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Editorial

Tranexamic Acid for the Prevention and Treatment of Postpartum Haemorrhage

Postpartum Haemorrhage (PPH) is a major cause of maternal mortality, accounting for one quarter of all maternal deaths world wide[1]. Uterotonics after birth are the only interventions that has been shown to be effective for PPH prevention[1,2]. Tranexamic acid (TXA) an antifibrinolytic agent has therefore been investigated as a potentially useful complement to this for both prevention and treatment of PPH.[3]

BIOCHEMICAL ACTION

In the haemostatic process, coagulation occurs rapidly at the site of damaged vessel by the buildup of a tight net of fibrin[2,4]. At the same time the fibrinolytic system removes the fibrin deposits that might cause permanent vascular occlusion, once vascular repair has taken place. Coagulation and fibrinolytic system are believed to be in a state of dynamic balance that maintains an intact vascular system[5,6]. Tranexamic acid is a potent antifibrinolytic agent that exerts it effects by blocking lysine, binding sites on plasminogen molecules and has potential to enhance the effectiveness of the patients own haemostatic mechanisms, consequently clot breakdown is inhibited and bleeding is reduced.

During delivery, when placenta separates from the uterine wall, physiologic and haemostatic changes occur sequentially to reduce bleeding[6,7]. Strong myometrial contraction, increased platelet activity massive release of coagulation factors and consequently a parallel increase in fibrinolytic activity[8]. While oxytocin administration enhances the first mechanisms, TXA administration might be able to counter the latter and thus facilitate the molecules and has the potential to enhance the effectiveness of the patient's own haemostatic mechanisms. Consequently clot a breakdown is inhibited and bleeding is reduced.

CONCLUSIONS:

Both theoretical arguments and results from RCT conducted indicate that TXA has promise in the prevention and treatment of PPH[8,10]. The available evidence from RCTS, which have focused mostly on PPH prevention after caesarean deliveries and Vaginal deliveries are of insufficient quality to reach any definitive conclusion, although it does suggest that TXA administration reduces postpartum blood loss[9,10].

In Bangladesh, 51% of maternal death is due to PPH and Eclampsia. It was stated at the work shop on preventing PPH and Eclampsia on 25th June, 2018 at MIS conference Room, DGHS, supported by UNFPA.

So, we have to give attention to find out the effective drug for prevention of PPH like Tranexamic acid and maternal mortality and morbidity will significantly reduced.

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Original Article

A Comparative Study between Patients of Diabetic & Non-diabetic Chronic Kidney Disease in Relation to their Estimated Glomerular Filtration Rate Value

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ABSTRACT

Background: *Chronic kidney disease (CKD) refers to an irreversible deterioration in renal function which classically develops over a period of years. Diabetic nephropathy, especially related to type II diabetes, has become the single most important cause of End Stage Renal Disease (ESRD) world wide. Survival rate after the onset of ESRD is shorter in diabetic population compared to that of non-diabetic population with similar clinical features.*

Objective: *To find out the difference between calculated GFR in patients with diabetic & non-diabetic chronic kidney disease.*

Method: *This cross-sectional comparative study was carried out in the department of Biochemistry, Chittagong Medical College. Study samples were collected from the department of Nephrology, Chittagong Medical College Hospital during the period of July 2013 to June 2014. Total 100 patients of both sexes were enrolled in this study. Among them 50 were considered as group A (diabetic CKD) and another 50 were considered as group B (non-diabetic CKD).*

Results: *The age range of Group A (Diabetic CKD) was 40-62 years and mean age was 51.27 (SEM±1.60) years and in Group B (Non-diabetic CKD) age range was 45-69 years and mean age was 60.12 (SEM±1.75) years. In group A (diabetic CKD) 66% were male and 34% were female and in group B (Non-diabetic CKD) 58% were male and 42% were female. The mean eGFR was 16.40 (SEM ± 0.67) ml/min/1.73m^2 in Group A (Diabetic CKD) and 17.88 (SEM ± 0.85) ml/min/1.73 m^2 in Group B (Non-diabetic CKD). Statistically significant (P<0.05) difference was found in mean eGFR among the two groups*

Conclusion: *The result showed that the mean eGFR in Diabetic CKD (Group A) was lower than the mean eGFR in Non-diabetic CKD (Group B).*

Keywords:
Estimated GFR, CKD, ESRD

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INTRODUCTION

Chronic kidney disease (CKD) is a world wide public health problem. It is a pathophysiologic process of multiple etiologies, resulting in the loss of nephron number and function. The prevalence and incidence rate of CKD patients are continuously increasing in all over the world including Bangladesh[1]. Emerging evidence from developing countries also indicates a high burden of CKD. It is expected to rise rapidly as when both the age of the population and the

prevalence of hypertension and diabetes increase [2].

Chronic Kidney Disease (CKD) is defined by KDIGO (Kidney Disease: Improving Global Outcome).The definition includes two broad headings- (ì) kidney damage that has continued for more than 3 months, as defined by structural or functional abnormalities of the kidney, with or without decreased glomerular filtration rate (GFR) or (ìì) eGFR<60ml/min/1.73m2 for >3months, with or without kidney damage [3].It has emerged as a non-communicable life-threatening disease. CKD increases not only the number of chronic dialysis patients but also mortality from cardiovascular diseases in both developing and developed countries [(2)]. Symptoms of kidney disease are generally mild. Patients often become conscious of CKD at the end stage of the kidney disease or when they suffer myocardial infarction or stroke [4].

