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Acknowledgements
Acknowledgements, if any, should be placed at the end of the body of the text and be limited to no more than 100 words. This section may be used to acknowledge the help of those who do not qualify for authorship or to acknowledge funding, donated resources, or significant material contributions to the research.

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An official organ of Ad-din Women's Medical College

Editorial

Zika Virus: A new threat right now

The Zika virus is probably a top-of-mind concern right now, and with good reason: This mosquito-borne virus is dominating headlines with its scary advance into the United States and potentially devastating consequences for pregnant women and their babies.

What is Zika virus?

The Zika virus is an insect-borne illness that can be primarily transmitted by infected Aedes mosquitoes. The name comes from the Zika Forest in Uganda where monkeys with the virus were first found in 1947.

Zika surfaced just over a year ago in South America and Brazil that has been disproportionately affected with thousands of babies suffering severe birth defects including brain damage in utero when their mothers contracted the virus. But it has now spread to more than three dozen countries and territories in America with local transmission taking place in two continents including USA according to the Centers for Disease Control and Prevention (CDC).

Why is it dangerous?

For the relatively few people who show signs of a Zika infection, the illness is often very mild but in pregnant woman, the effects can be devastating and can include pregnancy loss or a baby born with microcephaly may be associated with developmental delays, mental retardation seizures and in some cases can be fatal.

How is Zika transmitted?

Primarily through the bite of an infected Aedes species mosquito : (Ae.Aegypti and Ae.albopictus) Zika virus is transmitted to people. These are the same mosquitoes that spread dengue, yellow fever and chikungunya virus.

- These mosquitoes typically lay eggs in and near standing water in things like buckets, bowls, animal dishes, flower pots and vases.
- These mosquitoes are aggressive daytime biters but they can also bite at night.

From mother to child

- A pregnant woman can pass Zika virus to her fetus during pregnancy. A pregnant woman already infected with Zika virus can pass the virus to her fetus during the pregnancy or around the time of birth. To date, there are no reports of infants getting Zika virus through breastfeeding. Mothers are encouraged to breastfeed even in areas where Zika virus is found.
- Difference between congenital and perinatal transmission of Zika virus. Congenital or intrauterine transmission of Zika virus occurs when a woman is infected with Zika virus during her pregnancy but before delivery and the virus passes to the fetus.

  Perinatal transmission occurs when a woman is infected with the Zika virus within approximately 2 weeks of delivery, and the virus passes to the infant at or around the time of delivery. When an infant acquires Zika virus infection prenatally, the infant may develop symptoms such as maculopapular rash, conjunctivitis, arthralgia and fever.
- Postnatal Zika Virus Infection Infants and children can acquire Zika virus postnatally through mosquito bites.

Through sex

- Zika can also be passed through sexual transmission.

Through blood transfusion

- There have been multiple reports of blood transfusion transmission cases in Brazil. These reports are currently being investigated.

Through laboratory and healthcare setting exposure

- Prior to the current outbreak, there were four reports of laboratory acquired Zika virus infections, although the route of transmission was not clearly established in all cases.

What are the symptoms of Zika?

A Zika infection is similar to a mild case of the flu and may include such symptoms as a low-grade fever, headache, rash, muscle and joint pain and conjunctivitis (pink eye). Symptoms may last several days to a week.

Testing for Zika virus

All pregnant women should be assessed for Zika at prenatal visits in area. If one may have been exposed

either during travel to an active Zika infection area, live in an active area, or if could have been exposed through sexual contact, blood or urine tests to be done to see positive/negative for the virus, even if not showing symptoms.

Risks

Anyone who lives in or travels to an area where Zika virus is found and has not already been infected with Zika virus can get it from mosquito bites. Once a person has been infected, he or she is likely to be protected from future infections.

Prevention

No vaccine exists to prevent Zika but researchers from Florida State University, Johns Hopkins University and the National Institutes of Health have identified certain existing drugs that may be able to prevent the virus from replicating in the body and even protect fetal cells from being damaged. Most recently, it has been reported that scientists may have discovered an antibody that can help fight the virus.

What do to protect self and others

The best way to prevent Zika is to protect self from mosquito bites. If travel cannot be avoided, one should take every precaution to avoid mosquito bites, using mosquito nets including:

- Wearing shirts with long sleeves and pants, rather than shorts
- Using bug spray, which is safe for pregnant and nursing women.
- Treating clothes with insecticides eg. permethrin.
- Ridding home of any free-standing water.
- Pregnant women in any trimester should talk to the doctor or other healthcare provider before traveling to these areas and strictly follow steps to avoid mosquito bites during the trip.

While the Zika virus remains in the blood of an infected person for a few days to a week, according to the CDC, there is no current evidence to suggest that it poses a risk of birth defects in future pregnancies.

In conclusion a multidisciplinary approach is required to fight this threat against future generation.

Prof. Shireen Ayesha Siddiqua
Editor in Chief
The Journal of Ad-din Women's Medical College

Original article

Association of high density lipoprotein and low density lipoprotein with Serum Estrogen Level in Postmenopausal Women

Nahid yeasmin[1], Qazi Shamima Akther[2], Sayeeda Mahmuda[3], Khadija Begum[4]

Abstract

Objectives : Increased incidence of cardiovascular diseases in postmenopausal women may be due to hyperlipidemia caused by lower level of estrogen hormone. Its complications give rise to cardiovascular diseases, stroke in postmenopausal women. The study was carried out to observe the association of serum low density lipoprotein cholesterol (LDL-C) and high density lipoprotein cholesterol (HDL-C) with serum estrogen level in postmenopausal women.

Methods : This cross sectional analytic study was conducted in the Department of Physiology of Dhaka Medical College during the period of January to December, 2011. A total number of 90 female subjects were selected from different areas of Dhaka city. Among them, 60 postmenopausal women with age ranging from 50 to 60 years were taken as study group and 30 apparently healthy premenopausal women with age ranging from 20 to 30 years were included as control group for comparison. The study parameters low density lipoprotein cholesterol (LDL-C) & high density lipoprotein cholesterol (HDL-C) were estimated by enzymatic method in both groups. Serum estrogen level was estimated in order to assess the hormonal level of both groups. Data was analyzed by Unpaired Student's't' test and Pearson's correlation co-efficient (r) test as applicable.

Results : The mean serum LDL-C level was higher in postmenopausal women than those of premenopausal women and result was statistically significant. The level of mean serum HDL-C was significantly ($p<0.001$) lower in postmenopausal women in comparison to those of premenopausal women. In postmenopausal women serum estrogen level was lower than premenopausal women and serum estrogen level showed negative correlation with LDL-C level. HDL-C level showed positive correlation with serum estrogen level.

Conclusion : Present study revealed that there is association of low density lipoprotein cholesterol & high density lipoprotein cholesterol with serum estrogen level in postmenopausal women.

Keywords : Low density lipoprotein cholesterol, High density lipoprotein cholesterol, postmenopausal women

Introduction

Menopause is defined as the permanent cessation of menstruation resulting from the loss of follicular activity. It is recognized by the presence of amenorrhea for 12 consecutive months without any pathological and physiological factors. A new hormonal pattern is established at menopause, which is characterized by high levels of follicle stimulating hormone (FSH), luteinizing hormone (LH) and low level of estrogen[1]. Menopause has a wide starting range, but usually be expected in the range of 42-58 years[2]. After menopause, the morbidity and mortality from cardiovascular diseases(CVD) are increased. Postmenopausal women are 4-8 times more likely to die of coronary artery disease than premenopausal women[3]. Data from the Framingham study suggest that the rate of morbidity from coronary artery diseases accelerate more quickly in postmenopausal women than do those of males after the age of the 45 years[4].

In US it is estimated that one in every two women die of a heart related disorder, which represent more death than due to cancer, chronic lung diseases and accident combined5. Estrogen is a cardio protective hormone but in postmenopausal women due to lack of the estrogen, cardio protective function is lost and increases the coronary artery diseases[6]. However, several other physiological changes which develop during menopause may also influence the risk of cardiovascular disease, such as aging effect, decreasing resting metabolic rate and physical activity[7]. Due to lacking of estrogen, postmenopausal women have increased risk for central obesity, dyslipidemia, glucose intolerance and hypertension. Among these factors the dyslipidemia or hyperlipidemia seems to be the major issue[8].

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Association between derangement in lipoprotein metabolism and cardiovascular diseases has been supported by large epidemiological studies. They demonstrate a significant correlation between severity of atherosclerosis and high level of total plasma LDL-C. Low density lipoprotein cholesterol transports the cholesterol from liver to peripheral tissues and helps in formation of atherosclerotic plaque[4,6]. Estrogen has been noted to influence lipid metabolism by increasing hepatic synthesis of LDL-C receptor, resulting in an increased hepatic uptake of LDL-C and decreased in circulating LDL-C level[10]. Association between menopause and hyperlipidemia has been documented by several studies. Some studies suggested that the incidence of atherosclerosis and its complications are increase with increases in LDL-C level whereas the incidence decreases with increase in HDL-C level.-High density lipoprotein cholesterol (HDL-C) which is protective by reversing cholesterol transport, inhibiting the oxidation of LDL-C and by neutralizing the atherogenic effect of oxidized LDL-C[9]. Before menopause, women are found to be protected against cardiovascular disease by the typically lower LDL-C level and higher level of HDL-C compared with men of same age[11]. It is widely accepted that higher levels of LDL-C promote cardiovascular disease (CVD) whereas higher level of high density lipoprotein-cholesterol (HDL-C) has an important role against cardiovascular disease[13]. High level of LDL-C in postmenopausal women impairs endothelial cell function. This endothelial injury increases permeability and accumulation of LDL-C in intima of blood vessels[14].

So low levels of HDL-C in postmenopausal women would lead to excessive accumulation of cholesterol in the tissues and impair normal clearance of cholesterol from the arterial wall and so accelerate development of athero sclerosis[15].

Method

This cross sectional analytic study was conducted in the Department of Physiology, Dhaka Medical College during the period of January to December, 2011. A total 90 female subjects were selected from different areas of Dhaka city. Among them, 60 postmenopausal women with age ranging from 50 to 60 years were taken as study group (Group B) and 30 apparently healthy women with age ranging from 20 to 30 years were included as control group (Group A) (premenopausal). Subjects having history of heart, liver, kidney diseases, endocrine disorders and women taking hormone replacement therapy steroid, alcohol user, and smoker were excluded from the study. Detailed medical history, menstrual history and family history of the subjects were recorded. 5ml venous blood was collected with all aseptic precautions. Estimation of serum estrogen level was done by RIA method in the Department of Nuclear Medicine, Dhaka Medical College. Estimation of LDL-C and HDL-C were done in the department of Biochemistry, Dhaka medical college. Statistical analysis was done by Unpaired Student's't' test. Correlation was analyzed by Pearson's correlation co-efficient (r) test. P value <0.05 was taken as significance.

