditions. The following table is given below in detail:

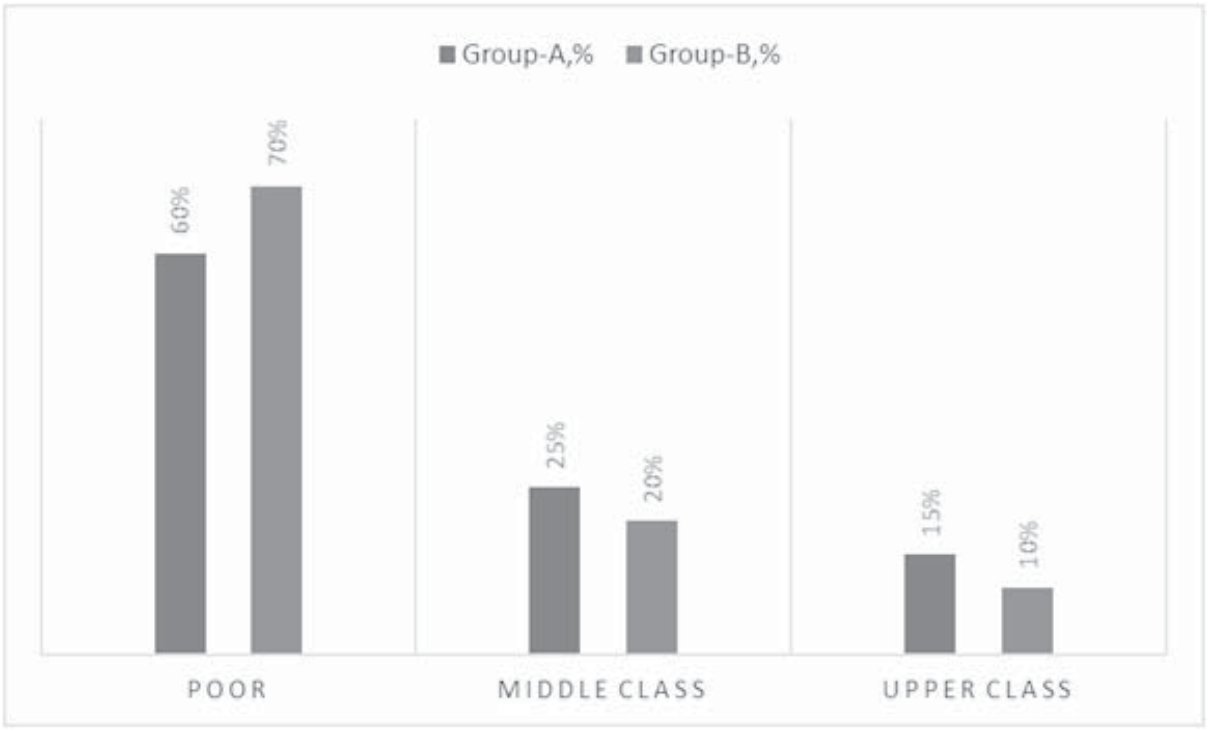

Figure-1: Distribution of the patients according to socioeconomic factors

Figure-2 shows TSH levels of the study subjects where Mean (±SD) TSH of the subjects were 0.95 ± 0.52 mIU/L and 0.93 ± 0.38 mIU/L in group A and group B respectively. No statistically significant differences were observed. The following figure is given below in detail:

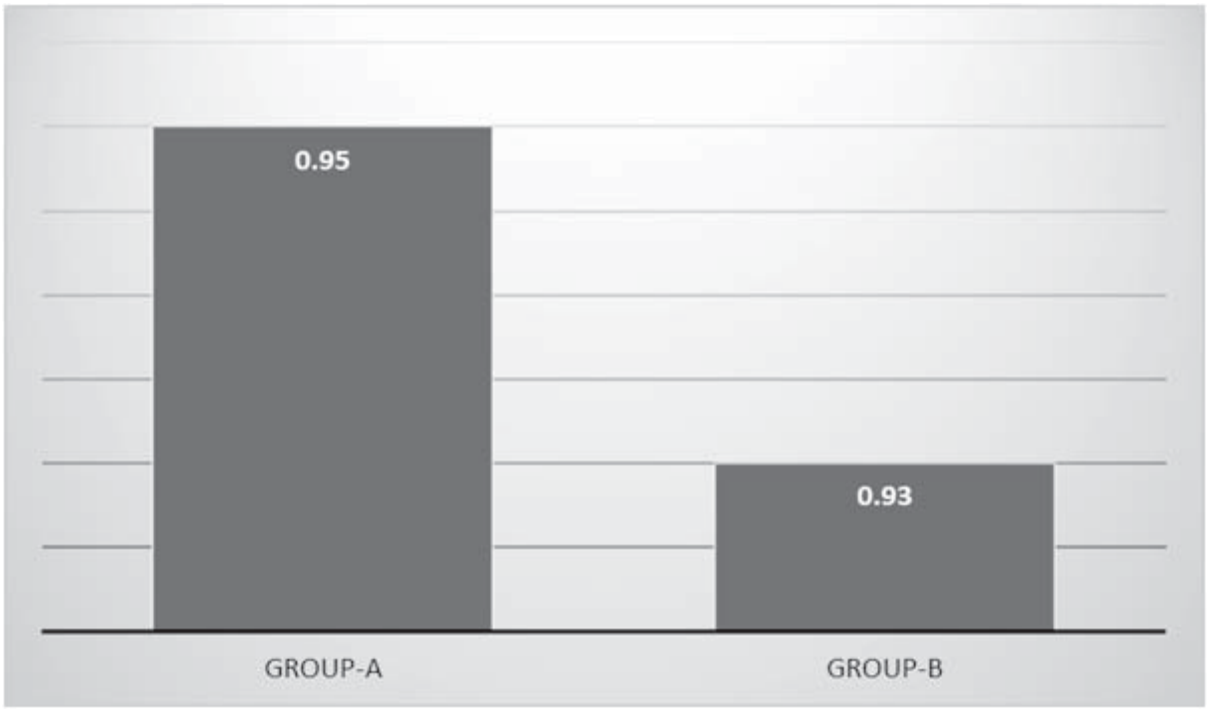

Figure-2: TSH levels of the study subjects.