Chronic kidney disease is a progressive loss in renal function over a period of months or years. Calculated GFR is essential for the diagnosis of CKD[5].The symptoms of worsening kidney function are non-specific, and might include feeling generally unwell and experiencing a reduced appetite. Chronic kidney disease is diagnosed as a result of screening of people known to be at risk of kidney problems like high blood pressure or diabetes. Chronic kidney disease may also be identified when it leads to one of its recognized complications like cardiovascular diseases or anemia [6].Chronic kidney disease is identified by a blood test for creatinine & calculated GFR. Higher levels of creatinine indicate a lower glomerular filtration rate and a decreased capability of the kidneys to excrete waste products. Creatinine levels may be normal in the early stages of CKD. The condition is discovered if urinalysis shows that the kidney is allowing the loss of protein or red blood cells into the urine. To fully investigate the underlying cause of kidney damage, various forms of medical imaging, blood tests and often renal biopsy are employed. These are done to find out if there is a reversible cause for the kidney malfunction.

The term "nondiabetic kidney disease" includes a variety of diseases. Those are often grouped together in epidemiologic studies and clinical trials. They differ widely in terms of patient's history, clinical presentation, risk of progression, and response to treatment. These diseases include glomerular diseases, vascular diseases, tubulointerstitial diseases and cystic kidney diseases [7].

Diabetes is the most common cause of kidney disease, accounting for nearly 44 percent of newly diagnosed cases[8]. In patients with diabetes screening for nephropathy should be done after about 5 years in type I diabetes and at the time of diagnosis of type II diabetes as onset of type II diabetes could not be identified definitely. It is the leading cause of premature death in young diabetic patients. The disease is progressive and may cause death two or three years after the initial lesions.The risk is higher if blood-glucose levels are poorly controlled. Once nephropathy develops, the greatest rate of progression is seen in patients with poor control of their blood pressure. People with high cholesterol level in their blood have much more risk than others. In the kidney, diabetic changes may lead to increased leaking of plasma proteins across the glomerular membrane and appearance of protein in the urine. The presence of urinary protein heralds the onset of diabetic kidney disease. It may contribute to the glomerular and tubulointerstitial damage that ultimately leads to diabetic glomerulosclerosis [9] .

Even when blood sugar is controlled, the disease can lead to chronic kidney disease (CKD) and kidney failure. Untreated CKD may progress to End Stage renal Disease (ESRD). Evidence suggests that some of this adverse outcome can be prevented and delayed by early detection and management of CKD [10]. To level of this incidence rates- The National Kidney Disease Outcomes Quality Initiatives (K/DOQI) and European Best Practice Guidelines, recommended the use of prediction equation to estimate the GFR from serum creatinine [11]. Numerous equations have been developed to calculate GFR in adults. The MDRD Study equation was developed in 1999. It is currently recommended for calculated GFR reporting in adults by the National Kidney Disease Education Program (NKDEP). It uses standardized serum creatinine, age, sex, and race (black versus white and other) to calculate GFR adjusted for BSA (ml/min/1.73m2). Here in this study we like to see the relative change in calculated GFR between diabetic and non diabetic CKD patients, whether there is any difference present or not [12]. Because many patients with

CKD follow a predictable clinical course following disease initiation, with progressive renal dysfunction ultimately resulting in ESKD. Critically, CKD is clinically silent in upto 90% patients until it has

reached an advanced stage. Patients who reach ESKD without prior contact with nephrology services experience greater co-morbidity and poorer survival following initiation of renal replacement therapy [1]. There is therefore an opportunity to detect patients with asymptomatic CKD by screening, with the aim of applying therapies to ameliorate disease progression.

MATERIALS & METHOD

This cross-sectional comparative study was designed to find out a difference between estimated GFR in diabetic & non-diabetic CKD patients. The study was carried out in the department of Biochemistry, Chittagong Medical College and the samples were collected from the department of Nephrology, Chittagong Medical College Hospital during the period of July 2013 to June 2014. Total 100 patients of both sexes were enrolled in this study; among them 50 were considered as group A (diabetic CKD) and another 50 were considered as group B (non-diabetic CKD). Patients' recruitment was done on the basis of chronic kidney disease without any cardiovascular instability, renal replacement therapy or dialysis. The collected data were analyzed by computer based software SPSS for windows verson 18. Data were expressed as mean ±SEM. Confidence level was fixed at 95% (P value d"5).

RESULTS

Table -1 shows Group A(Diabetic CKD) age range was 40-62 years and mean age was 51.27 (SEM ± 1.60) years and in Group B(Non-diabetic CKD) age range was 45-69 years and mean age was 60.12 (SEM ± 1.75) years. Significant statistical difference observed between the two groups (P = 0.02).

Comment: Mean age is significantly lower in Group A (Diabetic CKD) than in Group B(Non-diabetic CKD) (P < 0.05).

Table-1 : Distribution of age (years) among the study groups (with t-test significance)

	Study Group	N	Mean±SEM	Range	P value
Age	Group A (Diabetic CKD)	50	51.27±1.60	40 – 62	0.02
(Years)	Group B (Non-diabetic CKD)	50	60.12±1.75	45 – 69	

Table-2 shows sex distribution among the study groups. In group A (Diabetic CKD) 66% (N=33) were male and 34% (N=17) were female. In group B(Non-diabetic CKD) 58% (N=29) were male and 42% (N=21) were female.

Comment: In both groups male is higher than female.

Table-2 : *Distribution of sex among the study groups*

Sex	Group A (Diabetic CKD)		Group B (Non-diabetic CKD)		Total	
	N	%	N	%	N	%
Male	33	66.0	29	58.0	62	62.0
Female	17	34.0	21	42.0	38	38.0
Total	50	100.0	50	100.0	100	100.0

Table - 3 shows that mean serum creatinine was 3.9 (SEM ± 3.22) mg/dl in Group A (Diabetic CKD) and 2.7 (SEM ± 2.96) mg/dl in Group B(Non-diabetic CKD). There is significant statistical difference in serum creatinine level among the two groups (P < 0.05).

Comment: mean serum creatinine level is significantly higher in Group A(Diabetic CKD) than in Group B(Non-diabetic CKD).