Results

The value of mean low density lipoprotein cholesterol was higher in postmenopausal women than those of premenopausal women and the result was statistically significant ($p<0.001$). The mean value of high density lipoprotein cholesterol level in postmenopausal women was significantly ($p<0.001$) lower than those of premenopausal women(Table-I). Serum estrogen level was lower in postmenopausal women than that of premenopausal women and the result was statistically significant ($p<0.001$) (Figure 1). Distribution of parameters were observed in postmenopausal women and 35% of postmenopausal had LDL-C level within normal level (i.e.< 99 mg/dl) whereas 65% had above normal level in same group of women Again, 23.3% of postmenopausal had HDL-C within normal level (i.e.>50mg/dl), whereas, 76.7% had below normal level (Table-II). Moreover, serum estrogen level showed negative correlation ($r=-0.138$) with low density lipoprotein cholesterol level in postmenopausal women and result was statistically non-significant. In postmenopausal women the high density lipoprotein cholesterol level showed positive correlation ($r=+0.137$) with serum estrogen level and result was statistically non-significant. (Table-III)

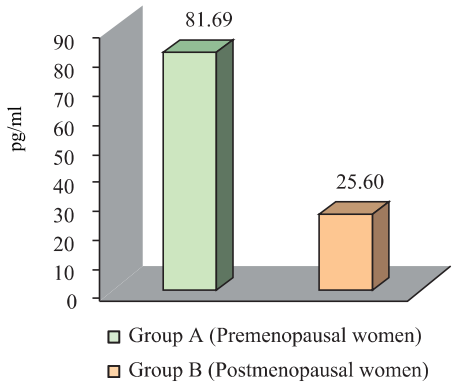
Table I : Age, low density lipoprotein(LDL-C) and high density lipoprotein(HDL-C) level in premenopausal and postmenopausal women

Groups(n)	Age (years)	LDL (mg/dl)	HDL (mg/dl)
A	3028.77±6.66	79.20±18.30	51.10±11.42
B	6053.90±5.75	114.93±28.97	41.33±10.79
Statistical analysis			
Groups	Age (p value)	LDL-C (p value)	HDL-C (p value)
A vs. B	0.0001***	0.0001***	0.0001***

Unpaired Student's 't' test was performed to compare between groups. The test of significance was calculated and p values <0.05 was accepted as level of significance.

Group A : Premenopausal women
Group B : Postmenopausal women
*** = Significant at P<0.001

Fig-1 : Mean serum estrogen level in premenopausal and postmenopausal women



Results are expressed as mean±SD

Table-II : Distribution of the subjects by the study parameters in postmenopausal women

Parameters	Group B (n=60)	No. (%)
Low density lipoprotein (mg/dl)		
<99	21	(35.0)
>99	39	(65.0)
High density lipoprotein (mg/dl)		
<50	46	(76.7)
>50	14	(23.3)

Table-I11 : Correlation of serum estrogen level with biochemical parameters in postmenopausal women

Parameters	Group B (n=60)	r	p
LDL-C		0.138	0.294^{ns}
HDL-C		+0.137	0.296^{ns}

Discussion

In the present study, the level of low density lipoprotein cholesterol and high density lipoprotein cholesterol in healthy premenopausal women were almost within normal range and also similar to reported by the several investigators from abroad[2-6].

In postmenopausal women the mean serum LDL-C level was higher than that of premenopausal women and the result was statistically significant. Similar types of findings were reported by different researchers of different countries[8,13,15]. On the contrary, similar observations were made by other researchers but they did not find any significant difference in LDL-C cholesterol level. This inconsistence of the result may be due to small sample size in their study.16Again, in our study, LDL-C showed negative correlation with serum estrogen level in postmenopausal women[13,15]. The result was consistence with the result of other study[17].

The serum level of HDL-C in postmenopausal was lower than those of premenopausal women and result was statistically ($p < 0.001$) significant. Similar types of findings were reported by different researchers of different countries[8,13,15]. On the contrary, similar observations were made by other researchers but they did not find any significant difference in HDL-C value between the groups. Again, HDL-C showed positive correlation with serum estrogen level in postmenopausal women. The result was consistence with the result of other study[17].

It has been suggested from research review that estrogen deficiency in postmenopausal women enhance adipose tissue deposition by increasing lipogenesis. So excess free fatty acid from adipose tissue, decrease the sensitivity of insulin. Thus insulin resistance is developed in postmenopausal women. Insulin resistance in adipose tissue causes increased activity of hormone sensitive lipase resulting in increased level of circulating fatty acids. These fatty acids are carried to the liver where they are converted to triacylglycerol and cholesterol. Excess triacylglycerol and cholesterol are releases as very low density lipoprotein, resulting in elevated serum LDL-C level[23].

In the present study, both LDL cholesterol level is higher but HDL-C level is lower in postmenopausal women than premenopausal women. This is most likely due to lower level of estrogen, as the measured value of estrogen was lower in postmenopausal women than premenopausal women. Furthermore, in the present study, LDL cholesterol showed negative correlation and HDL-C showed positive correlation with serum estrogen level in postmenopausal women. These correlations further support these findings. But exact mechanism is not elucidated by this type of study due to time and financial constraints.

Conclusion:

From this study, it can be concluded that higher value of LDL-C and lower value of HDL-C may present in postmenopausal women may be due to their lower level of estrogen hormone.

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Original article

Assessment of body composition of government primary school children in Dhaka city

Sharmin Rahman[1], Shamim Ara[2], Mohammad Adnan Khan[3], Afrose Ahmed[4], Sadia Rahman[5], Rahanur Akter[6]

Abstract

Objective : Parameters of the body composition such as percentage of body fat and total body fat are often used to evaluate physical abilities. These parameters are also used to assess nutritional status which is widely used in children. We can also use measurement of percentage of body fat and total body fat in children for clinical, research and epidemiological purposes. The present study was planned to determine difference in percentage of body fat and total body fat between boys and girls of four government primary school in Dhaka city.

Materials & Methods : This cross-sectional analytical type of study was conducted in the department of anatomy, Dhaka Medical College, Dhaka, from January 2012 to December 2012. The present study was performed on 400 government primary school children. Out of 400 children, 200 were boys and 200 were girls. The study population was divided into three groups A, B, C according to age and sex of the subject. Group A include age 9+ years, group B include age 10+ years and group C include age 11+ years old children. Each group was again subdivided into A_1, B_1 and C_1 for boys and A_2, B_2 and C_2 for girls. The subjects of this age group were the students of class III to class V. With the help of weighing scale and skinfold caliper measurements were recorded.

Results : Percentage of body fat and total body fat of group A_2, B_2 and C_2 were significantly greater ($P<0.001$) than group A_1, B_1 and C_1.

Conclusion : Studies with larger sample size could be necessary to identify more accurate results in different age groups among different population.

Key words : Body composition, total body fat, percentage of body fat.

Introduction

The assessment of body composition in childhood can be performed with several sophisticated techniques, but in many circumstances it is more desirable to utilize widely available and simple techniques such as anthropometry[1]. Measurement of body composition is proving increasingly important in clinical nutrition and research[2]. It is essential for monitoring childhood obesity in the world[3]. Assessment of total body fat and percentage of body fat is important in the management of illnesses like obesity, cardiovascular diseases and type 2 diabetes mellitus[4]. It is also a good method to measure level of fatness because it directly measures subcutaneous fat layers by measuring skinfold thickness[5].

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Different body size, shape and proportions are beneficial in different physical activities. Physical abilities of the players have marked effects on the skill of players and the tactics of the team. To evaluate these physical abilities, parameters of the body composition such as the percent body fat and somatotype components are often used[6].

Very low values of skinfolds indicate the depleted calorie reserves of the body and are correlated with malnutrition. Thus, variations in body mass, subcutaneous fatness and total body fat are good predictors of health and chronic diseases[7].

A marked change in body composition is the hallmark of pubertal maturation and result in typical male-female differences. Under the influence of the gonadal steroid hormones and growth hormone, the deposition of fat becomes maximally sexually dimorphic. Due to the influence of testosterone, boys have a simultaneous loss of fat in the limbs[8].

Prepubertal girls have greater levels of circulating estrogen than prepubertal boys that suggests a role of it in differences of fat distribution between both sexes[9].

Materials & methods

The study population was selected purposively from four government primary school in Dhaka city. The subjects of

this age group were the students of class III to class V. Out of 400 children, 200 were boys and 200 were girls. Each student was provided with an ID no. and a data sheet of personal information's was filled up for each student. So, there was no scope of repetition of students participating in the study. All the students of the class were included but data were collected only from those who fulfilled the criteria and participated willingly. Informed written consent was taken from the headmaster of the respective school and also from parents of the students for data collection. Date of birth of subjects was taken from the birth certificates which were collected from the office of the respective school. If birth certificates were not available from the school, then the date of birth of the students were collected from the parents. Age and sex wise distribution of sample is given in Table I. Those subjects who had completed 9 years of age but were less than 10 years even by one day were grouped under 9+ age group. Similar pattern was followed for other age groups as well. To take measurement of weight and skinfolds proper exposure was needed. Before exposure privacy was maintained. The measurement was taken in closed door room with the presence of an attendant (aya) of the respective school.

Weight was measured by weighing scale in kg. The subject was only with school dress without any extra clothing and extra things like pen, pencil, scale, water bottle, tiffin box in his/her hands or pockets. The subject was asked to stand bare footed on the scale facing forward. While both feet placed on the scale, weight was evenly distributed between the feet.

Skinfolds were measured by skinfold caliper in mm. A fold of skin and subcutaneous tissue was firmly raised between thumb and forefinger of the left hand and away from the underlying muscle at the marked site. Then the skinfold caliper was placed 1cm below the fingers of the left hand to measure thickness of the fold. During measurement the subject was asked to stand relaxed, except for the medial calf skinfold which was taken with the subject seated.

Triceps skinfold was taken with the subject's arm hanging loosely in the anatomical position. A line was drawn at the back of the arm connecting the acromion and the olecranon processes. A midpoint of the line was determined. Then a fold was raised at the determined site and measurement was taken[10].

Subscapular skinfold was taken by raising the fold on a line from the inferior angle of the scapula in a direction that was obliquely downwards and laterally at 45 degrees[10].

Percentage of body fat (BF%) was calculated by Slaughter et al equations[2].

Boys=1.21 (sum of 2 skinfolds) - 0.008 (sum of 2 skinfolds)^2 - 1.7

Girls =1.33 (sum of 2 skinfolds) -0.013 (sum of 2 skinfolds)^2 - 2.5

[BF% for children with triceps and subscapular skinfolds <35 mm]

Boys = 0.783 (sum of 2 skinfolds) -1.7

Girls = 0.546 (sum of 2 skinfolds) + 9.7

[BF% for children with triceps and subscapular skinfolds >35 mm]

Total body fat was calculated by following formula[6].

Total body fat (kg) = (Percentage of body fat / 100) x Body mass (kg)

Results

Results are showing in Table 1, 2, 3

Table I : Distribution of sample by age and sex

Group	Age limit (yrs)	No.of sample	Total
A_1 (Boys)	9+	68	136
A_2 (Girls)	(9 to <10)	68	
B_1 (Boys)	10+	66	132
B_2 (Girls)	(10 to<11)	66	
C_1 (Boys)	11+	66	132
C_2 (Girls)	(11to<12)	66	
Total			**400**

Table 2 : Percentage of body fat of boys and girls

Group	Percentage of body fat (Mean±SD)
A_1(n=68)	10.10±2.47(6.37 20.18)
A_2(n=68)	13.30±4.37(6.17 25.70)
P value	0.0001***
B_1(n=66)	10.69±3.72(3.87 21.04)
B_2(n=66)	14.28±3.99 (7.58 29.35)
P value	0.0001***
C_1(n=66)	11.71±3.55(6.37 22.73)
C_2(n=66)	15.71±4.65 (4.33 26.23)
P value	0.0001***

Table 3 : Total body fat of boys and girls

Group	Total body fat (kg) (Mean±SD)
A_1(n=68)	2.55±0.75 (1.28 5.85)
A_2(n=68)	3.32±1.30 (1.11 7.96)
P value	0.0001***
B_1(n=66)	2.85±1.27(1.04 6.63)
B_2(n=66)	4.41±2.12 (1.59 14.38)
P value	0.0001***
C_1(n=66)	3.38±1.35(1.53 8.07)
C_2(n=66)	5.35±2.47 (1.68 12.27)
P value	0.0001***

Figures in parentheses indicate range. Comparison between boys and girls done by unpaired Student's 't' test, * = significant at P<0.05, *** = significant at P<0.001

Discussion

In the present study, percentage of body fat of A2, B2 and C2 were higher than A1, B1 and C1 (P<0.001). Total body fat of A2, B2 and C2 were higher than A1, B1 and C1 (P<0.001).The findings of Chan, et al., Wickramasinghe, Lamabadusuriya, Cleghor n and Daviesand Yeung and Hui were significantly higher than the findings of the present study (P<0.001)[3,4,11]. The guardian of the study population was either small entrepreneur or third and fourth class employee of government and non-government organization. The monthly income of parents/ father/ mother/family was ranged from 15,000 to 20,000.