Table-2 shows the mean concentrations of insulin, glucosein the two phases of the menstrual cycle of both study groups. In group-A mean concentration of glucose was 70±12 whereas in group-B it was 72±11. The following table is given below in detail:

Table-2: The mean concentrations of insulin, glucose in the two phases of the menstrual cycle

Variable	Follicular Phase		Luteal Phase	
	Group -A	Group -B	Group -A	Group -B
Glucose (mg/dl)	70±12	72±11	71±13	93±13
Insulin(ul/ml)	9±2.01	9±1.01	10±2.01	11±3.00

Figure-3 shows the thyroid status of the study group wherein group-A, 21% had altered thyroid status, whereas in group-B it was 6%. The following figure is given below in detail:

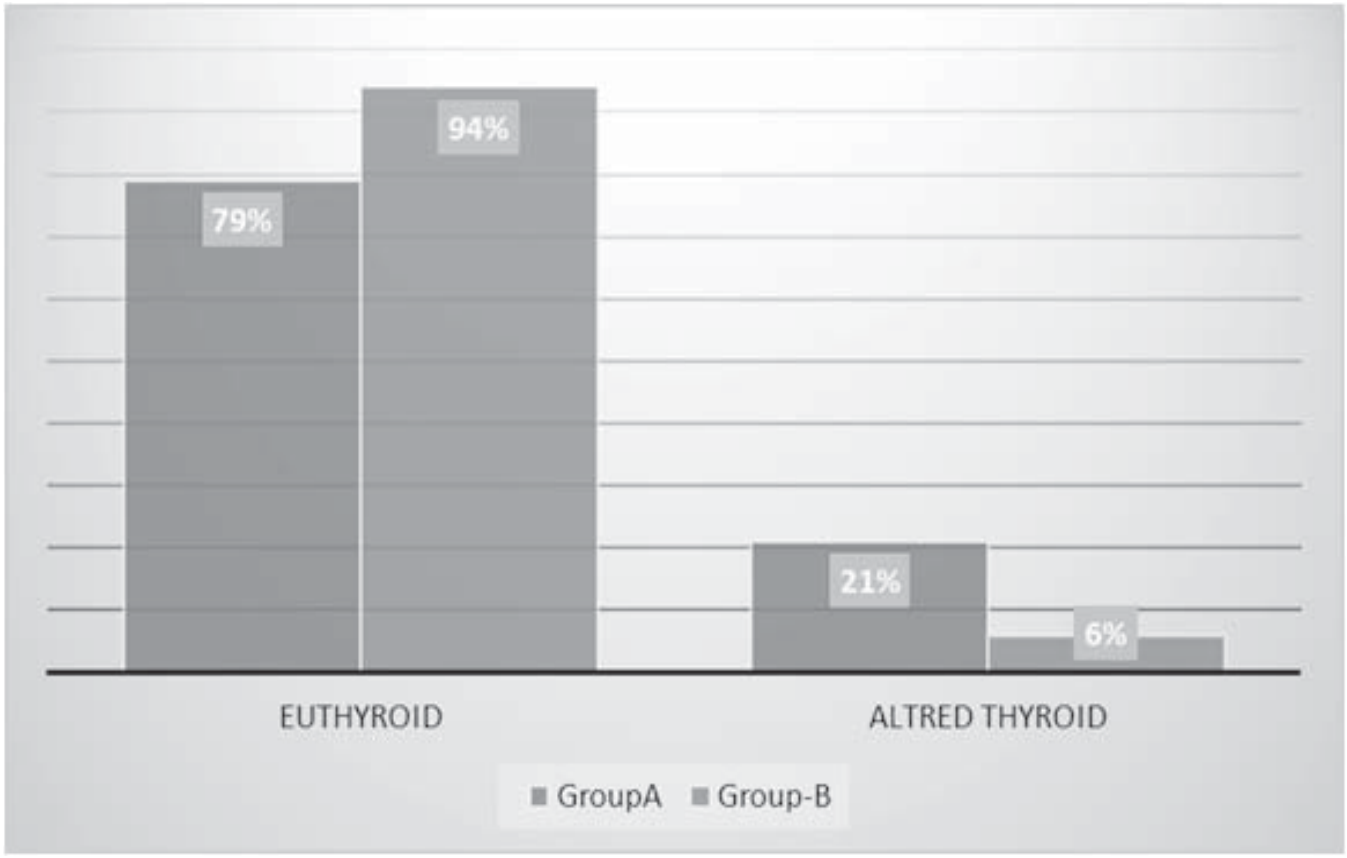

Figure-3: Thyroid status of the study groups.

Discussion

PMS epidemiological studies have not demonstrated a correlation between PMS and age, socioeconomic status, parity, diet, exercise, stress, characteristics of the menstrual cycle, or personality.[8] Overall, certain premenstrual symptoms are registered by approximately 75% of the general population. In most recent studies, in which strict, basic diagnostic guidelines for PMS are used, 3% to 8% of cycling women may be diagnosed with PMS. Approximately 40% to 50% of those seeking medical care meet PMS criteria.[9]If the diagnosis conditions include the complete absence of postmenstrual symptoms alone, 10% to 20% of women seeking medical care follow the PMS criterion.

Many women have signs of menstruation, but very few have extreme PMS. PMS is a well-defined premenstrual cluster of mainly affective symptoms that disturb the daily functioning of a woman.

PMS is diagnosed with prospective symptom mapping and should be distinguished from menstrual symptoms that are non-disruptive, major affective disorders, and other common medical and gynecological conditions.