Table-3 : *Distribution of Serum creatinine level (mg/dl) among the study groups*

	Study Group	N	Mean	± SEM	P value
Serum Creatinine (mg/dl)	Group A (Diabetic CKD)	50	3.9	3.22	0.04
	Group B (Non-diabetic CKD)	50	2.7	2.96	

Table - 4 shows that mean eGFR was 16.40 (SEM ± 0.67) ml/min/1.73m2 in Group A (Diabetic CKD) and 17.88 (SEM ± 0.85) ml/min/1.78 m2 in Group B(Non-diabetic CKD). There is significant difference in mean eGFR among the two groups (P<0.05).

Comment: Mean eGFR is significantly lower in Group A (Diabetic CKD) than in Group B (Non-diabetic CKD).

Table–4: *Distribution of eGFR (ml/min/1.73m^2) among the study groups*

	Study Group	N	Mean	± SEM	P value
eGFR (ml/min/1.73m^2)	Group A (Diabetic CKD)	50	16.40	0.67	0.01
	Group B (Non-diabetic CKD)	50	17.88	0.85	

Table– 5 : *Distribution of eGFR (ml/min/1.73m^2) according to CKD stages among the study groups*

CKD stages	Group A (Diabetic CKD)			Group B (Non-diabetic CKD)			P value
	Number	Mean	± SEM	Number	Mean	± SEM	
CKD Stage 3	9	34.22	0.79	9	38.11	1.46	0.03
CKD Stage 4	13	20.92	1.00	14	22.07	0.78	0.01
CKD Stage 5	28	8.93	0.21	27	8.96	0.31	0.05

Table -5 shows that in stage 3 mean eGFR was 34.22 (SEM ± 0.79) ml/min/1.73m2 in Group A(Diabetic CKD) and 38.11 (SEM ± 1.46) ml/min/1.73m2 in Group B(Non-diabetic CKD) . There is significant statistical difference in eGFR among the two groups in stage 3 CKD (P < 0.05). The table also shows that in stage 4 mean eGFR was 20.92 (SEM ± 1.00) ml/min/1.73m2 in Group A (Diabetic CKD) and 22.07 (SEM ± 0.78) ml/min/1.73m2 in Group B (Non-diabetic CKD) . There is significant statistical difference in eGFR among the two groups in stage 4 CKD (P < 0.05). The table also shows that in stage 5 mean eGFR was 8.93 (SEM ± 0.21) ml/min/1.73m2 in Group A (Diabetic CKD) and 8.96 (SEM ± 0.31) ml/min/1.73m2 in Group B (Non-diabetic CKD). There is no significant statistical difference in eGFR among the two groups in stage 5 CKD (P < 0.05).

Comment: In stage 3 and 4 CKD Mean eGFR is significantly lower in Group A (Diabetic CKD) than in Group B (Non-diabetic CKD). But in stage 5 CKD there is no significant statistical difference in Mean eGFR in Group A (Diabetic CKD) and in Group B (Non-diabetic CKD).

DISCUSSION

Chronic kidney disease (CKD) is one of the common health problems in the world and more common in developing countries like Bangladesh. This study tried to evaluate if there was any significant difference in eGFR among the diabetic and non-diabetic chronic kidney diseased patients. The present study enrolled 100 patients suffering from chronic kidney disease of which fifty (50) patients were diabetic and another fifty (50) patients were non-diabetic. The mean age of the patients of group A(Diabetic CKD) was significantly lower than group B(non-diabetic CKD) patients (P<0.05).This means that the onset and progression of CKD in diabetic patients are earlier than in non-diabetic patients.[13]Among the 100 participants in group A(diabetic CKD) 66% were male and 34% were female and in group B(Non-diabetic CKD) 58% were male and 42% were female.

According to staging of CKD the mean serum creatinine level in patients of group A (Diabetic CKD) was significantly higher by statistical analysis in stage 3 and stage 4 than in patients of group B (Non-diabetic CKD). Statistically significant difference was not found among the two groups (P<0.05) in stage 5 CKD. But among the total study group the mean serum creatinine level was significantly higher in group A (Diabetic CKD) patients than in group B(Non-diabetic) patients.

This study was designed to find a difference between eGFR in diabetic & non-diabetic CKD patients. The

result showed that the mean eGFR in Group A (Diabetic CKD) was lower than the mean eGFR in Group B (Non-diabetic CKD) in stage 3 and stage 4 CKD. The finding is consistent with the study of Nelson et al .[14] and Unsal et al.[15] they found out that there was more fall of eGFR in CKD patients having long standing diabetes than those without having diabetes. Present study shows that there was no statistically significant difference between the two groups of patients in stage 5 CKD which is also consistent with the study of Stojkeva et al.[16] They have found that at the end stage of CKD there was no significant difference in eGFR level and the result was all through same for all causes of CKD. But in case of total study group the study result shows that the mean eGFR of group A (Diabetic CKD) was lower than that of group B(Non-diabetic CKD). This result is similar with the work of Daniel et al.[17] But in a study done by Stojkeva et al.[16] found no difference in eGFR level in diabetic and non-diabetic CKD patients.

Low HDL level are parts of metabolic syndrome. High TG and low HDL (Dyslipidemia) and hyperurecemia are associated with early atherosclerotic change in diabetic nephropathy patients; these reduce renal blood flow and rapid fall of GFR.[18] For this reason diabetic nephropathy patients rapidly progress to ESRD than other causes of chronic kidney disease.[18]Additionally, it has been proposed that the presence of both conditions lead to increased inflammation and oxidative stress, increased total peripheral resistance, and impaired left ventricular relaxation which increases the risk for CVD events.[19]

As compared to non-diabetic individuals, hemodialysis in patients with DM is associated with more frequent complications, such as hypotension (due to autonomic neuropathy or loss of reflex tachycardia), more difficult vascular access and accelerated progression of retinopathy. Survival after the onset of ESRD is shorter in diabetic population compared to that of non-diabetics with similar clinical features.[19]

To reduce the number of opinion in favour and against, better inclusion and greater number of cases are required for further extension of studies and re-establishment of the hypothesis.