Dissimilarities of the findings of the present study with the findings of the other researchers may be due to the selection of study population of different age group, different socio-economic status, different nutritional status and different categories like sportsman.

Conclusion

Only four government primary schools were included in this study. So the children of the present study do not represent all primary school children of Bangladesh. Further studies with larger sample size are recommended to get more precise picture in order to produce a more comprehensive data in different age group of male and female in Bangladesh. Studies with different category of people are also recommended.

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Original article

Association of birth trauma with genital prolapse – a study of hundred cases

Mahbuba Akhter[1], Ferdousi Chowdhury[2], Rina Haider[3]

Abstract

Objective : Genital prolapse is a common gynaecological problem both in developed and developing countries. This spectrum of problem creates a social and economic burden on society of enormous magnitude. The study was conducted to identify the factors which favor to develop genital prolapse

Methods : This Cross sectional descriptive study was carried out during the period from July 2006 to December 2006. The study was conducted on 100 cases, in department of Obstetrics and Gynecology of Bangabandhu Sheikh Mujib Medical University, Dhaka from July to December, 2006.

Results : In the present study, 99% of the deliveries were conducted at home by TBA or by Dai. 42% women had 1-4 and 58% women had 5or more children. Fifty two percent of the patients had difficult and prolonged labour 20% patients developed prolapse after menopause.45% women had early resumption of heavy work.30%patients had chronic constipation and 9% had chronic cough.

Conclusion : Vaginal birth is associated with risk of development of uterovaginal prolapse and risk is increased with number of vaginal birth, mismanaged labour & puerperium.

Keywords : Uterovaginal prolapsed, Aetiological aspects, Birth trauma, intrapartum care.

Introduction

The pelvic floor and its support systems have been a site of keen interest for gynecologists, urologists, surgeons and anatomists. Integrity of this system is needed for the storage and controlled evacuation of urine and faeces along with an accommodation during sudden changes in intra-abdominal pressure and in pregnancy. An intact pelvic floor ensures that all the visceral structures are in their normal positions. Genital prolapse in one of the most common clinical conditions met in the day-to-day gynecological practice, especially amongst the parous women. The entity includes descent of the vaginal wall or the uterus.It is, in fact, a form of hernia. This is very relevant in our country and is one of the frequent causes of morbidity in women. It is responsible for over 20% of all gynecological operations[1]. The exact prevalence of prolapse is difficult to determine because the social embarrassment discourages women from seeking medical advice. Some women are asymptomatic and some are unaware that help is available. It has been estimated that a half of parous women loose pelvic support, resulting in some degree of prolapse and that, of these women, 10-20% seek medical care[2]. In developing countries like Bangladesh, genital prolapse is associated with repeated and mismanaged vaginal deliveries. Vaginal delivery with consequent injury to the supporting structures is the single most important acquired predisposing factor in producing prolapse[3]. The prolapse is unusual in cases delivered by caesarean section. Reproductive health plays an important role behind the cause and development of prolapse[5]. In this study much emphasis is given on causes and factors related to prolapse. It is hoped that it may help in determining the methods that can be used to minimize genital prolapse.

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Methodology

This cross sectional descriptive study was conducted in department of Obstetrics and Gynecology of Bangabandhu Sheikh Mujib Medical University, Dhaka. The study was conducted on 100 cases, from July to December, 2006. Data was collected through the use of prepared questionnaire and by thorough physical examination, for recording all relevant parameters, which was in structured format.

Study Result

The study was carried on 100 cases of genital prolapse, who attended gynae outdoor and indoor of BSMMUH. The results are presented here in tables or graphs.

Fig-1 : Distribution of patient by age

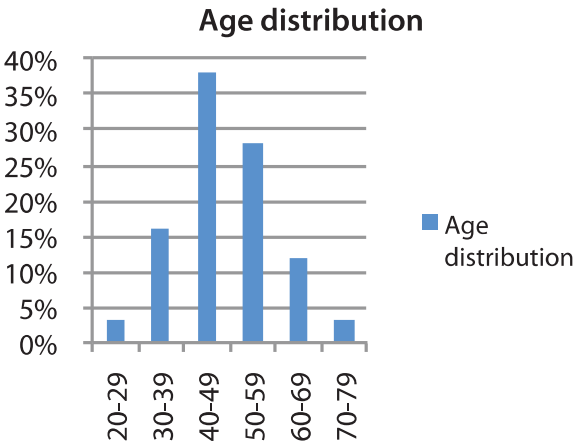

Table-1 : Distribution of patients by Socio economic condition

Income group	No of Patients	Percentage (%)
Low	54	54
Middle	34	34
High	12	12
Total	100	100

Fig-2 : Distribution of patients by Parity

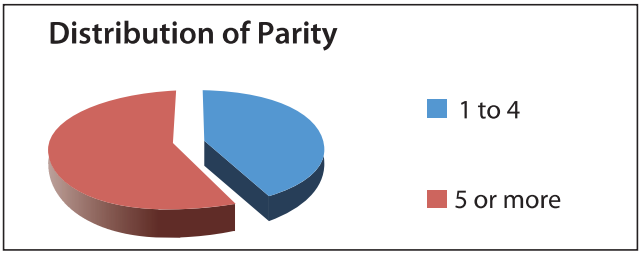

Table-2 : Distribution of patients by conduction of Delivery

Delivery Conducted by	No. of Patients	Percentage (%)
Dai	49	49
TBA	50	50
Doctor	1	01
Total	100	100

Table-3 : Cases with or without difficult labour

Duration of labour	No. of patients	Percentage (%)
Prolonged labour pain and difficult deliveries	52	52
Labour without difficulties	48	48
Total	100	100

Table-4 : Distribution of patient by presenting symptoms

Presenting symptoms	No.	Percentage (%)
Something coming down p/v	100	100
Pelvic heaviness	9	9
Backache	34	34
Urinary symptoms		
Increased frequency	44	44
Burning micturition	38	38
Difficulty in emptying bladder	34	34
Urinary incontinence	20	20
Discharge per vagina	36	36
Total	100	100

Table-5 : Distribution of patients by associated Risk Factors

Risk factors	No.	Percentage (%)
Early resumption of work after delivery	49	49
Lifting heavy weight	45	45
Chronic constipation	30	30
Chronic cough	9	9
Total	100	100

Fig-3 : Distribution of patients by Relation of Prolapse with menopause (oestrogen deficiency) as a risk factor.

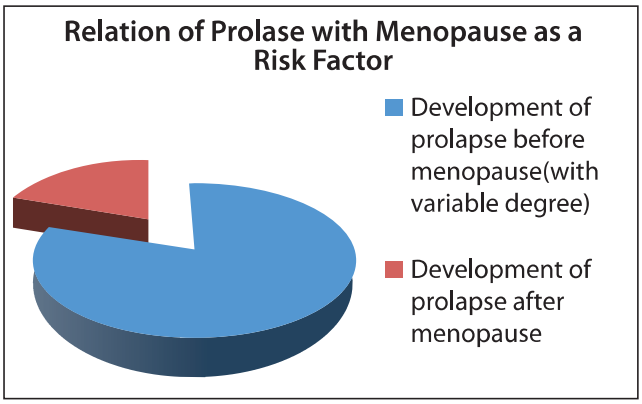

Table-6 : Distribution of patients by degree of anemia

Anaemia	No. of Patients	Percentage (%)
Not anaemia	30	30
Mild anaemia	53	53
Moderate anaemia	17	17
Severe anaemia	0	0

Discussion

In the present study, age of the patients ranged from 20-70 yrs. Highest incidence 38% was found in the age group 40-49 yrs. The incidence is also nearer to incidence in other developing countries[6,11], but does not correlate with the age incidence of developed countries like California[4], where it was shown that peak age incidence is 50-89 yrs. In the developed countries life expectancy is more than developing country again process plays more important role in development of prolapse. In developing country early age incidence is due to early marriage and high parity at a younger age[8].

In the present study, 99% of deliveries were conducted at home by TBA or by Dai. 99% women were multipara. Fifty two percent of the patients had difficult and prolonged labour, 49% of the patients did not take proper nutrition adequate rest during puerperium instead did heavy household works during puerperium. Early resumption of heavy works before revert back of pelvic organs to their normal anatomical position, is attributing factor in developing prolapse. These findings suggest that there is some mismanagement in conduction of labour and also of puerperium that resulted in development of prolapse[10].

If it considers about the inherent weakness of pelvic supportive tissue, this might have been there. But here the women in this study did not observe any protrusion of tissue per vagina before child birth and 80% of them developed features of prolapse after the first or subsequent difficult child birth, which suggest birth trauma is the main causative factor of developing prolapse of the women[7]. Many patients had aggravation of mild symptom after menopause. Estrogen deficiency in previously traumatized pelvic floor (during child birth), might have cause further weakening of the pelvic supports. Regarding relation of prolapse with menopause, 80% observed protrusion of variable degree before menopause and 20% patients developed prolapse after menopause. In these cases causative factor would be oestrogen deficiency leading to atrophy of pelvic supports[5].

Associated risk factors like chronic cough was present 9% cases, chronic constipation in 30% cases, heavy works like lifting heavy weights was in 45% cases. All these factors causes chronically increase in intra abdominal pressure attributing to genital prolapse[12].

In the study, genital bulge, i.e. protrusion of tissue per vagina was the commonest symptom, which was 100%. Pelvic heaviness which is earlier symptom was found in 9% cases. Increased frequency of micturation was in 44% cases, burning sensation during micturation in 38% cases, difficulty in emptying bladder was in 34% cases, urinary incontinence in 20% cases. Discharge per vagina and backache were present in 36% & 34% cases respectively. In the study made by Evauf, Prebeuk in Sweden, 15% of patients reported pelvic heaviness, 4% genital buldge and 12% difficulty in defaecation[9]. The incidence of protrusion of tissue per vagina is much lower in this study. This is probably due to conscious patients in the developed countries who seek medical care earlier.

Out of 100 patients, 53% of the patients had mild and 30% had no anaemia. A study in Gambia showed significantly increased odds of prolapse in the presence of moderate or severe anaemia compared with those who were non-anaemic and mildly anaemic[9]. Present study is not consistent with this observation. In this study, most of the patients were from low socio-economic backgrounds, which correlate with the comment by Lukman that under-nutrition which is more pronounced in poor people, as cause of poor tissue tensile strength of the pelvic supporting system may be a possible co-factor in the pathogenesis of pelvic organ prolapse[3]. Poor socioeconomic conditions also suggest poor maternity service, was the most important social factor for genital prolapse.