In this study, relative to controls, the decreased level of blood glucose and insulin resistance in the PMS community during the luteal and follicular phases may worsen symptoms of PMS. Despite the fact that our discoveries exhibited the fundamentally expanded degree of blood glucose and insulin opposition in the controls during the luteal stage contrasted with the follicular stage, announced information from the PMS bunch demonstrated no huge contrasts between those factors during the luteal and follicular stages.

In our investigation, the blood glucose levels and insulin obstruction were altogether lower during the luteal and follicular stages in the PMS bunch contrasted with those of the controls. Diminished blood glucose levels on the thirteenth day of menses were the most reduced among the times of the feminine time frame tried. In like manner, during the luteal and follicular stages, no huge contrasts in the insulin focus between the two study bunches were watched. Albeit undocumented proof demonstrates that the signs and side effects of PMS happen a couple of days before the beginning of monthly cycle, this investigation found that the unsettling influences of glucose homeostasis started from the follicular stage and proceeded into the luteal stage. It is realized that nutrient D invigorates insulin emission through its immediate activity on the pancreatic beta cells and its backhanded activity by extracellularly normalizing calcium levels. [5,6,7] Also, one study detailed that the constructive outcomes of progesterone on the insulin focus have been seen in the two people and monkeys after glucose organization. [10] Based on such proof, it has been recommended that patients with PMS experience insulin decrease prompting a diminished degree of progesterone and nutrient D. [11]

As indicated by the information of one study, the specific explanations behind the absence of huge contrasts in insulin fixation saw between the PMS bunches are not completely clear; enlistment strategies and contrasts in ecological foundation as well as other obscure related variables might have assumed a job. It is likewise conceivable that the unidentified factors that add to changes in insulin discharge during the period might be static that is, either continually discouraged or continually raised in patients with PMS. Then again, at whatever point the grouping of blood glucose is low, insulin emission is reduced.[12]

Conclusion

From our study, we can conclude that the lower level of blood glucose and insulin resistance in the PMS group during the follicular and luteal phases of the menstrual cycle compared to those of healthy women. The lower blood glucose and thyroid dysfunction in the PMS group compared to controls was noticeable. Likewise, according to the data from this study, hypoglycemia is a stimulating factor of PMS symptoms.

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Original Article

Outcome of Fixation of Stable Osteoporotic Pertrochanteric Fracture by Dynamic Hip Screw in Elderly Patients

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Abstract

***Objective**: To evaluate radiographic and functional outcomes of dynamic hip screw (DHS) fixation for treatment of stable osteoporotic pertrochanteric fracture in elderly patients.*

***Material and methods:** In this prospective study, a total 30 cases were studied from January 2019 to Decemebr 2019 through non randomized purposive sampling. All the patients were between 50 to 84 years of age and operated within 5 days of fracture by close reduction and internal fixation by dynamic hip screw with four hole slide plate under C-arm guidance. Postoperative functional outcome was assessed clinically by Harris hip score and radiologically by seeing the radiological evidence of union. Postoperative follow up was conducted at 3th, 6th and 12th months.*

***Results:** The mean age was 65.8±6.9 years with female dominancy (83.3%). Fall in slippery ground was the most common cause of injury (86.7%). Most of the patients were grade 3 osteoporosis according to Singh's index. Postoperatively, 66% patients had good to excellent functional outcome with mean Haris hip score of 81±6.610. Mean union time was 3.7±1.04 with range from 3 to 5 months. Complications were cut out of screw in one case and varus collapse of the fracture in two cases.*

***Conclusion:** Our results indicate that dynamic hip screw yields good outcomes in fixation of stable osteoporotic pertrochanteric fracture.*

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Introduction

Pertrochanteric fractures are common problems in elderly patients. Operative stabilization permits early mobilization and minimizes complications of prolonged recumbency[1]. Stable pertrochanteric fractures are preferably fixed by sliding hips crews[2, 3, 4]. In general, for the treatment of unstable pertrochanteric fractures, two options exist: extramedullary or intramedullary stabilization. Each device has its advantages and disadvantages. The advantage of extramedullary fixation, such as dynamic hip screw (DHS), is the relatively simple, safe and forgiving surgical technique[5]. The DHS remains the implant of choice because of its favourable results and low rates of non-union or hard ware failure [2,3,4] but the complication rates of the DHS are higher in unstable pertrochanteric fractures; despite the wide spread use of the DHS, cut-out rates of 5–17% have been reported in the literature[3,6,7,8] . The most common mode of failure of a DHS is cut-out of the lag screw from the femoral head [9, 10] followed by lift-off of the plate from the femur [3,4,11.] Wolfgang et al.[12] reported a 19% mechanical and technical complication rate with unstable pertrochanteric fractures treated with sliding hip[4] osteosynthesis of the fracture. So this study was conducted to see outcome of the fixation of osteoporotic stable pertrochanteric by DHS in elderly persons.

Materials and Method

Between January 2019 and Decemebr 2019, thirty patients with stable pertrochanteric fracture with osteoporosis came to Jahurul islam Medical College Hospital were included in the prospective study. Purposive sampling done according to availability of the patient and strictly considering the inclusion and exclusion criteria.

Inclusion criteria were:

1) Age over 50 years

2) Stable pertrochnateric fracture according to AO classification AO31A1.1, AO31A1.2 [13]

3) Osteoporotic bone Singh's index ≤3[14].

Exclusion criteria were:

1) Unstable pertrochanteric fracture, AO31A2.2 to Ao31A3[13].

2) Patient with uncontrolled medical co-morbidity like uncontrolled DM, MI, electrolyte imbalance. Demographic variable are age, sex, occupation. Clinical Variables are type of osteoporosis, fracture type, duration between injury and surgery, associated injury. Outcome variable are functional outcome which will be measured by Harris hip score[15] radiological outcome by union of the fracture. Union was defined as bridging of three of the four cortices and disappearance of fracture line on the plain radiographs for a patient who was able to bear full weight. Non-union was defined as a fracture that did not heal within six months. All patients were preoperatively assessed, treated by dynamic hip screw with 04 holes side plate fixation. Each patient was followed up at 3rd, 6th, 12th month. Analysis was done by SPSS 20.0 for windows software.