CONCLUSION

The result showed that the mean eGFR in Diabetic CKD(Group A) was lower than the mean eGFR in Non-diabetic CKD(Group B) and there was significant statistical difference in mean eGFR level in between the two groups ($P<0.05$). Diabetic nephropathy, especially related to type-2 diabetes, has become the single most important cause of ESRD worldwide. Survival rate after the onset of ESRD is shorter in diabetic population compared to that of non-diabetic population with similar clinical features. So, this study is particularly important in a region like our country, where screening for nephropathy among adult diabetes is often not performed at all due to limited resources and where the treatment options for end stage renal disease are limited. It would be even more important in order to slow progression and prevent complications as the incidence of diabetes continues to increase in this region alarmingly. A further study may be suggested to different zone of the country including different medical college of Bangladesh to evaluate the variety of results and observations.

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Original Article

Frequency of Minimal Hepatic Enchephalopathy in Cirrhotic Patients in A Tertiary Level Hospital in Bangladesh

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ABSTRACT

This study was done to investigate the frequency of minimal hepatic encephalopathy (MHE) in cirrhotic patients in a tertiary level hospital (BIRDEM General Hospital) in Bangladesh. This observational cross sectional study done in the in-patient and out-patient departments of BIRDEM General Hospital from August 2013 to July 2014 included eighty-five patients selected by non random sampling. Demographic, clinical and biochemical data were obtained. Cognitive function was tested using Bangla adaptation of mini mental state examination (BAMSE) to ensure normal mental and neurological state, followed by psychometric tests- Number connection test-A (NCT-A) and Digit Symbol test (DST) to detect MHE . The frequency of MHE in this study was 64.7% and varied by Child-Pugh-Classification (CPC) - CPC-B: 35.2% and CPC-C: 72.05%, P = 0.005). Cirrhotic patients were found to have a high frequency of MHE that is proportionate to the degree of liver function.

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INTRODUCTION

Minimal hepatic encephalopathy (MHE) has been defined as a condition in which patients with cirrhosis regardless of its etiology, demonstrates neuro-psychiatric and neuro-physiological defects, yet, having a normal mental and neurological status through global clinical examination[1]. MHE predicts the development of overt HE and is associated with poor survival. It's negative impact on daily living among other reasons, has led some authors to suggest that the failure to diagnose this condition could be classified as a medical error[2,3]. The prevalence of MHE was reported to vary from 10% to 84%, depending on the diagnostic techniques used and patients selected for the studies[1]. Many diagnostic techniques have been used to detect MHE. Among these tests, only psychometric test can be administered easily in epidemiological studies. In a variety of psychometric tests listed in the medical literature, DST and NCT part A (NCT-A) were reported to have the advantages of simplicity and reliability[4,5,6,7]. The combination of these two tests was commonly applied in epidemiological studies. Patient with minimal hepatic encephalopathy may improve, remain unchanged or deteriorate and develop overt encephalopathy over a long-term follow-up. The frequency of MHE increases as the severity of liver disease increases[8]. In view of a high frequency of MHE in patients with liver disease, it is important to understand its impact on future clinical outcomes, such as occurrence of overt HE, quality of life and survival, and to determine whether treatment of MHE can induce improvements in these outcomes. Several studies that looked at the frequency of development of overt HE in cirrhotic patients found that those with MHE developed overt HE more often during follow up than those without MHE[9]. Gut-derived nitrogenous substances are universally acknowledged to play a major role in the pathogenesis of hepatic encephalopathy and pathogenesis of MHE is thought to be similar to that of overt HE. Specifically, ammonia is thought to be

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a critical factor in the pathogenesis[10]. The INASL Working Party recommends that all patients with cirrhosis be screened for the presence of MHE using a standard battery of psychometric tests, PHES, CFF or ICT, depending upon the availability of tests and their validation for local populations from different parts of the world. Patients whose index psychometric or computerized test results do not indicate pathology should be screened every 6–12 months[11]. All patients with liver cirrhosis should be subjected to testing for MHE. Special attention should be given to those who have cognitive symptoms and high-risk groups such as active drivers, patients handling heavy machines or reporting decline in work performance[12]. Although named "minimal", MHE can have a far-reaching impact on quality of life, ability to function in daily life and progression to HE . In view of the reported high prevalence of MHE and its presumed negative effect on daily life, routine screening of cirrhotic patients for MHE and treatment of MHE is recommended[9,14,15].

Cirrhotic patients with MHE more frequently develop episodes of overt HE than those without MHE[16]. Among cirrhotic population, if the frequency and factors associated with MHE can be determined, the patients will be benefited from preventive measures and timely treatment. There is hardly any local data available on minimal hepatic encephalopathy among cirrhotic patients in our country. Therefore, The current study has been designed to find out the frequency of MHE. It will help in providing ideas for the policy makers to formulate proper intervention strategies among the cirrhotic patient with MHE who are at risk of developing overt HE. This will significantly improve the quality of life and prevent morbidity and mortality related to cirrhosis with encephalopathy.

MATERIALS AND METHODS:

This was an observational cross sectional study carried out in Department of GHPD, BIRDEM General Hospital from August 2013 to July 2014.Using a precision based calculation, minimum sample size required at 5% level of significance and 95% confidence level 293. But due to time constraints, 85 patients were taken.