Conclusion

Women in Bangladesh constitute a high risk group for genital prolapse because of lack of maternity health service. Maternity care during antenatal, intranatal and postnatal period will provide safe motherhood and good obstetric practice. All these measures will lower the rate of development of genital prolapse. Correction of chronic cough and constipation, avoidance of heavy physical works are also necessary to lower the incidence of genital prolapse. Our government and many non-government organizations are trying to provide maternity health services and updating the training program for skilled birth attendant and it is hopeful that these services will lower maternal mortality and morbidity along with minimizing the incidence of genital prolapse.

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Original article

In vitro evaluation of the quality of different trade brands of Co-Trimoxazole tablet formulation by qualitative assay methods

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Abstract

Objectives : In vitro evaluation of different trade brands of co-trimoxazole tablet formulation was done in this study by conducting assay of different quality control parameters like average weight, friability, disintegration & hardness test.

Methods : This was a cross sectional analytic study done from July, 2007 to June, 2008. A total sixty tablets from each batch of different trade brands were collected from the local market & evaluated by the qualitative assay methods.

Result : Quality control parameters of most of the brands were within normal limits of BP standard (Disintegration time-15 mins, Hardness-4-10 kg, Friability <1 % weight loss, Average weight 444 –516 mg for single strength & 888-1032 mg for double strength formulations except excipients). Four batches of different trade brands (Code U,O,S,N) did not comply with BP standard. Disintegration time of Code U (37.50 mins.) exceeded the normal limit & the Code O just reached the upper limit (14.58 mins) of normal. Hardness of Code O (4.02 kg) was at the lower limit of normal. Code O completely failed in friability test and Code S (10.65% weight loss) exceeded the normal limit. Average weight of Code N (821.26 mg) was below the normal limit of BP specification.

Conclusion : This study included only 17 trade brands which are not sufficient to generalize widespread existence of substandard preparations of co-trimoxazole. It needs further similar studies by taking more number of samples.

Key words: In vitro, evaluation, quality, co-trimoxazole, qualitative assay

Introduction

The use of ineffective and poor quality drugs may lead to serious health hazards including treatment failure, adverse drug reactions, development of drug resistance, increased morbidity and mortality. Drug quality is a great concern worldwide, particularly in many developing countries. Recent reports indicate that the availability of substandard drugs has reached in a disturbing proportion in resource -poor settings, such as in most Asian countries. The reported percentage of substandard drugs range from 2% to >60%[1]. Quality assessment study of some of the marketed drug product could give an insight into the quality of the products[2]. Co-trimoxazole is a combination of sulfa methoxazole (SMZ) & trimethoprim (TMP).

During the last three decades co-trimoxazole had occupied a central role in the treatment of various infections & has also been particularly useful for several other specific clinical conditions. However, changing resistance patterns and the introduction of newer broad-spectrum antibiotic have led to the need to carefully redefine the appropriate use of this agent in clinical practice[3].

Suspicion and concern about the quality of co-trimoxazole in the market are due to its;

- easy availability and
- popularity in our country as a broad spectrum agent against a variety of infections
- high consumption rate
- inclusion in essential drug list
- previous reports of being substandard.

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Our government has limited manpower and facilities to cope with the country's fast expanding pharmaceutical sector. There are only two drug testing laboratories and 37 drug supervisors for entire country, which account for the poor supervision in this sector.

Quality test of drug can be performed in any medical college laboratory. This may reduce the burden on central drug testing laboratory which is always overburdened with sample testing from all over the country. So drug administration of Bangladesh will be able to utilize the medical college laboratories (pharmacology and biochemistry) for random testing of alleged and suspicious samples from the market in a cost effective way.

So, this study was done to ascertain the general standard of quality of different trade brands of Co-trimoxazole tablet formulation in our country and to suggest means for detection of substandard drugs in a cost effective way.

Materials and methods

This cross sectional analytic study was done in the Department of Pharmacology & Therapeutics, Sher-E-Bangla Medical College and the Chemist Laboratories Limited, Barisal during the period of one calander year from July, 2007 to June, 2008.

Samples : A total of 21 batches of co-trimoxazole tablet formulations from 17 trade brands, of which 8 batches were of single strength & rest 13 batches were of double strength formulations were collected from the local market by convenient sampling. Coding was done to avoid bias. Decoding was not done as it was not the objective of investigator to identify any alleged manufacturers. Sixty tablets from each batch were taken for evaluation of drug quality. All the samples were within their expiry dates.

Tests of some physical parameters such as average weight, friability, hardness and disintegration were done in the qualitative assay. The results were analyzed manually and were presented in tables.

Apparatus : (1) Metler Balance 2) Tablet Disintrigration Test Apparatus (3) Tablet Friability Test Apparatus (4) Manual Hardness Tester.

Methodology

Average weight : Ten tablets from each batch of different co-trimoxazole tablet formulation were taken. Each tablet was weighted individually on metler balance & average weight of ten tablets was determined.

Hardness test : Five sample tablets from each batch of different co-trimoxazole tablet formulation were taken. One sample tablet was mounted on the edge of the hardness tester and piston was screwed until the tablet was held lightly in the extreme end of the tester. The weight mark of this point was recorded as the 1st weight. Then the piston was screwed up to the point at which the tablet breaks up and the weight at this broken point was recorded as 2nd wt. The hardness of the tablet was calculated by subtracting the 1st wt from the 2nd wt. In this way hardness of other 4 sample tablets was calculated and the mean hardness was recorded. That was the hardness of that specific batch of specific trade brand.

Friability test : Ten sample tablets from each batch of different co-trimoxazole tablet formulation were taken. The total weight of 10 tablets was taken by metler balance (1st wt), then these 10 tablets were placed in the drum of the friability tester. The drum must be cleaned before. The drum was rotated 100 times and tablets were removed from the drum. Any loose dust was removed from the tablets and again weighed the tablets (2nd wt).

Then the friability of those tablets was calculated by using following formula;

$$\text{Friability weight loss} = \frac{\text{1st wt} - \text{2nd wt}}{\text{1st wt}} \times 100\ \%$$

Disintegration time test : Five sample tablets from each batch of different co-trimoxazole tablet formulation were taken & placed in five tubes of disintegration time tester, a disc was added to each tube. The assembly was suspended in the beaker containing distilled water inside the tester, then the tester was started and the state of the tablet was observed. The time was noted at which the first and the fifth tablet were completely disintegrated. This time range was taken as disintegration time for specific batch of specific trade brand. All samples were assayed according to methods outlined in the individual drug monographs of the BP 2007, except for dissolution test which used USP-32[4].

Procedures for qualitative assay are given in the appendix.

Result

In the present study qualitative analysis of different trade brands of co-trimoxazole tablet formulations was done.

Table-1 : Distribution of table according to average weight, Disintegration Time, Friability and Hardness of co-trimoxazole tablet formulation of different trade brands (single strength formulation):

Sample Code	Avg. wt. (mg)	Disintegration Time (secs)		Friability (%wt loss)	Hardness (kg)
		Range	Avg		
A	619.69	7-12	10	0.69%	7.90
B	607.81	95-120	112	0.33%	7.66
C	562.82	51-90	40	0.79%	4.40
D	619.36	12-18	15	0.44%	7.05
E	613.94	32-52	42	0.55%	8.10
F	520.72	246-315	280	0.42%	5.85
G	595.64	18-30	24	0.95%	6.85
H	550.55	76-132	104	0.96%	5.80

Table-2 : Distribution of table according to average weight, Disintegration Time, Friability and Hardness of Co-trimoxazole tablet formulation of different trade brands (double strength formulation):

Sample Code	Average wt (mg)	Disintegration Time (secs)		Friability (%wt loss)	Hardness (kg)
		Range	Avg		
I	1061.07	35-45	40	0.12%	10.00
J	1008.16	58-65	62	0.22%	10.05
K	1007.73	183-415	299	0.39%	10.15
L	1007.54	30-130	80	0.50%	10.00
M	1014.94	75-126	100	0.51%	10.15
N	821.26	400-480	440	0.94%	6.75
O	919.95	850-900	875	Failed	4.02
P	1080.54	60-480	270	0.31%	10.15
Q	1005.27	74-106	90	1.06%	10.15
R	992.29	20-55	37	1.01%	10.00
S	1058.37	15-45	30	10.65%	8.10
T	1058.15	215-270	242	0.43%	10.05
U	1064.58	2223	2223	0.48%	10.15

According to British Pharmacopoeia Disintegration Time limit up to 15 minutes for uncoated tablet formulation, Friability <1% weight loss, Hardness 4-10 kg & the limits for Average weight varies from 444 - 516 mg (excepting exipients) which correspond to quantity of active ingredients of Sulfamethoxazole and Trimethoprim (92.5 to 107.5 %). Table-1 showing the average weight, disintegration time, friability and hardness of single strength of co-trimoxazole tablet formulations in which average weight varied from 520.72 - 619.69 mg (including exipients), disintegration time varied from 10-280 seconds, hardness varied from 4.40 - 8.10 kg, friability varied from 0.33- 0.96 % weight loss.

Table-2 showing the average weight, disintegration time, friability and hardness of double strength formulation of co-trimoxazole tablet in which average weight varied from 821.26-1080.54 mg, disintegration time varied from 30 sec to 2223 sec (37.05 min), hardness varied from 4.02-10.15 kg, friability varied from 0.12-10.65 % weight loss & average weight varied from 821.26 mg -1080 mg.

Discussion

In this study, researcher analyzed the quality of different trade brands of Co-trimoxazole tablet formulations available in the local market. For this, different quality control parameters, such as Disintegration time, Friability, Hardness & Average weight were assayed by using methods given in British Pharmacopoeia.

Two batches of two trade brands did not comply regarding disintegration time. Disintegration time of one batch (code U - 2223 sec/37.05 min) exceeded the normal limit & another batch (code O - 875 sec) just reached the upper limit of normal. A study done in Nigeria in 2010 showed that 1 out of five(20%) co-trimoxazole tablet formulations was failed in disintegration time test[5]. This finding is not in agreement with the finding of the present study. This inconsistency may be due to very small number of samples in their study which gave increased percentage of disintegration time test failure.

In friability test most of the samples were within normal range of British Pharmacopoeial specification (<1% weight loss) except for two batches of two trade brands. One batch failed in friability test (code O - double strength formulation) and friability of another batch (code S-10.65% weight loss) exceeded the normal range of <1% weight loss according to British Pharmacopoeia. In a study 2 out of 11 co-trimoxazole tablet formulations

(18.18%) failed in friability test[4]. This finding is not similar with the finding of present study. This inconsistency may be due to less number of samples used in their study which gave increased failure rate in friability test.

Only one sample Code no O, had a hardness of 4.02 which is just around the lower limit of normal (4-10 kg). Average weight of most formulations was within normal range exceptone batch (code N -821.26) which is below the normal range. Hardness & average weight could not be compared with other studies because of the unavailability of concrete data from existing literature.

No attempt was made to find out the cause of poor quality of the drug. The co-trimoxazole trade brand that failed in quality test might be due to poor manufacturing practice, inadequate quality assurance or control, or possible decomposition of the raw materials. The decomposition is possible when drugs are stored under conditions conducive to chemical degradation of the active ingredients particularly in tropical countries.

This study included only 17 trade brands which are not sufficient to generalize widespread existence of substandard preparations of co-trimoxazole. This needs to be confirmed by further similar studies by taking more number of samples. Moreover bioequivalence study of various brands of co-trimoxazole may also reveal the existence of substandard preparations. So bioequivalence study may be conducted in future such study. As our drug administration has limited facilities to cope with the detection of suspicious samples from the market, the medical colleges can be utilized for detection of substandard drugs. The department of pharmacology and biochemistry can help sample analysis and reduce the burden on drug testing laboratories.