Results

In this study the highest number of patients 15(50%) were observed in the 6th and lowest number of patient 1(3.3%) was observed in 8th decades. The mean age was 65.8±6.9 years old with range from 50 to 80 years. Table-I shows distribution of patients by age.

Table I: Distribution of cases according to age (N=30)

Age (in years)	Fre quency	Percent
50-59	5	16.7
60-69	15	50.0
70-79	9	30.0
80-89	1	3.3
Total	30	100.0

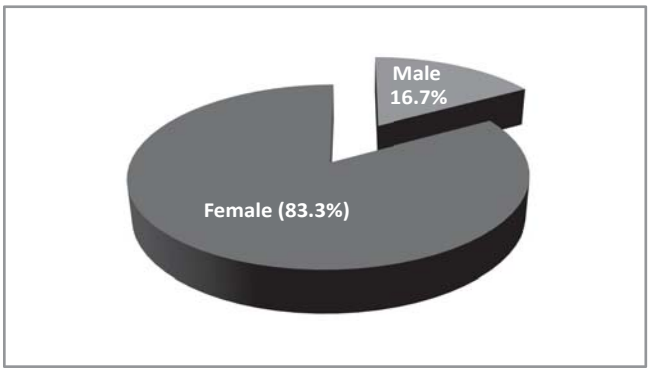

Figure 1: Gender distribution in pie chart shows, Male was 5(16.7%) and Female 25 (83.3%).

Patients sustained injury by fall in slippery ground 26, fall from height 03, RTA 01. All stable pertrochanteric fracture of femur AO type was included. Among them 17 patient was AO type 31A1.1 type, rest of the 17 patient were AO type 31A1.2 type.

The Singh's index was assessed from antero-posterior radiographs of the contralateral hip. Regarding singh's index 18(60%) patients were in 3, 11(36.7%) patients were in 2 and 1(3.3%) patient was in 1.

All patients were treated with a DHS using a four-hole side plate fixed with four bicortical screws and weight bearing afterwards, healed uneventfully except one case.

The average tip–apex distance was 22.3±3.9mm (range14–28mm). In three cases, it was more than 25mm (26,27 and 28mm).

Radiological union was observed 10 patient in 3 month, 12 patient in 12 month, 7 patients in 5 month, one patient fail to union. The mean union time was 3.7±1.04 with range from 3 to 5 months.

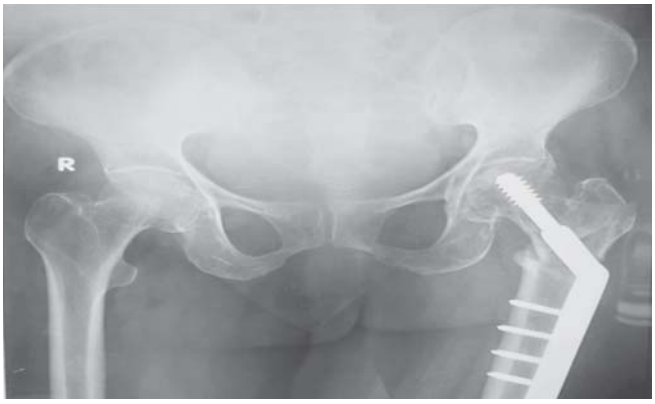

Figure: 2 show radiological union.

Table-II: Union time (N=30)

Union time (in months)	Frequency	Percent
00	1	3.3
3.00	10	33.3
4.00	12	40.0
5.00	7	23.3
Total	30	100.0

One fractures had nonunion at 24 weeks due to cut out of the screw (3.3%), two patients had a varus collapse of the fracture (6.6%).

In the final grading as per Harris hip score (Table-III), 6 patients had excellent results (score 90–100), 14 had good results (score 80–90) and 9 had fair outcome (score 70–80) and 1 case had poor outcome. The mean postoperative Harris hip score was 81±6.61. P value is ≤0.05 is considered as significant (Table-III).

Table-III: Final Harris hip score (N=30)

Harris hip Score	Frequency	Percent
less than 70	1	3.3
70-79	9	30.0
80-89	14	46.7
more than 90	6	20.0
Total	30	100.0

Discussion

Successful outcomes of pertrochanteric fractures depend on many factors: the age of the patient, the patient's general health, the time from fracture to treatment, concurrent medical treatment, the adequacy of treatment and stability of fixation.

In this study, the highest number of patients 15(50%) were observed in the 6th and lowest number of patient 1(3.3%) was observed in 8th decades. The mean age was 65.8±6.9 years old with range from 50 to 80 years. It is

clear from many studies that elderly people suffer from pertrochanteric fracture more often than any other age group. In the study of Michiel H.J.Verhofstada and Chrisvander Werken the median age was 80.0 years (range22—96) with 85% of patients over 65 years old.[16]

In our study, male 5 (16.7%) and female were 25 (83.3%) with a male: female ratio of 1:5. Michiel H.J.Verhofstad and Chris van der Werken showed 48 male and 100 female with male: female ratio 1:2.08[16], that was dissimilar to our study.

In Present study, the mean union time was 3.7±1.04 months with range from 3 to 5 months. Siwach, et al showed mean union time is 13.14 weeks in there study which is close to our study. [17]

Regarding Harris hip score sixty six percent patients had good to excellent functional outcome with mean Harris hip score of 81±6.61. In the series of Mohsen et al. the mean Harris hip score was 88.04±7.51. [18] In the present study the follow up period is shorter than Mohsen et al & the mean Harris hip score is slightly lower and expected to increase gradually in subsequent follow up.

Among 30 cases one fractures had nonunion at 24 weeks due to cut out of the screw (3.3%). Two patients had a varus collapse of the fracture (6.6%). Maohsen et al. found 3% device failure[18] & Siwach et al found 1% varus collapse in their study with dynamic helical hip system. [17]

Conclusion

The DHS allows impaction at the fracture site, shorter operating time, no need for osteotomy; good bone healing and low rate of complication. As seen from the result of this study, pertrochanteric fracture with osteoporosis can be treated with dynamic hip screw. This method offered appraisable clinical and functional recovery with limited complication with early rehabilitation.