Adult cirrhotic population aged 18 years or more attending GHPD out-patient department or admitted in GHPD of BIRDEM General Hospital, Dhaka without sign, symptoms of overt hepatic encephalopathy (altered mental status, flapping tremor), diagnosed on the basis of clinical evaluation and biochemical investigations were recruited. Patients with clinical features suggestive of cirrhosis from inpatient and outpatient departments of GHPD were subjected for investigations including complete blood count, liver function tests- serum total bilirubin, serum alanine aminotransferas (ALT), serum aspartate aminotransferase (AST), serum total protein, serum albumin, prothrombin time, renal function tests (blood urea, serum creatinine), serum electrolytes and serum ammonia. Serological tests for hepatitis B and hepatitis C were performed by ELISA (enzyme linked immunosorbant assay). Patients who had symptoms and signs suggestive of overt encephalopathy, renal impairment (AKI or CKD), H/O of gastrointestinal bleeding within last one month, had sedative or psychotropic drugs within two weeks prior to admission or having any other serious medical or surgical condition were excluded from the study. Cognitive state was assessed by Bangla Adaptation of Mini Mental State Examination (BAMSE). The Bangla adaptation of mini–mental state examination (BAMSE) is a brief 30-point questionnaire test that can be used to screen for cognitive impairment. It was developed by Kabir & Herlitz (2000) in the University of Stockholm. [17] Those whose score was above 24 were enrolled for the study. Then two tests, NCT-A and Digit-symbol test were used for screening of minimal hepatic encephalopathy. Reports of laboratory investigations were collected from patients documents. Data was analyzed by computer with the help of SPSS (Statistical Package for Social Sciences) version 16. Statistical analyses was done by using appropriate statistical tool like 'chi-square' test, student's 't' test, where applicable. Statistical significance was set at 0.05 level and confidence interval at 95% level.

RESULT

Eighty-five patients who fulfilled the inclusion criteria were included in the study.

Mean age was 55.78(±10.30) years. Majority 52(61.18%) were male and 33(38.82%) were female.

Table 1: *Mean score of Bangla adaptation of mini mental state examination (BAMSE) and psychometric tests of study population (N=85)*

	Mean (±SD)	Range
BAMSE Score	27.23(±1.06)	25-30
NCT-A Score (Seconds)	38.92(±7.62)	25-49
DST Score (Seconds)	125.75(±38.49)	60-240

Table1. shows that mean BAMSE score were 27.23 (±1.06), Mean NCT-A score was 38.92(±7.62) seconds and Mean DST score was 125.75 (±38.49) seconds in the study population.

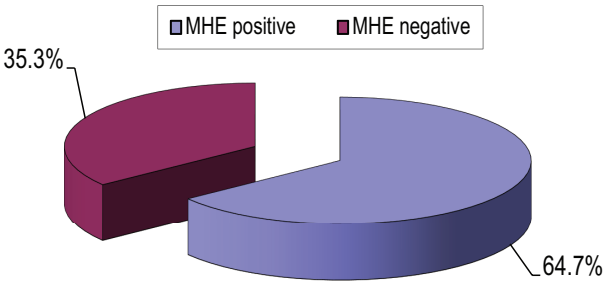

Figure-1: *Frequency of MHE positive and negative cases among study population (N=85)*

Figure-1: shows that among the 85 subjects included in the study, 55 (64.7%) met the criteria for MHE.

Table 2: *Comparison of mean scores of BAMSE and psychometric tests between MHE positive and negative cases (N=85)*

	MHE		
	Positive	Negative	P
	Mean (±SD)	Mean (±SD)	value
BAMSE score	27.18(±0.81)	27.33(±1.42)	0.53
NCT-A (seconds)	42.96(±4.22)	28.04(±1.60)	<0.001
DST(seconds)	142.30(±31.60)	81.13(±5.87)	<0.001

Table shows mean BAMSE score of MHE positive group was 27.18(±0.81) and MHE negative group was 27.33 (±1.42) (p>0.05). Mean NCT-A score in MHE positive patients was 42.96 (±4.22) seconds and in MHE negative patients 28.04 (±1.60) seconds (p<0.001). Mean DST was 142.30 (±31.60) seconds in MHE positive cases and 81.13(±5.87) seconds in MHE negative cases (p<0.001).

DISCUSSION

This was an observational cross sectional study done in BIRDEM general hospital from August 2013 to July 2014 to find out the frequency of minimal hepatic encephalopathy among cirrhotic patients attending inpatient and outpatient departments. In the present study, mean age of the study population was 55.78(±10.30) years.. Compared with the study done by Koziarska et al that showed mean age was 54.5 ± 11.8 years and in another study by Li et al, they reported mean age 53.4±11.9 years which are similar to this study[18,23]. This study showed majority 52(61.18%) were male and 33(38.82%) were female. The study by Wang et al also supports male predominance, as they found 68.6% male patients and 31.2% female. Mean BAMSE scores in this study were 27.18 (±0.81) in MHE positive and 27.33 (±1.42) in MHE negative groups, which showed no significant difference (p >0.05). This finding is consistent with that of Koziarska et al who found MMSE score 27.7 ± 1.8 in MHE positive and 27.5±2.0 in MHE negative groups, which was also not significant (p>0.05)[18]. Mean NCT-A score in MHE positive group was 42.96(±4.22) seconds and 28.04(±1.60) seconds in MHE negative group. Mean DST score was 142.30(±31.60) seconds in MHE positive and 81.13(±5.87) seconds in MHE negative. Both were statistically significant (P<0.05). Sharma & Sharma in their study found that there was significant difference between MHE negative and positive groups in NCT-A (29.1±12.3 vs. 50.4±14.0 sec, P = 0.001). Sharma et al showed that DST score in MHE positive group was 113.7±30.7 seconds and MHE negative group was 60.2±27.4 seconds[19]. Both the tests showed statistically significant difference (P<0.001). Bajaj et al found that NCT-A score in MHE positive cases were (32±11) seconds whereas in MHE negative cases it was (22±6) seconds which was significantly different (P<0.0001)[20].