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Original article

A clinicopathological study on dysfunctional uterine bleeding at perimenopausal age group

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Abstract

Objective : Dysfunctional uterine bleeding is a form of abnormal uterine bleeding when there is absence of organic disease of the genital tract. The objective of this study was to find out the clinical and pathological aspect of women presenting with dysfunctional uterine bleeding at perimenopausal age group.

Methodology : It was a hospital based prospective observational study carried out in the Department of Obstetrics and Gynaecology, Ad-Din Women's Medical College Hospital, Dhaka. Total 62 consecutive patients of DUB who were admitted selected for the study population from July 2011 to March 2012. The clinical presentation and histopathological reports (following dilatation and curettage or hysterectomy) of 62 DUB patients were observed. Twelve of these patients subsequently found to have organic pathological conditions were excluded from the study. Data was analyzed statistically.

Results : Of the studied 62 patients 44 (70.96%) were found to have DUB, 12(19.35%) had organic pathology, and rest 6(9.67%) were found to be normal. Histopathological findings revealed 28(63.63%) cases had proliferative endometrium, 6 (13.6%) had secretory endometrium, while 4 (9.09%) had cystic hyperplasia, only one (2.27%) had atypical hyperplasia and 3(6.8%) cases had atrophic endometrium.

Conclusion : Despite the low incidence of endometrial atypical hyperplasia and carcinoma in perimanopausal women, but they do occur.

Key words : Dysfunctional uterine bleeding, perimenopausal age group, endometrial thickness, LNG-IUS, thermal ballon ablation.

Introduction

Dysfunctional uterine bleeding is a common problem. It affects women's health both mentally, physically and socially. Among women aged 30 to 49 years, one in 20 consults her general practitioner each year with menorrhagia, making DUB one of the most often encountered gynaecological problems. About 30% of all women report having had menorrhagia, and it accounts for two thirds of all hysterectomies and most of the endoscopic endometrial destructive surgery[1].

The generally accepted definition of dysfunctional uterine bleeding is abnormal uterine bleeding which occurs without any clinically detectable organic, systemic and iatrogenic causes[2]. In half of women with menorrhagia there is no organic cause. So, DUB is a diagnosis of exclusion. As DUB can occur during the life span of a woman any time from menarche to menopause but commonly occurs in two extremes of life. About 10% of outdoor patients in gynae department present with DUB[3].

In the first 18 months after menarche, the immature hypothalamo-pituitary-ovarian axis may fail to respond to estrogen and progesterone, resulting in anovulation[4,5] In obese women, the non-ovarian endogenous estrogen may upset the normal menstrual cycle[6].

As menopause approaches, decreases in hormone levels or irresponsiveness to hormones also may lead to anovulatory DUB.

The term includes a variety of separate entities such as mid-month staining, premenstrual staining, normal uterine bleeding occurring at larger than normal interval, profuse or prolonged uterine bleeding of normal duration. The pathology of dysfunctional uterine bleeding is largely unknown, but it occurs in both ovulatory and anovulatory menstrual cycles[4].

Ovulatory dysfunctional uterine bleeding occurs secondary to defects in local endometrial haemostasis, such as (i) Local disorder of prostaglandin receptors in the endometrium (ii) increase of fibrinolytic activity in the endometrium (iii) increase in capillary fragility.

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Anovular type of bleeding present in 10% of reproductive age group probably represents dysfunction of hypothalamic-pituitary-ovarian axis resulting in continued estrogenic stimulation of endometrium. Anovolar type of bleeding occurs due to systemic disorder, secondary to endocrine, neurochemical or pharmacological mechanisms[5].

In most patients dysfunctional uterine bleeding associated with anovulation, and anovulatory bleeding is common in the pubertal and perimenopausal periods. During these transitional states, the abnormal bleeding has a physiological basis and is secondary to an oestrogen withdrawal. Anovulatory bleeding can also be associated with chronic anovulation. The chronic unopposed oestrogen that characterizes this disorder causes a continuous proliferation of the endometrium. This can result in abnormal bleeding and increases the risk of developing endometrial cancer. Only 2% of endometrial cancer occurs before age 40. The goals of treatment for anovulatory bleeding are to stop the acute bleeding, avert future episodes, and prevent long term complications.

In contrast to normal menstrual cycles which are characterized by a regular balance between gonadotrophin & ovarian hormone resulting in ovulation and cyclical uterine bleeding is chacraterized by an imbalance between adenohypophysis and ovary. Since the endometrium is the target of this endocrine imbalance, abnormal bleeding is merely a symptom of endocrine dysfunction[7].

Diagnosis should be suspected by history along with meticulous examination and confirmed by endometrial biopsy.

Methodology

It was a hospital based prospective observational study. Total 62 patients were selected in this study according to inclusion criteria.

Inclusion criteria

All the patients with abnormal uterine bleeding without any organic or systematic causes were included in this study.

Exclusion criteria

Patients with abnormal uterine bleeding but having organic or systematic causes were excluded.

Results

The study revealed that of the 62 cases 70% were in the age group of 45-52 years and only 12% of cases fall in age group of 53-55 years (table-1). Forty two percent patients had menorrhagia and only 4% had sudden 2/3 bouts of bleeding in postmenopausal women. Other clinical presentations were polymenorrhagia 32%, polymenorrhoea in 14% and continuous bleeding in 8% of the cases (table-2).

Through trans-vaginal ultrasonography (TVS), endrometrial hyperplasia was detected 66%. Endometrial atrophy was found 4% and 30% patients had normal endometrium (table-3). According to Histopathology only 12(19.35%) had organic pathology (table-4). Of the 12 patients with organic pathology, 41.66% were suffering from fibroid uterus, 25% had adenomyosis, 16.66% had endometrial polyp. Equal number of patients had (8.33%) carcinoma cervix and pelvic inflammatory disease (table-5).

All of 44 DUB cases' samples sent to histopathology laboratory for tissue diagnosis. Findings include 28(63.63%) cases had proliferative endometrium, 6 (13.6%) had secretory endometrium, while 4 (9.09%) had cystic hyperplasia, only one (2.27%) had atypical hyperplasia and 3(6.8%) cases had atrophic endometrium (table-6).

Among 50 patients, medical treatment was received by 35 where synthetic progesterone was used in 24 (68.57%), combined pill in 6 (17.14%) and tranexamic acid in 5 (14.28%). In case of surgical intervention among 44 patient only curettage was done in 10 (22.72%), curettage with hysterectomy in 8 (18.18%), medical therapy with hysterectomy in 8 (18.18%), medical therapy with curettage and hysterectomy in 14 (31.81%) and lastly direct hysterectomy in 4 (9.09%).

Table-1: Distribution of patients according to age group (n-60).

Age group	Number	Percentage (%)
40-44	9	18
45-48	23	46
49-52	12	24
53-55	6	12
Total	62	100

Table-2 : Distribution of patients by to various clinical presentation of (DUB) (n=50)

Category	No. of patients	Percentage %
Menorrhagia	21	42
Polymenorrhoea	7	14
Polymenorrhagia Sudden 2/3 of bleeding in postmenopausal	16	32
women	2	4
Countinuous	4	8

Table-3 : Distribution of patients by to Ultrasonographic (TVS) findings of endometrial thickness (n=50)

Category	No. of patients	Percentage %
Hyperplasia	33	66
Atrophic	2	4
Normal endometrium	15	30

Table-4 : Distribution of patients by histopathology findings.

Category	No. of patients	Percentage %
DUB	44	70.96
Organic pathology	12	19.35
Normal endometrium	6	9.67

Table-5 : Distribution of the patient according to organic pathology n-12

Category	No. of patients	Percentage %
fibroid uterus	5	41.66
adenomyosis	3	25
endometrial polyp	2	16.66
pelvic inflammatory disease	1	8.33
carcinoma cervix	1	8.33
Total	12	100

Table-6 : Distribution of patients by Histopathological findings of endometrium (n=44)

Category	No. of patients	Percentage %
Profilerative phase	28	63.60
Secretary phase	6	13.60
Atrophic endometrium	3	6.80
Cystic hyperplasia	4	9.09
Atypical hyperplasia	1	2.27

Table-7 : Distribution of patients by Mode of treatment of DUB patients in present series (n = 50)

Mode of treatment		No.	Percentage %
Medical (n = 35)	Synthetic progesterone	24	68.57
	Oestrogen & Progesterone (Combined pill)	6	17.14
	Tranexamic Acid +NSAID Naproxen)	5	14.28
Surgical (n = 44)	Curettage only	10	22.72
	Curettage followed by hysterectomy	8	18.18
	Medical therapy followed by hysterectomy	8	18.18
	Medical therapy+curettage followed by hysterectomy	14	31.81
	Direct Hysterectomy	4	9.09

Discussion

Regarding age group these findings were somehow comparable to study done by Muzaffar et al[8].

In a study of 1000 cases of DUB, Sutherland found that 14% patients had organic pathology. In another study, 20 patients (20%) out of 100 cases showed organic pathology9, in the study done by Banerjee, 20 patients (28.5%) out of 70 showed organic pathology[10] which were more or less similar to the present study.

DUB patients may come with different types of menstrual disorders e.g menorrhagia, polymenorrhagia, polymenorrhoea, metrorrhag ia even intermenstrual bleeding. But most common form is functional polymenorrhoea and polymenorrhagia. Jeffcoate stated that 50% patients present with DUB with polymenorrhoea and polymenorrhagia[11].

Begum showed 78% had menorrhagia, 12.5% polymenorrhoea and polymenorrhagia, 8.75% continuous bleeding and 1-2% had intermenstrual bleeding[9]. In the study reported by Banerjee, 54% had menorrhagia, 30% polymenorrhoea and 14% continuous bleeding[10]. In the present study, 42% suffered from cyclical bleeding, 32% had polymenorrhagia, 14% had polymenorrhoea and 4% had post menopausal bleeding which is more or less similar to Jeffcoate study[12].

USG is a valuable tool in evaluating women presenting with a complaint of abnormal vaginal bleeding by demonstrating anatomic finding frequently not discernible on pelvic examination, such as small cyst leiomyoma and even endometrial carcinoma and in

evaluating the endometrium in terms of its thickness. USG can also be of value in confirming some diagnoses that are generally made clinically by exclusion such as break through bleeding from oral contraceptive[1].

Goldstein et al. studied of 111 cases, by TVS, found that 31(27.9%) women had an abnormal endometrium hyperplasia in 13.5%, polyps in 5.4%, sub-mucous myoma in 5.4% and adenocarcinoma in 3.6%[13].

In this study USG was done mainly by TVS route and 66% revealed hyperplasia, 30% normal and 4% atrophic endometrium.

In another study the two most common findings were proliferative and secretory endometrium. This finding is similar to the other studies[14]. Endometrial hyperplasia is a precursor of endometrial cancer. The incidence of endometrial hyperplasia without and with atypia peaks in early 50's and early 60's respectively[15,16].

In the study by Vercillini et.al histopathological report of endometrium showed atypical hyperplasia in (0.7%) and endometrial carcinoma in (0.5%) in her group-3 (45-50 years)[17]. Histopathological findings of the present study, was about similar to the above studies.

In choosing the most appropriate and effective medical treatment, some help may be gained from endometrial histology in the second half of the cycle.