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Original Article

A Comparative Study of Efficacy and Safety of Oral Itraconazole Versus Terbinafine in Treatment of Tinea Corporis and Tinea Cruris

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Abstract

Objectives: *Tinea infections are the common fungal infections aggravated by hot and humid climate. Itraconazole and Terbinafine are commonly used oral antifungal agent for the same. They are being used as pulse and continuous therapy for different types of fungal infection. This present study was designed to compare the efficacy and safety of oral Itraconazle and Terbinafine in treatment of patient with tinea corporis and tinea cruris.*

Materials and Methods: *This randomized comparative study was done in the Department of Dermatology and Venereology, Jahurul Islam Medical College Hospital, Bajitpur, Bangladesh, on patients with tinea corporis and tinea cruris. Patients were randomly divided into two groups of 45 each and were given oral itraconazole in (Group A) and oral terbinafine in (Group B) for a period of 4 weeks. Final assessment was done at week 4 by observing sign and symptoms i,e physician assessment 4 point scale and microscopic KOH examination. All the data were analysed by SPSS version 22. A P value of <0.05 was considered as statistically significant.*

Result: *Final evaluation at the end of week 4 showed a cure rate of 76% in Itraconazole group (Group-A) as compared to 69% of patients in Terbinafine group (Group-B). No definite adverse effect was noted in either group.*

Conclusion: *Although Itraconazole showed a higher cure rate in comparison to Terbinafine, but the difference was not statistically significant.*

Keywords: *Itraconazole, Terbinafine, Tinea corporis, Tinea cruris.*

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Introduction

Tinea are fungi that invade and multiply within keratinized tissues (skin, hair and nail) causing infection [1]. Based upon their genera tinea can be classified into three groups; Trichophyton (which causes infection on skin, hair and nail), Epidermophyton (which causes infection on skin and nail) and Microsporum (which causes infection on skin and hair). Based upon mode of transmission these have been classified as anthropophilic, zoophilic and geophilic. Finally based upon the affected site these have been classified clinically into tinea capitis (head), tinea faciei (face), tinea barbae (beard), tinea corporis (body), tinea manum (hand), tinea cruris (groin), tinea pedis (foot) and tinea unguium (nail), other clinical variant include tinea imbricata, tinea pseudoimbricata and Mejocchi granuloma[2].

Tinea infections are the most common fungal infections affecting 20%-25% population globally. They are common in geographical areas with higher humidity. Over population and poor hygienic living conditions also contribute to tinea infections[3]. Hot and humid climate of Bangladesh make tinea a very common superficial fungal infection of skin[4]. There are many drugs now being used orally for the treatment of tinea infections such as griseofulvin, fluconazole, ketoconazole, itraconazole and terbinafine. Among them itraconazole and terbinafine are newer oral antifungal agent with better pharmacokinetic profile.

Itraconazole is a wider spectrum triazole group of fugistatic drug which inhibit sterol 14 α demethylase impairing biosynthesis of fungal ergosterol, an essential component of fungal cell membrane[5]. Similarly Terbinafine is a broad spectrum allylamine group of drug with fungicidal activity which inhibit squalene 2,3 epoxidase enzyme thus inhibit fungal biosynthesis of ergosterol[6,7]. These two drugs have been used conventionally as pulse and continuous therapy in case of any sorts of tinea infections. Here the present study was designed to compare the efficacy and safety of oral itraconazole versus terbinafine in the treatment of tinea corporis and tinea cruris.

Materials and Methods

This randomized comparative study was conducted in the Department of Dermatology and Venereology, Jahurul Islam Medical College Hospital, Bajitpur, Bangladesh in the year 2020.

A total of 90 patients including both male and female of age 18-60 years suffering from both clinically and mycologically confirmed tinea corporis and tinea cruris were included in the study. Patients with history of hypersensitivity to study drugs, pregnant and lactating women, patient receiving treatment with systemic immunosuppressive agent, patient with pre-existing renal, hepatic or cardiac disease, patient with contact dermatitis, atopic dermatitis, Psoriasis or any other skin diseases were excluded from the study.

Recruited patients were randomly allocated into two study groups of 45 each. All the patients of both the groups were demographically of similar characteristics. Systemic itraconazole was given in (Group A) and terbinafine in (Group B) for a period of 4 week. The itraconazole was given at a dose of 200mg once daily and terbinafine 250mg once daily. During the screening visit a detailed medical history was obtained and a thorough cutaneous examination was performed in each patient. Various clinical sign and symptoms such as pruritus, scaling, erythema were rated according to a 4 point physician assessment scale of 0-3 (0=absent, 1=mild, 2=moderate, 3=severe).

Blood was tested for haematological profile and biochemical test such as liver function test and renal function test were done at the start of therapy. After commencement of therapy patient were followed up at week 2 (1st follow up visit) and at week 4. Clinical assessment was made at each visit about sign and symptoms such as pruritus, scaling, erythema and any adverse effect from the prescribed drugs.

Final efficacy assessment was done at the end of week 4 with the combined evaluation of mycological result and the sum of clinical scores according to following scheme.

A. Complete cure: Considered in patient with absence of clinical sign and symptoms and negative (KOH) microscopic examination. Post inflammatory pigmentary changes were not taken into account.

B. Mycological cure: Considered in patient with minimal residual sign and symptoms (clinical scores <2) with negative (KOH) microscopic examination.

C. Failure: Considered in patient with no or minimal improvement of clinical sign and symptoms with positive (KOH) microscopic examination.

All the data were recorded in a predesigned questionnaire and evaluated in to SPSS software. Patients unwilling to give voluntary consent were excluded from the study. Ethical clearance was taken from the ethical review committee of the institution. All the data were analysed by SPSS version 22. A p value of <0.05 was considerd as statistically significant.