In this study, we found that among the 85 cirrhotic patients attending inpatient and outpatient departments of GHPD in BIRDEM General Hospital in the study period, 55 patients met the criteria for minimal hepatic encephalopathy. From this data, we found the frequency of minimal hepatic encephalopathy to be 64.7%. Maldonado-Garza et al (2011) found that the prevalence of MHE was 55.8% among cirrhotic patients[21]. Li et al (2004) found MHE prevalence in cirrhotic patients in China was 50.9%[23]. It is to be noted that the prevalence of MHE has been reported in as many as 20%"84% of cirrhotics, depending on which methods or tools are used and fixed diagnostic cut-offs (Prasad et al 2007)[22]. From the above observations, it can be concluded that the frequency of minimal hepatic encephalopathy (MHE) in this cross sectional population of cirrhotic patients was 64.7%. Although the researcher in every steps of this study had taken optimum care, still some limitations existed. The study was conducted in a selected center. So, it cannot represent the whole community. Further randomized controlled study with larger sample size is needed to verify the significance.

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Original Article

Cost Effectiveness of Locally adopted Dietary Regimen in the Treatment of Wasting Malnutrition

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ABSTRACT

Background: *Malnutrition is a major public-health problem for developing world. Malnutrition is not only a direct cause of death among children, but it is also indirectly a significant underlying factor for child mortality. WHO proposed a dietary regimen to solve the problem in resource limited country like Bangladesh. But it is difficult to implement the WHO protocol properly due to lack of necessary logistic support. So we used a locally adopted peanut based new dietary regimen (DMCH regimen) which is available and easy to make.*

Objective: *Current study aimed at evaluating the effectiveness of locally adopted peanut based DMCH dietary formula in the treatment of wasting malnutrition in comparison to WHO regimen in terms of rate of recovery*

Methodology: *This was a randomized control trail conducted at Department of Pediatrics in Dhaka Medical College and Hospital from April 2013 to April 2014.Eighty chuldren of age between 6 months to 59 months and weight for height Z score < – 3 were included in the study. Children were allocated in control (WHO group) and study group (DMCH group) and received WHO regimen & DMCH regimen respectively . Outcome was assesed in terms treatment cost of two groups. Daily weight gain, duration of achieve target weight were also compared.*

Result : *In DMCH group the time taken to achieve target weight was 13.61days which was around one day less than that of WHO group (14.50) and per day rate of weight gain was higher by around 3.28 gm/kg/day (p value=0. 000). Most importantly daily treatment cost was higher by around 16.37 taka per day (p value=0.001) in WHO group.*

Conclusion: *DMCH dietary regimen is less expensive than WHO regimen.*

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Keywords:
Wasting, Weight for height Z score, WHO regimen, locally adopted diet, malnutrition

INTRODUCTION

The situation of child malnutrition is a silent emergency. According to joint child malnutrition report (UNICEF /WHO/World Bank)-2014, 159 million child were stunted, 95 million under weight and 16 million severely wasted [1]. Nearly half of all deaths in children under 5 are attributable to under nutrition. This translates into the unnecessary loss of about 3 million young lives a year [2]. The economic consequences represent losses of 11 percent of gross domestic product (GDP) every year in Africa and Asia[3], whereas preventing malnutrition delivers $16 in returns on investment for every $1 spent[3] While South Asia has the highest proportion and numbers of malnourished children, Bangladesh is one of the three countries in this region that accounts for half the world's malnourished children[4]. According to BDHS (2014) report 14% children are wasted and 33% are underweight in Bangladesh[5]. Severely malnourished children have a high mortality rate, even in the 1990s, mortality rates was as high as 49%[6].

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Severely malnourished patients need intensive medical and nursing care. Optimum management of these acutely ill children and a good outcome depends on an evidence based prescriptive regimen of care. WHO has advocated a protocol and various agencies have adopted it according to their need and available facilities. But High case fatality rate in hospitals has been attributed to faulty case management due to lack of knowledgeable staff and absence of resources or high cost of treatment. To address this issue and for better management of severe malnutrition, Department of Paediatrics, Dhaka Medical College hospital has introduced a dietary regimen based on peanut. (Latter on, we will mention it as a DMCH regimen). Peanut is a third most important source of vegetable protein. It is easily available also. Peanut has traditionally been used as a source, of oil. In recent years, several cereals and legumes-based foods using peanuts as protein supplements have been developed to alleviate protein calories malnutrition problem. Peanut in the form of flour, protein isolates, and meal in a mixed product have been found to be very desirable from a sensory quality point of view.

This study was conducted to determine the cost effectiveness of locally adopted DMCH dietary regimen (F-75 & F-100 peanut based) for the management of wasted children. This study also determined the effectiveness of DMCH regimen based on achievement of target weight.

MATERIALS AND METHODS

This was a randomized control trial conducted at the Department of Pediatrics, Dhaka Medical College Hospital, during the period from April 2013 to April 2014. Sample size was calculated using standard formula Children between 06 months to 59 months of age & weight for height Z score < -3 were included. Children having bipedal edema, complication like shock, chest in drawing, severe anemia and illness that can lead to secondary malnutrition (tuberculosis, chronic diarrhea, etc.) were excluded from the study.

A total of 80 children were included in this study. Children were randomized by lottery method into two groups as DMCH (study group) and WHO group (control group).Each group comprises of 40 children. For each child, a detailed history including feeding history & thorough physical examination findings (weight, heiight/lenght, MUAC, edema) on admission and daily follow up were recorded in a predesigned structural questionaire. Weight were measured by digital weight machine and up to 5 gram to precision was considered.