Progesterone may be used to arrest severe uterine bleeding by large dose in case of endometrial hyperplasia or administered cyclically either in second half (from 15th to 25thday), particularly with premenstrual spotting or throughout the cycle (15thto 25th day) in cases of endometrial hyperplasia. Fraser treated 10 women with ovulatory menorrhagia with progesterone at a dose of norethisterone 5 mg three times daily or MPA 10 mg three times from day 5 to 215. Similarly high dose of NE in 22 women decreased MBL significantly[11].

In the study by Begum, 26 patients were treated by synthetic progesterone. In the present study, 24 out of 35 patients were advised synthetic progesterone. Twenty two patients had good cycle control after 3-6 months of regimen. In 4 patients bleeding had controled during taking drug but started to bleed again when drug was discontinued. One patient responded poorly and 2 did not come for follow up. Progesterone acts better in anovular bleeding.

Combined OCP has great advantage of correcting any abnormality of menstrual cycle and producing regular bleeding as well as reducing the amount MBL. In the study by Begum, 11 patients were treated by low- dose oral contraceptive cyclically for 3-6 months. Of these patients, 8 resumed normal cyclical bleeding later on, failure occurred in 3 in the form of break through bleeding or irregular bleeding. In the study by Banerjee, 8 patients treated by OCP for 3-6 months in a cyclical bleeding and success rate were 100%[10].

In present study, 11 patients were advised to continue, OCP as they were taking pills and their bleeding was under control. 8 patients were symptom free for 3-6 months and in 3 patients, response was not satisfactory. Response was more or less similar to first reference.

Antifibrinolytic agents are potent inhibitor of fibrinolysis and have shown to normalize or reduce MBL in 50% case. It is effective in most types of menorrhagia, Milsum, Bonner and Sheppard18 treated 75 cases with tranexamic acid, of which 75% showed reduction in bleeding. In present study, 5 patients were treated by tranexamic acids. Among them 3 patients were symptom free for 3-6 months and 2 patients developed spotting. Response rate was quite satisfactory.

Hysterectomy is justified when conservative treatment fails and blood loss impaired the health of the patient. Presence of endometrial hyperplasia with atypia is an indication of hysterectomy. In the study, by Begum, 50 patients out of 80 (62.5%) underwent hysterectomy who had previous curettage but showed no improvement, 33 patients had direct hysterectomy and all of their families were complete. Banerjee in his study showed that 33 out of 50 patients (66%) underwent hysterectomy and 21 patients were 41-45 years of age and 12 were above 45 years. In the present study, 34 patients out of 50 had hysterectomy. Among them, 4 had hysterectomy as primary treatment and the remaining 8 patients had medical treatment followed by hysterectomy and 14 patients had medical treatment and curettage followed by hysterectomy and 8 patients had curettage[18].

Conclusion

The present study showed DUB most common in perimenopausal age group (>40 years). Histopathological evaluation of endometrium helps exclude the local causes and establishes the diagnosis of DUB, clinical correlation to histopathological findings and finally helps to determine the mode of management.

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Review article

Placental morphology and anemic pregnancy: morphology of Placenta significantly changes in anemic pregnancy

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Abstract :
Placenta is the vital organ for the maintenance of a normal pregnancy. Fetal growth and well-being depend on the functional and structural component of the placenta because Placenta is the home for this spirit! soul for nine months. Anaemia in pregnancy is common and one of the risk factor in pregnancy . Foetal hypoxaemia develops consequent to maternal anaemia and stimulates placental growth. In anaemia, significant changes are occurring in gross morphological structure of the placenta. The ability of the fetus to grow and prosper in uterus is presumed to be a function of the placental surface area available for the exchange of respiratory gases and nutrients. So, ultimately anaemia has a great impact on health of fetus as well as mother.

By the application of proper knowledge about morphological changes of placenta in anaemic pregnancy, both the maternal and fetal well being can be maintained.

Keywords : maternal anaemia, gross morphology of placenta,.

Introduction

Pregnancy is a healthy and welcoming process and children are God's blessing to a couple as well as to that family. Bangladesh is a developing country. Anaemia is one of the most common risk factors in the area of obstetrics and perinatal medicine. Anaemia in pregnancy is associated with an increased incidence of both maternal and fetal morbidity and mortality 87% of women have nutritional anaemia in pregnancy due to iron deficiency Maternal mortality due to anaemia in Bangladesh was 4% in1991[1]

Most of the female in child bearing age have mild to moderate degree of anaemia due to nutritional deficiency According to WHO, a level of Haemoglobin below 11 gm/dl during pregnancy is an indication of anaemia. But in South Asia, anaemia is diagnosed when the lowest antenatal haemoglobin is <lOg/d[2]. Placenta is an organ that is essential to the survival of the fetus of the mammals. Placental hypertrophy associated with maternal anaemia, which is probably a compensatory physiological response to ensure adequate oxygen supply to the fetus[3] Maternal anaemia causes the development of a big placenta[4].

It undergoes continuously throughout gestation a morphological changes such as in weight, structure, shape, and function in order to support prenatal life[6]. Babies born with a disproportionately large placenta are at greater rick for hypertension in later life[5]. Examination of the placenta can yield information that may be important in the immediate and later management of mother and infants. A one minute examination of the placenta performed in the delivery room provides information that may be important to the case of both mother and infant.

Anatomical and physiological background of placenta :

Placenta [plusen´tu] Pronunciation Key or **afterbirth**, organ that develops in the uterus during pregnancy. Placenta may be defined as any intimate apposition or fusion of fetal organs to maternal tissues for the purpose of physiological exchange[5]. It is an unique characteristic

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of the higher (orplacental) mammals.

The human placenta is a discoid, deciduate, haemochorial chorioallantoic placenta (DeCherney 2003) due to maternal blood comes into direct contract with the foetal trophoblast.

Placenta at term, an average volume of some 500 ml (range 200 - 950 ml), average weight about 500g (range 200-800 g), average diameter 18.5 cm (range 15.0-20.0 cm), average thickness 2.3cm (range 1.0-4.0 cm) and an average surface area of about 300 cm^2. Thickest at its centre (the original embryonic pole) it rapidly diminishes in thickness towards its periphery where it continues as the chorion leave[6].

Macroscopically, its foetal or inner surface, covered by amnion, is smooth, shiny and transparent and the mottled appearance of the subjacent chorion. The umbilical cord is attached near the center of the foetal surface, and branches of the umbilical vessels radiate out under the amnion from this point, the veins being deeper and larger than the arteries. Variations in this arrangement are possible - sometimes the umbilical cord is attached to the edge of the placenta or even to the membranes beyond the margin of the Placenta - but these differences appear to have little effect on normal function. Maternal surface is rough and spongy. Maternal blood gives it a dull red color (Dutta, 2003). The maternal surface is finely granular and mapped into some 15-30 lobes by series of fissures or grooves. The lobes are often somewhat loosely termed cotyledons and the grooves correspond to the bases of incomplete placental septa. The Maternal portion of the placenta amounts to less than one fifth of the total placenta. Only the decidua basalis and the blood in the intervillous space are of maternal origin[7].

Placental circulation

Placental circulation consists of independent circulation of blood in two systems :

- Utero-placental circulation
- Feto-placental circulation

Uteroplacental Circulation

(Maternal circulation):

It concerns with the circulation of maternal blood through the intervillous space. A villi system and 150 ml lying in the intervillous space. As the intervillous blood flow at term is estimated to be 500-600 ml per minute, the blood in the intervillous space is completely replaced about 3 to 4 times per minute. The villi depend on the maternal blood for their nutrition, thus it is possible for the chorionic villi to survive for a varying period even after the fetus is dead. The pressure within the intervillous space is about 10 to 15 mm Hg during uterine relaxation and 30-50 mm Hg during uterine contraction. In contrast, the fetal capillary pressure in the villi is 20-40 mm Hg[8].

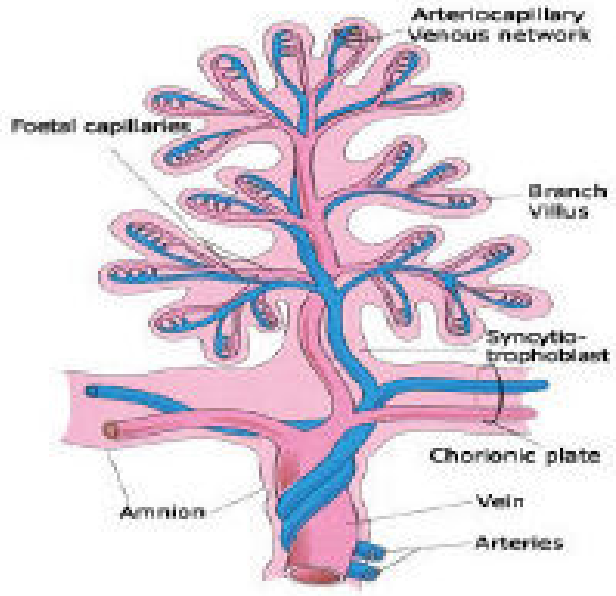

Fig-1 : Foetal Circulation through placenta (from Collins, 2005)

Feto-placental circulation

The two umbilical arteries carry the impure blood from the fetus. They enter the chorionic plate underneath the amnion, each supplying one half of the Placenta. The arteries break up into small branches, which enter the stems of the chorionic villi. Each in turn divides into primary, secondary and tertiary vessels of the corresponding villi. The blood flows into the corresponding venous channels either through the terminal capillary networks or through the shunts (Fig. 01). Maternal and fetal blood streams flow side by side, but in opposite direction. This counter current flow facilities maternal exchange between the mother and fetus. The villus capillary pressure varies from 20-40 mm Hg. The fetal blood flow through the placenta is about 400 ml per minute. This is mainly facilitated by the pumping action of the fetal heart[8].

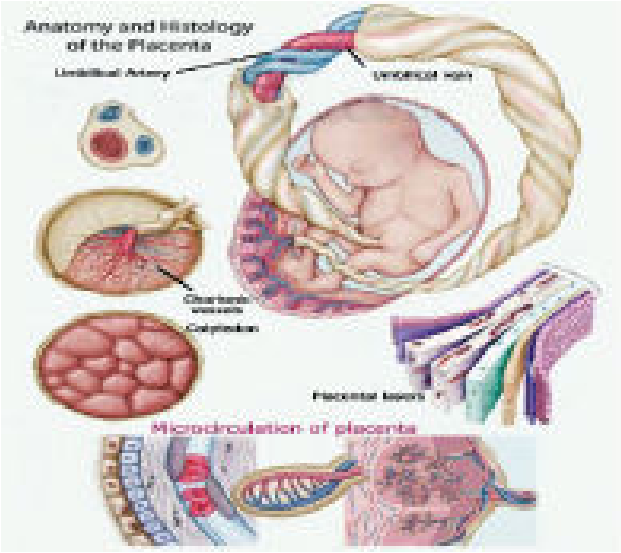

Fig-2 : Showing the gross morphology and histology of placenta (from science-art.com)

Structure of the placenta

Placental tissues are arranged as chorionic plate, basal plate and, between the two villus stem, their branches and the intervillous space.

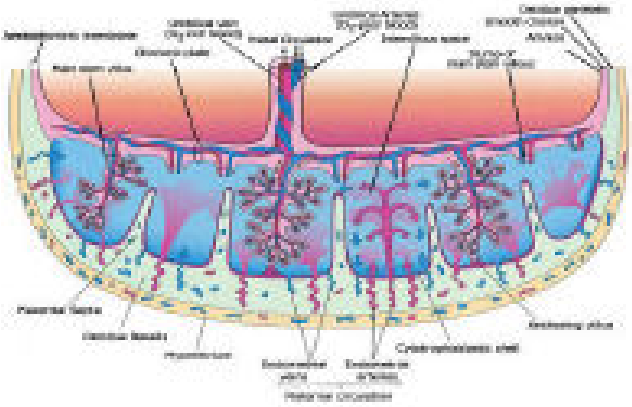

Fig-3 : Photograph of fine dissection of placenta showing the vascular pattern of chorionic vessels

Development of the placenta

The placenta has two parts, develop from two different individual. Chorionic frondosum froms fetal part and decidua basalis froms maternal part.