Result

A total of 90 patients were randomly assigned treatment and included in the study. Half of the patient 45 in (Group-A) were treated with itraconazole at a dose of 200mg once daily, while the other half, 45 in (Group-B) were treated with terbinafine 250mg once a day. The mean age of the patients were 31.27 ±2.54 (mean±SD) and 30.58 ±3.17 (mean±SD)years respectively in group A and group B. Male patients were 50 (55.56%) and female patients were 40 (44.44%) as shown in (Table-I). Efficacy assessment was done by two expert dermatologists at the end of week 4.

Complete cure (i,e clinical and mycological clearance) was achieved in 28 (62.22%) and 27 (60%) in itraconazole and terbinafine group respectively. Mycological cure was seen with itraconazole in 6 (13.33%) and with terbinafine in 4 (8.89%) (Table-). All the failures in both the groups itraconazole 11 (24.44%) and terbinafine 14 (31.11%) had tinea corporis and tinea cruris. None of the patient showed any significant adverse effect in both itraconazole and terbinafine groups that warrant discontinuation of treatment.

Final evaluation showed a cure rate of 76% with itraconazole in comparison to terbinafine 69% in the treatment of tinea corporis and tinea cruris.

Table I: Demographic Characteristic of Patients in Both Groups.

Characteristic	Number (%)	Group -A Itraconazole	Group -B Terbi nafine
Patients	90	45	45
Sex Distribution :			
Male	50 (55.56)	25	25
Female	40 (44.44)	20	20
Age :			
Mean ±SD	30.92 ±1.86	31.27 ±2.54	30.58 ±3.17
Age Distribution :			
≤ 20	24(26.67)	12	12
21 – 30	26(28.89)	13	13
31 – 40	24(26.67)	12	12
41 – 50	12(13.33)	6	6
50 – 60	4(4.44)	2	2
BMI (mean±SD)	26.84±1.14	27.11±0.64	26.69±0.81

Table II: Cure rate of tinea in Group-A and Group-B.

Result	Itraconazole (Group -A)	Terbi nafine (Group -B)	Total	P Value
Complete cure	28 (62.22%)	27 (60%)	55	0.105
Mycological cure	6 (13.33%)	4 (8.89%)	10	0.24
Failure	11 (24.44%)	14 (31.11%)	25	0.11

Pie chart showing effectiveness of

Itraconazole (Group-A) and Terbinafine (Group-B).

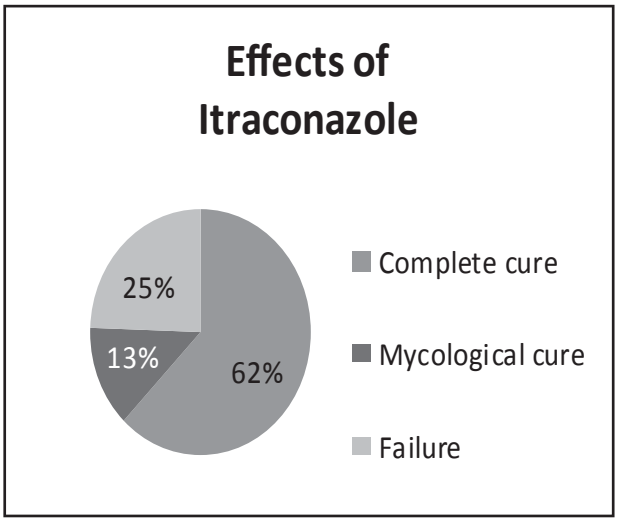

Fig 1 : Effects of Itraconazole

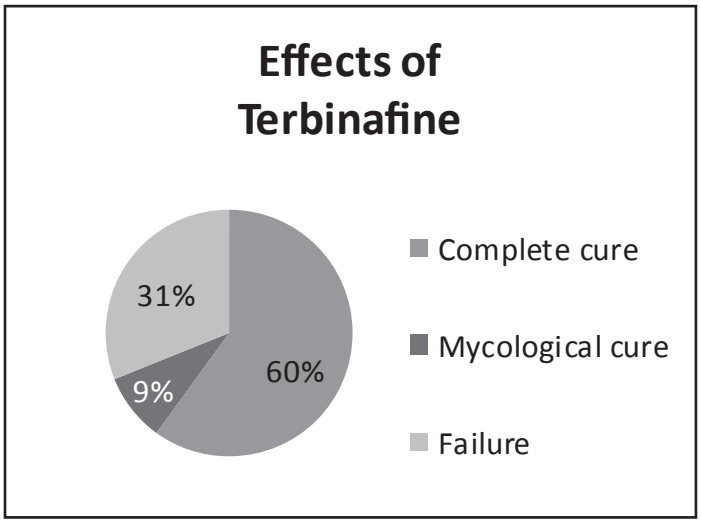

Fig 2 : Effects of Terbinafine

Discussion

Wide spread resistance to conventional oral antifungal agents with increasing clinical failure rate warrant the search for an effective first-line antifungal drug that bring about rapid clinical and mycological cure in tinea corporis and tinea cruris.

Itraconazole is a triazole antifungal drug which is increasingly being used as a first line drug for tinea corporis & tinea cruris, but it is being given for a longer period as compared to before. [8,9]

Similarly, Terbinafine is an allylamine group of antifungal drug is also being used increasingly for tinea corporis and tinea cruris with a standard dose of 250 mg once daily for 2 weeks.[10]

The most common side effects of Itraconazole are gastric upset, headache, taste alteration, jaundice and rarely can it cause hypokalemia and heart failure [9]. On the other hand Terbinafine can cause gastric upset, headache, altered taste, altered liver function test and rash; rarely can it cause blood dyscrasias and hepatitis [11]. However in our study, mild adverse effects such as gastrointestinal upset, headache and taste disturbances were observed in few patients of both groups, but none were severe enough to discontinue treatment.