Both groups were managed in two phases. i.e. initial phase and rehabilitation phase. In initial phase F- 75 diet used in WHO group and peanut based locally adopted diet (76 calorie/ 100 ml with 0.9gm protein / 100 ml used in DMCH group. In rehabilitation phase F- 100 diet used in WHO group and peanut based locally adopted diet (100 calorie/ 100 ml with 2.9gm protein / 100 ml) used in DMCH group.

Play therapy, nutritional educations were same for both groups. Outcome of treatment was assessed in terms of, cost of treatment, time to achieve target weight and rate of weight gain.

The target weight for height Z score was set upto >-2. Daily and total treatment cost were recorded. Necessary approval from institutional ethical committee and informed written consant was taken from parents prior to data collection . Statistical ananlysis was done by using SPSS version 17 . Test of significant were calculated from $\div^2$ test & t test. p value of was <0.05 was considered as significant.

MATERIALS

DMCH Dietary regimen (Pea-nut based):

Starter formula (F-75):	Cost	Calorie	Protein
Ingredient			
Milk powder=30 gm	Tk 16.00	120 kcal	7.74gm
Sugar=105gm	Tk 5.00	420 Kcal	
Oil=20ml	Tk 1.50	180Kcal	
Peanut=05gm	Tk 0.50	30 Kcal	1.31gm
Minerals & vitamins	Tk 0.50		
Water make up to 1000m			
Total	Tk.23.50/1000ml	760Kcl/1000ml	9.05gm/1000ml

Catch-up formula (F-100):

Ingredient	Cost	Calorie	Protein
Milkpowder=70gm	Tk. 36.75	280 Kcal	18.7gm
Sugar=65gm	Tk. 3.05	260 Kcal	
Oil=35ml	Tk. 2.85	315 Kcal	
Peanut=25gm	Tk. 2.50	150 Kcal	6.55gm
Minerals& vitamins	Tk 0.50		
Water make up to 1000ml			
Total	Tk.45.65/1000ml	995 Kcal/1000mll	25.25gm/1000ml (2.5gm/100ml)

The electrolytes and mineral were supplied separately. Potassium 3-4 mmol/kg/daymagnesium 0.4-0.6 mmol /kg/day, multivitamin supplementation, folic acid 1mg/day (5mg on day one), zinc 2mg/kg/day were given from 1st day. Elemental iron (3mg/kg/d) was given only when child gaining weight usually on days 7±1 and onwards.

WHO Dietary regimen:

Starter formula (F-75): **Catch-up formula (F-100):**

Ingredient(F-75)	Cost	Ingredient(F-100)	Cost
lk powder=35 gm	Tk. 18.30	Milk powder= 110gm	Tk. 57.70
Sugar=100gm	Tk. 05.00	Sugar=50gm,	Tk. 2.50
Oil=20ml	Tk. 1.80	Oil=35ml	Tk. 2.70
Mineral mix & vitamins=20ml	Tk. 0.50	Mineral mix & vitamins =20ml,	Tk. 0.50
Water make up to 1000ml		Water make up to 1000ml.	
Total =	Tk.25.60/1000ml		Tk.63.40/1000ml

Mineral mix contains Potassium Chloride 224gm, Tri potassium citrate 81gm, Magnesium Chloride 76gm, Zinc Acetate 8.2gm and Water 2500 ml.20ml of electrolyte mineral solution was to added 1000ml of milk food.

RESULTS

A total of 80 children were studied in two groups, 40 for WHO and 40 for DMCH group. None died in either of the groups. Hence data of 80 children were produced for final analysis.

Table 1 illustrated the distribution of the socio-economic characteristic in both the groups. No statistically significant difference exist in the distribution of gender, place of residence and socioeconomic status across two groups

Table 2 showed that, mean age for WHO group was 21.5 months whereas it was 17.3 months in DMCH group. No statistical significant difference ($p>.05$). in age was apparent. Anthropometric measure, in terms of weight height/length and MUAC were also indifferent in the two groups ($p>.05$).

Table 3 illustrated that, in DMCH regimen rate of weight gain was 17.2 gm/day and with WHO regimen it was 13.9 gm/day. So in DMCH regimen it was significantly higher ($p< .000$). In DMCH group mean time taken to achieve target weight was 13.6 days and 14.5 in DMCH and WHO group respectively but the difference was not statistically significant ($p= 0 .307$).

Table 4 showed the average treatment cost in two groups ($p<.001$). Both total treatment cost ($p<0.001$) and per day treatment cost ($p<0.001$) were significantly less in DMCH regimen.

Table-1: *Socio-demography*

Variables	Values	Group		Total	Analysis
		DMCH	WHO		
Sex	Male	14 (46.7%)	13 (43.3%)	27 (45.0%)	χ^2=.07 p=.79
	Female	16 (53.3%)	17(56.7%)	33 (55.0%)	
Residence	Urban	5 (16.7%)	3 (10.0%)	8 (13.3%)	χ^2=.59 p=.75
	Slum	22 (73.3%)	24 (80.0%)	46 (76.7%)	
	Rural	03 (10.0%)	3 (10.0%)	6 (10.0%)	
Socioeconomic status	Low	29 (96.7%)	30(100.0%)	59 (98.3%)	χ^2=1.02p=.31
	Middle	01 (3.3%)	00 (0.0%)	1 (1.7%)	

Table illustrates the distribution of the socio-economic characteristic in both the groups. No statistically significant difference exist in the distribution of gender, place of residence and Socioeconomic status across two groups.