Placental barrier

In spite of close proximity, there is no mixing of the maternal and fetal blood. The two are separated by tissues called placental membrane or barrier. In early pregnancy, it consists of :

(1) syncytiotrophoblast

(2) cytotrophoblast

(3) basement membrane

(4) stromal tissue and

(5) endothelium of the fetal capillary wall with its basement membrane.

The endothelium is about 0.025 mm thick. Near term, there is attenuation of the syncytial layer.

Physiology of Placenta.

The placenta is attached to the uterus, and the fetus is connected to the placenta by the umbilical cord. The placenta draws nourishment and oxygen, which it supplies to the fetus, from the maternal circulation. In turn, the placenta receives the wastes of fetal metabolism and discharges them into the maternal circulation for disposal. It also acts as an endocrine gland, producing estrogen, progesterone, and gonadotrophin.

Shortly after delivery of the fetus the placenta is forced out by contractions of the uterus. Severe hemorrhage may occur if the placenta does not emerge in its entirety or if the uterus fails to contract properly.

It could be said that the placenta puts a little 'PEP' into the baby's life by being involved in production, exchanges, and protection[9].

Pathophysiology

The architecture of the placenta has been claimed to be changed in maternal diseases like anaemia[2,11,13,] hypertension,[12.13] & eclampsia[10]. Although to some extent these changes may be compensatory responses.

Role of Hb= O_2 transport from lungs to tissues, decrease, causes tissue hypoxia, responsibl e for all manifestations of anaemia [Dora Mbanya].

The placental weight higher in the iron deficiency group compared with control group.Thangaleeta, et al. in 1994 Teasdale, 1980 studied with 17 placentas between mid-gestation to term in only normal pregnancy. He observed that two stages are clearly discernible in the development of the human placenta. The first stage of growth, which terminates at approximately 36 weeks of gestation, is characterized by a progressive increase in parenchymal components. The second stage, which extends from around 35 weeks to term, is called the maturation stage because it is characterized by

substantial fetal growth but without any increase in placental functional tissues.

In 2006, Baumann et al. observed hypoxia in any condition such as anaemia causes reduced birth weight due to reduced blood flow and oxygen delivery. Placental weight was higher in anaemic group as compared to the controls[4]. They observed that there was a significant difference in both the placental weight and placental diameter among the different groups and grossly calcification were more in anaemic group.

Anaemia and pregnancy:

Anaemia is one of the most common risk factors in the area of obstetrics and perinatal medicine. Anaemia in pregnancy is associated with an increased incidence of both maternal and fetal morbidity and mortality[11].

About 87% of women have nutritional anaemia in pregnancy due to iron deficiency (ICMR Bull 2000). According to WHO, a level of Haemoglobin below 11 gm/dl during pregnancy is an indication of anaemia. But in South Asia, anaemia is diagnosed when the lowest antenatal haemoglobin is <10g/dl[14]

In Global Perspective iron deficiency is the most common nutrient deficiency in the world, and the most common cause of anaemia in pregnancy linked to reduced iron reserves, which may exist prior to conception. It is estimated that 60 million pregnant women worldwide are anaemic; of these, some 4 million live in industrialized countries. The prevalence of iron deficiency anaemia in pregnancy varies among countries[11]. A half of all pregnant women about 50% to 59% in Bangladesh are Anaemic[12]. In general, it is low during the first trimester and increases during the second trimester. About 50% of iron deficiency anaemia occurs after the 25th gestational week[8].

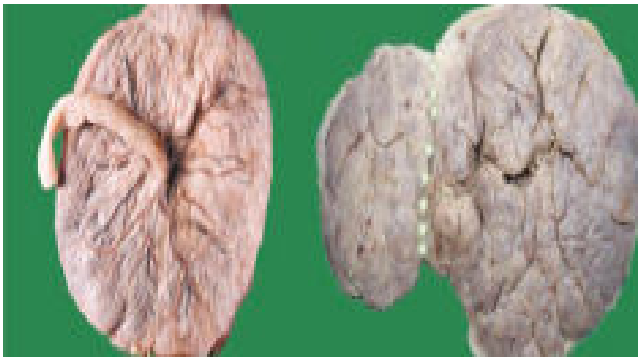

Fig-4 : Irregular type of placenta in anaemic group

Foetal iron metabolism is completely dependent on maternal iron delivery and iron transport from the mother to fetus across the placenta. Placental transferring receptors play a key role in binding circulating transferrin, which releases incorporated iron on the placental side[6]. Iron enhances placental superoxide dismutase activity, which scavenges superoxide radicals and protects the foetus from their deleterious effects.There is a U-shaped relationship between maternal haemoglobin and birth weight i.e. haemoglobin levels above 11.0 g/dL and below 9.0 g/dL show a 2-3 fold increase in the risk of delivering a low birth weight infant[8].

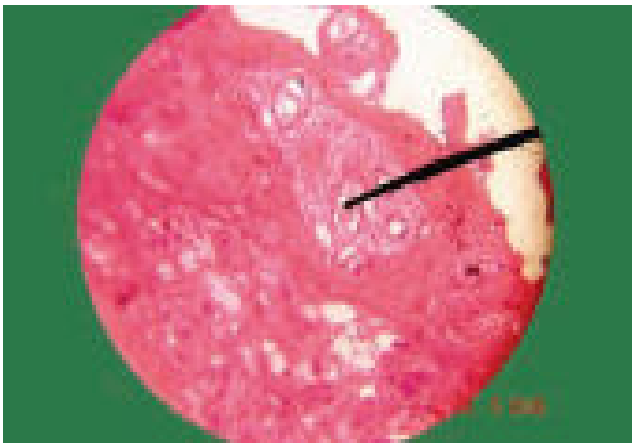

Fig-5 : Photomicrograph indicates Haemolysis of foetal capilliary of moderate anaemic group (x40 objective H & E stain)

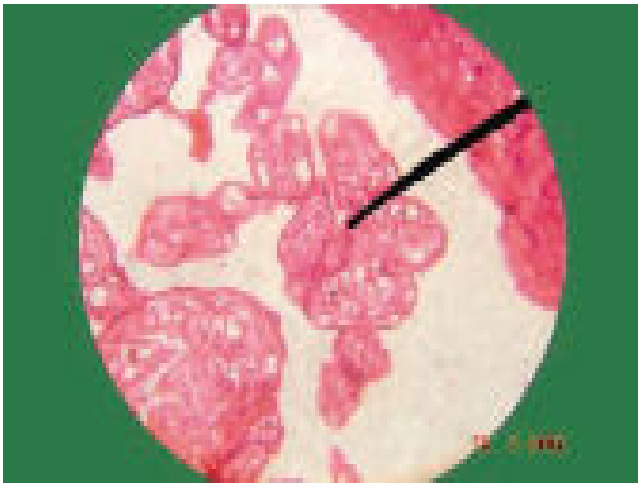

Fig-6 : Photomicrograph of placenta of moderate group of anaemia showing infraction marked by indicator (H & E x 40 objectives).

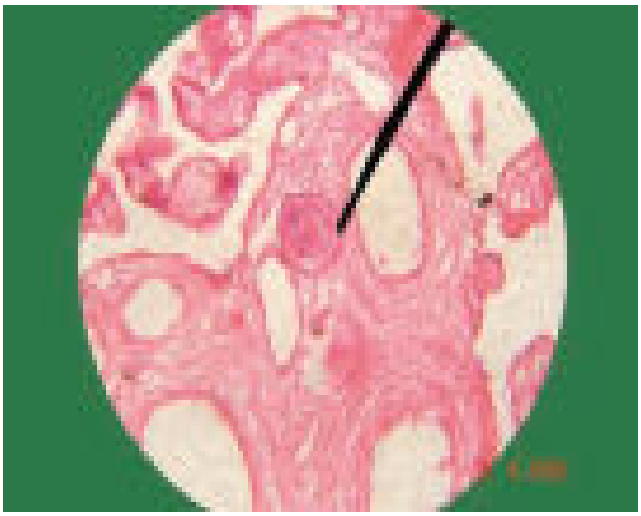

Fig-7 : Photomicrograph of placenta showing the intervillous thrombus (marked by indicator) H & E x 40 objective

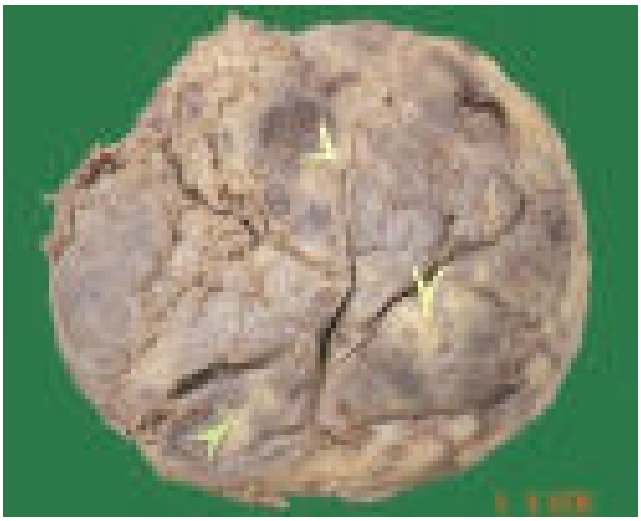

Fig-8 : Photograph of placenta showing diffused infarction on maternal surface marked by Arrow Sign

Placental hypertrophy associated with maternal anaemia, which is probably a compensatory physiological response to ensure adequate oxygen supply to the fetus[2]. Thagaleeta et al. observed a significant difference in diameter among different groups[13]. The highest diameter was 18.80 cm in moderate anaemia Placental weight & thickness has been taken as an indicator of placental function1. Increases in placental weight in case of maternal anaemia have therefore frequently been interpreted as evidence of compensatory hypertrophy for reduced oxygen supply. Braumafln 1993 observed that in hypoxic condition like anaemia, thickened placenta causes reduced birth weight due to blood flow and oxygen supply is happened in oedematous thickened placenta[11].

Placental weight has been taken as an indicator of placental function. Increases in placental weight in case of maternal anaemia have therefore frequently been interpreted as evidence of compensatory hypertrophy for reduced oxygen supply.

Some studies[4,5,13] observed that the maternal anaemia was associated with placental hypertrophy. Lao and Wong[3] observed that placental weight was higher in anaemic group.

Conclusion

It should be emphasized that the placenta is a tool that is easily and non-invasibly available for gross morphological and histological study. These characteristics of the organ are unique and the future researcher may make the best used of it for identifying how much changes occur in syncytial knot, vasculosyncytial membrane of placenta in anaemic mothers. Immunocyto chemistry against transferring receptor using a monoclonal anti-body may be performed in a paraffin-embedded block section for determining the functional condition of the peripheral villi. Again, using the perfused placenta cotyledon preparation may be done to understand the controlling factor of vascular tone in foeto placental circulation in hypoaxic condition. Grossly placental chorionic plate growth may be measured using computerized imaging technique.