Both itraconazole and terbinafine are highly lipophilic and keratinophilic. They persist in the stratum corneum of hair in high concentrations for 3 – 4 weeks after therapy is discontinued. These levels are well above the

minimum inhibitory concentration for most of the dermatophytes and hence sufficient to inhibit fungal growth. [12]

The result of our study found that itraconazole had a cure rate of 76% in comparison to terbinafine 69% in the treatment of tinea corporis and tinea cruris but statistically significant difference was not observed between the two groups regarding complete cure and mycological cure($P>0.05$). Study done by Anuradha Bhatia et al [13] in Ludhiana, Punjab, India on tinea corporis and tinea cruris have found a cure rate of 91.8% with itraconazole and 74.3% with terbinafine. Another study in Kathmandu, Nepal conducted by Nabin Bhakta Shakya et al[14] on tinea cruris have found a cure rate of 91.4% with itraconazole and 82.9% with terbinafine. While in another study, 2 weeks of itraconazole found to have higher cure rate in treating tinea capitis caused by T. violaceum than 2 weeks of terbinafine [15].On the contrary, reverse was found in treatment of toe nail onychomycosis, where terbinafine found to be more effective than itraconazole. [16]

Both the drugs were well tolerated and had good safety profile, but when taken into account the response rate for complete cure and mycological cure, itraconazole showed a higher cure rate over terbinafine and moreover the treatment cost for patient with itraconazole was relatively lower than those of terbinafine for the same duration of therapy.

Conclusion

Itraconazole had higher clinical and mycological cure rate and less failure rate as compared to terbinafine but the difference was not statistically significant. We had some limitations in our study- the sample size was small and the duration of study was short, further research with larger groups and longer study period is required to support these findings.

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Case Report

Olmesartan Induced Enteropathy in A 63-Year Old Woman: A Case Report.

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Abstract

Background: *Olmesartan medoxomil is one of eight marketed Angiotensin II Receptor Blocker (ARB) for the treatment of high blood pressure. Olmesartan associated enteropathy (OAE) has been described in several case reports, subsequently, the US Food and Drug Administration included severe sprue-like enteropathy as an adverse effect of Olmesartan. We report a case of Olmesartan associated enteropathy (OAE) in a 63 year old woman.*

Case: *We report a case of 63 year old woman who presented with dyspepsia, bloating and chronic diarrhoea. Initial investigations were almost normal except for a low potassium level. Stool studies including fecal leukocytes, fecal fat staining, Clostridium difficile toxin PCR, rotavirus ELISA, bacterial cultures, and Giardia and Cryptosporidium antigen testing all returned negative. Tests for other ova & parasites were negative as well. Serological test for HIV was negative. Upper GI endoscopy revealed scalloping of duodenal mucosa at the second part of it & biopsy showed the presence of villous atrophy along with raised intra epithelial lymphocytes (IEL). Serum IgA level was normal & anti tTG IgA was negative. Gluten free diet didn't seem to be working. A course of tetracycline failed & an empirical course of prednisolone showed only short term benefit with recurrence of symptoms after discontinuing it. Colonoscopy with terminal ileoscopy was also normal along with a normal biopsy report, excluding microscopic colitis. After careful review of foods & drugs, Olmesartan was discontinued, resulting in dramatic improvement of symptoms within a month of discontinuation.*

Conclusion: *Several case reports have described the effects of Olmesartan on gut, giving rise to the term of Olmesartan associated enteropathy (OAE). Clinicians should always be aware that Olmesartan can cause an enteropathy clinically and histologically similar to celiac disease.*

Key words: *Olmesartan, Enteropathy, Olmesartan associated enteropathy (OAE).*

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Background

Olmesartan medoxomil is one of eight marketed Angiotensin II Receptor Blocker (ARB) for the treatment of high blood pressure[1]. It was approved in 2002 in the USA, and in 2003 in the European Union, for the treatment of hypertension. Olmesartan associated enteropathy (OAE) was first described in a case series by Rubio-Tapia et al[2] in 2012; subsequently, the US Food and Drug Administration[1] included severe sprue-like enteropathy as an adverse effect of Olmesartan. The diagnosis of OAE relies on high clinical suspicion, demonstration of histological changes associated with enteropathy and negative coeliac disease (CD) serology.[3] Patients with Olmesartan induced enteropathy typically present with diarrhea, weight loss, nausea, vomiting, and low albumin. Although biopsy findings mimic those of celiac disease, Olmesartan induced enteropathy can be distinguished from celiac disease by the presence of normal celiac serologies and, importantly, by the absence of a response to a gluten-free diet.[2]

The presence of small bowel villous atrophy and negative serologic testing for celiac disease represents a difficult dilemma in clinical practice[4]. The differential diagnoses include several intestinal disorders (e.g., bacterial overgrowth, ulcerative jejunitis, protein-losing enteropathy, T-cell lymphoma, and tropical sprue)[5], even though in recent years similar findings have been also reported following the use of drugs[6-9]. To the latter it has been recently added Olmesartan, sometimes responsible for an enteropathy and malabsorption mimicking celiac disease[2]. Olmesartan associated enteropathy (OAE) is increasingly being recognized as a major differential diagnosis in patients with villous atrophy and negative coeliac disease (CD) serology. We report a case of Olmesartan-associated enteropathy (OAE) in a 63 year old woman who presented with dyspepsia, abdominal bloating & chronic diarrhoea.

Case

A 63 years old woman was admitted to the Gastroenterology department with the complaints of dyspepsia, abdominal bloating & chronic diarrhoea for last 6 months. On query she gave a history of weight loss of about 10 kg in last 6 months. She didn't give any history of abdominal pain, fever or passage of bloody stool. She was hypertensive & was on Amlodipine-Olmesartan combination for last 2 years with optimal control of blood pressure.

On examination she was mildly dehydrated. Other system examinations including abdominal examination revealed no abnormality. Except for mild hypokalemia the blood count, hepatic & renal function & serum albumin were within normal limit. Stool studies including fecal leukocytes, fecal fat staining, Clostridium difficile toxin PCR, rotavirus ELISA, bacterial cultures, and Giardia and Cryptosporidium antigen testing all returned negative. Tests for other ova & parasites were negative as well. Serological test for HIV was negative.