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Case Report

A Case of Juvenile Papillomatosis- "Swiss Cheese Disease" of Breast

Sadia Armin Khan[1], Abu Ahmed Ashraf Ali[2], Abdus Salam[3], Sayeda Samina Hossain[4], Anusree Sarker[5], Ayesha Arman[6], Sharupa Chowdhury[7]

Abstract :
Juvenile papillomatosis (JP) is a breast tumor of young women featuring atypical papillary duct hyperplasia and numerous cysts, first described as a clinicopathologic entity in 1980. The disease is of interest because of the youth of these patients and the fact that the pathologic elements resemble those considered to be precancerous in older women. Recently a case of JP in a 16 years old female was treated and followed in this hospital. The patient noticed a large tumor, 6cm in diameter, on the medial side of the right breast. She underwent an excisional biopsy and pathology demonstrated JP. According to literature, wide local excision is adequate to control the lesion in most cases. Careful clinical surveillance is indicated for any woman who has juvenile papillomatosis and for her female relatives.

Introduction

Papillary lesions of breast have varied morphological, radiological, and pathological features. Such lesions are characterized by formation of epithelial growth that have both the luminal epithelial and the outer myoepithelial cell layers, supported by a fibrovascular stroma[1]. Papillomas of the breast can be divided into solitary papillomas, juvenile papillomatosis, and multiple papillomatosis[2]. Their malignant potentials vary and may have an impact on patients' decision making process.

Case Report

A 16-year-old woman presented with a lump in right breast. Her past medical history unremarkable and she had no significant breast cancer-related family history. Previous breast cytology revealed fibroadenomatoid and fibrocystic changes. Ultrasound (USG) of the lesion revealed an irregular but circumscribed mass containing solid and cystic regions thought to possibly represent thought to possibly represent an atypical (cystic) fibroadenoma (Fig. 1). The patient was elected to undergo excisional biopsy of the mass. Gross evaluation of the specimen revealed a 5.8X3.8X2.8 cm well-circumscribed nodule with diffusely cystic cut surfaces. Some of the cysts contained cloudy fluid and there were scattered foci of chalky yellow-white fat necrosis. Microscopic evaluation revealed a well-demarcated lesion with an admixture of fibrocystic changes including multiple apocrine cysts, adenosis, ducts with prominent fibrovascular cores suggestive of benign intraductal papilloma and prominent duct expansion by usual ductal hyperplasia. Chronic inflammation and foamy macrophages were present in areas of previous cyst rupture.

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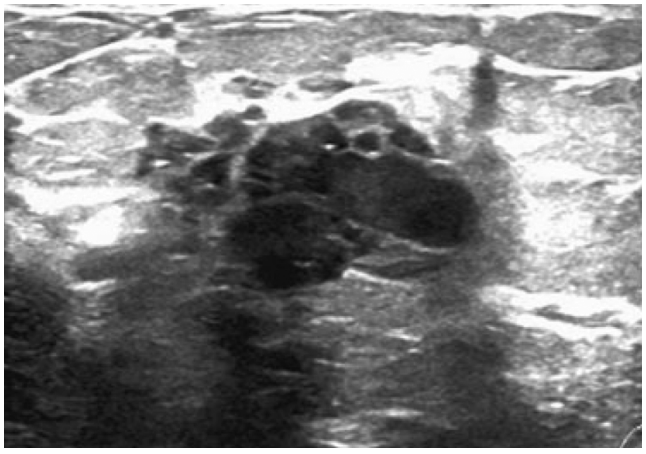

Fig-1: Ultrasound image demonstrating an irregular mass with circumscribed margins. Presence of multiple areas of hypo-echogenicity indicating cystic areas.

No significant architectural or cytologicatypia was present. These histopathologic features were characteristic of juvenile papillomatosis (JP) or "Swiss cheese disease" as it is sometimes referred due to its multicystic appearance (Fig. 2).

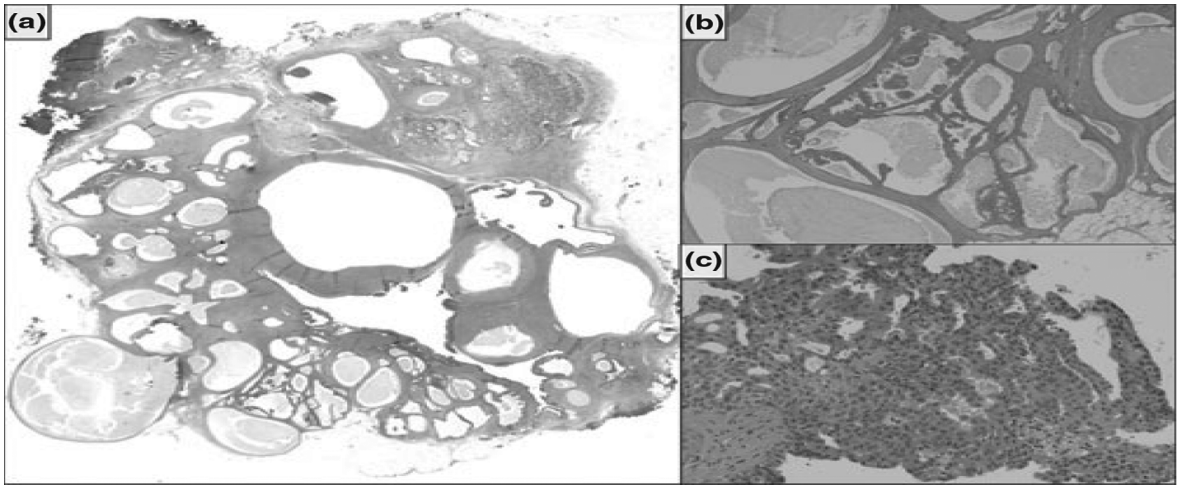

Fig-2 : Whole-mount section from the excisional biopsy specimen showing multiple cysts interspersed with more solid regions, imparting a "Swiss cheese" appearance (a). Higher power images of the lesion including a cluster of simple and apocrine cysts filled with inspisated secretions (b) and ducts expanded by florid usual ductal hyperplasia with intermixed apocrine metaplasia (c).

Discussion

This case is a diagnostic and therapeutic challenge, taking into account the patient's age and the controversial treatment recommendations.

Juvenile or cellular fibroadenomas are an uncommon variant of fibroadenoma. JF are well-circumscribed lesions and, generally, surgical excision is advised for any rapidly growing mass in the adolescent breast, even if it has been previously characterized as benign by core biopsy[3]. The surgical management of JP is a complete excision with histological confirmation. This process is usually effective, and incomplete excision invariably leads to recurrence. The concern should be greatest for women with a positive family history of breast cancer and recurrent bilateral JP[4].

In 1980, Rosen et al[5] reported 37 cases of papillomatosis in young females with a mean age of 19 years (range, 10–44 years), and defined this novel disease as JP due to its clinical and microscopic features. Thus far, ~400 cases of JP have been reported, the majority in Caucasian females aged <30 years at the time of diagnosis. Cases of JP in Asian individuals were rare and thus, fewer reports exist. Whether the difference in incidence between Caucasian and Asian populations is due to genetic or environmental factors remains unclear.

The typical manifestation of JP is a unifocal tumor, commonly located in the upper outer quadrant or outer half of the breast, and is firm, well-circumscribed, mobile, painless and generally measures <3 cm in diameter. Reports of bloody nipple discharge were unusual[6]. When the clinical diagnosis was determined prior to surgery, it was typically fibroadenoma. Mammography is not routinely recommended for diagnosis or follow-up in females <35 years; however, the few reported mammographic findings regarding JP revealed a well-circumscribed homogeneous opacity, which is similar to that observed in fibroadenomas and cysts[7]. Ultrasonography is the preferred imaging technique for JP patients as it facilitates with the differentiation between JP and similar cystic lesions, fibroadenomas, phyllodes tumors, intracystic papillomas and breast cancer[8].

Sonographically, the JP lesion presented as a poorly-defined heterogeneous mass with various small, round, echo-free areas, predominantly observed close to the border of the lesion[9]. Microscopically, the typical histopathological features are duct papillomatosis with or without epithelial atypia, apocrine and non-apocrine cysts, duct stasis and sclerosingadenosis[5]. Papillomatosis and cysts are the dominant diagnostic criteria of JP. A case report describing the fine-needle aspiration cytology of JP revealed the tumor to be comprised of sheets of hyperplastic breast epithelium with areas resembling fibroadenoma, and containing macrophages and apocrine cells. Although it is difficult to diagnose JP solely by its cytology, a combination of clinical and cytological findings may facilitate with the diagnosis of JP. There is no evidence to associate hormonal agent use or reproductive history with the occurrence of JP in young individuals, nor to associate JP with the maternal use of teratogenic agents during pregnancy[5].

Various breast disorders in children and young adults must be distinguished from JP. Rosen[5] described rare types of papillary duct hyperplasia, which are observed in adolescence, including papilloma, papillomatosis and sclerosing papillomatosis.

The most common symptom of papillary duct hyperplasia is the presence of a mass, although certain cases also exhibited nipple discharge, or presented with nipple discharge alone; however, all of these lesions lacked the cystic component that is characteristic of JP. Breast cancer is rare in children, however, when it does occur it most commonly takes the form of a secretory carcinoma and presents as a long-standing breast mass, which is occasionally painful. Nipple discharge is rarely identified. Secretory breast cancer is characterized by the presence of abundant intracellular and extracellular secretions, and intracytoplasmic vacuoles. Furthermore, immunoperoxidase staining for α-lactalbumin is typically positive in secretory carcinoma, but negative in JP[10]. Rosen et al6 reviewed 84 cases of JP in 1982 and identified that 26% of the patients had a family history of breast cancer in at least one female relative. The majority of breast cancer cases were observed in older, secondary relatives (for example grandmothers or great aunts), although instances of maternal breast carcinoma were also reported. This may have been due to the young age of the JP patients and, therefore, the patients' mothers or young female relatives may not have reached the peak age of breast cancer incidence. Bazzocchi et al[11] observed that 33% of JP patients had a family history of breast cancer. These findings indicate that JP may be a marker of breast cancer in the family of the JP patients, thus, a thorough medical follow-up is recommended for JP patients and their families. Furthermore, microscopic evaluation revealed that breast carcinoma coexisted with JP in certain cases. Bazzocchi et al[11] identified that 15% of the JP patients presented with a coexisting carcinoma and Rosen et al[6] described three cases of other types of cancer coexisting with JP (n=84). Two of the patients exhibited secretory carcinoma (one arising from JP and another with contralateral secretory cancer) and the two patients had a maternal history of breast cancer. In addition, although the follow-up data was insufficient, the JP patients appeared to be at an increased risk of developing breast cancer. A previous study of 41 patients with a median follow-up period of 14 years demonstrated a 10% incidence of subsequent breast carcinoma in patients with JP[10]. Although the risk of breast cancer should not be exaggerated, patients exhibiting any one of the following characteristics should be closely monitored for the subsequent development of breast cancer:

i) positive family history of breast cancer
ii) atypical proliferative lesions
iii) bilateral lesions
iv) multifocal lesions
v) recurrence of JP.

Patients with a positive family history of breast cancer and recurrent bilateral JP are considered to be at the greatest risk. Further studies with a longer follow-up period are required to determine the incidence of breast cancer in patients with JP.

In conclusion, the recommended treatment strategy for JP is complete excision of the cancerous lesion to reduce local recurrence. On consideration of the current literature, it is prudent to advise an annual clinical follow-up, including a physical examination and/or ultrasonography of the breasts for JP patients, and for the patients' female relatives, particularly those with a family history of breast cancer and with recurrent or bilateral JP.

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