She attempted to avoid several potential food triggers like wheat products, milk products, salads & fiber containing foods with no effect on her symptoms. An endoscopy upper GI was done, which showed gross scalloping of mucosa at the second part of duodenum. Biopsy from the second part of duodenum revealed villous atrophy along with increased intra epithelial lymphocytes (IEL).

Based on these reports, anti tTG IgA was sent along with serum IgA level & gluten free diet was started. Serum IgA level was 284 mg/dl (70-400 mg/dl) & anti

tTG IgA was negative (<3U/ml). And the clinical condition didn't improve at al even after strictly sticking to a gluten free diet for a month.

Colonoscopy with terminal ileoscopy was performed which revealed no abnormality. Moreover, biopsy samples were also negative for microscopic colitis. A trial of tetracycline also failed to resolve symptoms. She was then prescribed an oral course of prednisolone empirically, targeting the gut inflammation. Symptoms resolved rapidly within few days, but relapse of symptoms occurred as soon as prednisolone was weaned.

A critical review of patient's food & medication history was done. And subsequently Olmesartan was discontinued following different reports of enteropathy induced by Olmesartan worldwide. Olmesartan was replaced by losartan. After about two weeks of discontinuation of Olmesartan, symptoms started getting better & she became symptom free after about a month of discontinuation of Olmesartan.

A repeat endoscopy upper GI was done 6 months after discontinuation of Olmesartan, which showed complete resolution of the endoscopic findings at the second part of duodenum. She continues to feel absolutely symptom free on losartan, after about a year of discontinuation of Olmesartan, with a gain of 7 kg weight during this period.

Discussion

Olmesartan medoxomil is one of eight marketed Angiotensin II Receptor Blocker (ARB) for the treatment of high blood pressure[1]. It was approved in 2002 in the USA, and in 2003 in the European Union, for the treatment of hypertension.

Olmesartan-associated enteropathy (OAE) was first described in a case series by Rubio-Tapia et al[2] in 2012; subsequently, the US Food and Drug Administration[1] included severe sprue-like enteropathy as an adverse effect of Olmesartan. The diagnosis of OAE relies on high clinical suspicion, demonstration of histological changes associated with enteropathy and negative coeliac disease (CD) serology.[3] Dong et al[10] reported a higher incidence of gastrointestinal adverse events with Olmesartan when compared with other ARBs in a cohort of over 1.5 million patients, of whom 350 790 were on Olmesartan.

At present, the mechanisms responsible for the onset of enteritis after Olmesartan use are unknown[2]. The effect of Olmesartan on the intestinal mucosa is thought to be immune-mediated.[11] Transforming growth factor-β (TGF-β) is a multifunctional cytokine that plays a role in gut haemostasis.[11] Olmesartan has a higher affinity to block angiotensin II receptor (ATR) type-1, leaving angiotensin free to bind ATR type-2. This results in modulation of TGF-β, which in turn leads to histological changes on the small bowel mucosa.[11] Two pathways have been proposed, including (1) the inhibitory effects of angiotensin II receptor blockers (ARBs) on transforming growth factor β, and (2) a disproportionate activation of angiotensin II receptor type 2 (AT2) receptors by angiotensin II after blocking AT1 receptors with olmesartan, which results in apoptosis of enterocytes.[2,12]

Patients with Olmesartan induced enteropathy typically present with diarrhea, weight loss, nausea, vomiting, and low albumin. Although biopsy findings mimic those of celiac disease, Olmesartan induced enteropathy can be distinguished from celiac disease by the presence of normal celiac serologies and, importantly,

by the absence of a response to a gluten-free diet.[2] Histological changes described in Olmesartan induced enteropathy can range from intraepithelial lymphocytosis and lymphocytic proliferation of the lamina propria to marked villous atrophy.[13]

In 2012, Rubio-Tapia et al. identified 22 patients on Olmesartan who developed clinical features of chronic diarrhea, weight loss, and sprue-like enteropathy, evidenced by villous atrophy and mucosal inflammation on intestinal biopsy.[2] Notably, all 22 patients experienced resolution of symptoms upon withdrawal of Olmesartan and discontinuation of a gluten-free diet.[1] Steroids may ameliorate symptoms in 95% of cases.[13]

In our case the patient presented with dyspepsia, bloating and chronic diarrhoea. Initial investigations were almost normal except for a low potassium level. Stool studies including fecal leukocytes, fecal fat staining, Clostridium difficile toxin PCR, rotavirus ELISA, bacterial cultures, and Giardia and Cryptosporidium antigen testing all returned negative. Tests for other ova & parasites were negative as well. Serological test for HIV was negative. Upper GI endoscopy revealed scalloping of duodenal mucosa at the second part of it & biopsy showed the presence of villous atrophy along with raised intra epithelial lymphocytes (IEL). Serum IgA level was normal & anti tTG IgA was negative. Gluten free diet didn't seem to be working. A course of tetracycline failed & an empirical course of prednisolone showed only short term benefit with recurrence of symptoms after discontinuing it. Colonoscopy with terminal ileoscopy was also normal along with a normal biopsy report, excluding microscopic colitis. After careful review of foods & drugs, Olmesartan was discontinued, resulting in dramatic improvement of symptoms within a month of discontinuation.

Conclusion

Small intestinal villous atrophy and inflammatory infiltrates with negative celiac serologies (sprue-like enteropathy) presents a diagnostic challenge. The differential diagnosis is broad and includes autoimmune and drug-induced enteropathies, malignancies, infections, post-infectious enteropathy, and immunodeficient disorders. Several case reports have described the effects of Olmesartan on gut, giving rise to the term of Olmesartan associated enteropathy (OAE). Clinicians should always be aware that Olmesartan can cause an enteropathy clinically and histologically similar to celiac disease.

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