Table -2: *Comparison of age, weight, height and MUAC in WHO and DMCH regimen group*

	WHO		DMCH		Test statistics	
	Mean	SD	Mean	SD	T	p value
Age(+/-) (Month)	21.5	12.14	17.37	8.45	-1.759	.082
Wight(+/-) (Kg)	5.8	1.44	5.137	1.23	-2.293	.052
Length/Height(+/-) (Cm)	70.7	8.11	68.1	5.98	-1.703	.093
MUAC(Cm) (+/-)	10.2	0.87	9.8	1.12	-1.720	.089

Among the two comparing groups (WHO and DMCH) no statistically significant difference in age (p >.05) is apparent. Anthropometric measure, in terms of weight (p>.05), height/length (p >.05) and MUAC (p >.05), were also indifferent in the two groups.

Table-3: *Outcome of treatment*

Variables	WHO		DMCH		Test statistics	
	Mean	SD	Mean	SD	T	p value
Time to achievetarget weight (days)	14.5	3.494	13.6	4.254	-1.028	.307
Rate of weight Gain (gm/day)	13.9	3.869	17.2	3.815	3.658	.000*

With DMCH regimen rate of weight gain was 17.2 gm/day and with WHO regimen it was 13.9 gm/day. So in DMCH regimen it was significantly higher (p< .000). In DMCH group mean time taken to achieve target weight was 13.6 days and in WHO group it was 14.5 days .So in DMCH group it was around one day less.

Table-4: Average treatment cost per patient

Variables	WHO		DMCH		Test statistic	
	Mean	SD	Mean	SD	T	p value
Treatment cost(Taka)	792.9	333.27	504.4	211.75	-1.224	.001
Per day cost (Taka)	52.9	13.50	36.5	9.12	-6.245	.001

Average treatment cost in two groups were compared in the table. Both total treatment cost (p<.001) and per day treatment cost (p<.001) were significantly less in DMCH regimen.

DISCUSSION

Between two comparing groups no statistically significant difference in age (p value =0.082) was seen. Anthropometric measurement, in terms of weight (p value=0.052), height/length (p value=0.093) and MUAC (p value = 0 .089), were also in similar range in two groups. Outcome of treatment was assessed in terms of, time to achieve target weight (hospital stay) and rate of weight gain. Cost effectiveness was measured by calculating the amount of feeding required to achieve the target weight and price of ingredients

During the study no child died in either of the groups, a study conducted by Talukder, et al [7] using ICMH protocol showed a mortality rate of 4.5% among severely malnourished children. Hossain et al.[8] found mortality rate 6.7% with ICMH protocol. Similar mortality rate was also observed by Kabir, et a [9]. Another study was conducted in Chittagong Medical College Hospital (Banani et al 2008) with traditional diet: water, milk and sugar. But there mortality rate was high (9.8 percent).

Average time to achieve target weight after the intervention was not statistically different in two groups; however in DMCH group the time taken to achieve target weight was one day less than WHO group. A study in Brazil also showed that average time to achieve target weight was same between WHO regimen and locally adopted dietary regimen[10].

Rate of weight gain was measured by researcher following up the patient every day in gm/kg/day. With DMCH regimen rate of weight gain was higher by around 3.3 gm/kg/day than WHO regimen, which was significant (p value=0 .001). Peanut based biscuits were given to children suffering from moderate malnutrition in Malawi study. Rate of weight gain was not reported in that study, however 66% achieved weight gain and no change of 34% children after 3 weeks treatment[11].

A study[12] conducted on 30 children with malnutrition at ICMH and a local private hospital compared the efficacy of WHO dietary regime with another locally adopted regime called ICMH regimen. They reported almost similar time to achieve target weight. However the study enrolled both marusmus and kawarsiorkor. A study by Devdas [13] reported that the children fed with peanut fortified millet and rice diet experience greater height, weight, greater arm and chest development and higher haemoglobin concentration.

Treatment cost is an important determinant of compliance and feasibility in resource limited country like Bangladesh. Hence we compared the cost of treatment with two dietary regimens. We considered both daily cost and total cost in Bangladeshi taka. Both total treatment cost and per day treatment cost (P<0.001) was significantly less in DMCH regimen. In DMCH group the average cost of treatment was less than 500 taka and daily cost of around 36 taka. In WHO group the total cost was around 792 taka and each day patients have to spend more than 50 taka.

CONCLUSION

Although WHO regimen was considered as standard, our study finding illustrates that locally adopted DMCH regimen is cost effective than WHO regimen.

RECOMMENDATION

As the study conducted in a single center and sample size was small, so there is a scope for multicentre study in larger sample size in this important issue.

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Original Article

Study of Antibiotic Sensitivity Pattern in Urinary Tract Infection at a Tertiary Hospital

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Abstracts

This study was conducted in a tertiary hospital at Mymensingh, Dhaka, Bangladesh between august 2013 and January 2014 to check the changing pattern of antibiotic sensitivity among uropathogens causing urinary tract infections (UTI). A total of 135 urine culture sensitivity reports were analyzed. The predominant growth of single bacteria was seen in all (100%) samples. The most common organisms isolated were Escherichia coli, klebsiella, and Staphylococcus aureus. (These represented 93.33%, 126; 4.44%,6; 2.22%,3 and of isolates respectively). 100% of sensitive to meropenem imipenem, next 85.7% of amikacin ,80% gentamicin and 73.68% of nitrofurantoin. Very high rate of resistance was seen against cephradin,nalidixic acid ,co amoxyclav ,amoxycillin (100%), cefuroxime (66.7%) ciprofloxacin (63.4%) ceftriaxone (58.8%).

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INTRODUCTION

Urinary tract infections (UTIs) are some of the most common infections experienced by humans, exceeded in frequency among ambulatory patients only by respiratory and gastrointestinal infections. Neonates, girls, young women, and older men are most susceptible to UTIs. In women, bacterial cystitis is the most common bacterial infection. Urinary tract infection is said to exist when pathogenic microorganisms are detected in the urine, urethra, bladder, kidney, or prostate with or without the presence of specific symptoms. In most instances, growth of more than 10μ organisms per milliliter from a properly collected midstream "clean-catch" urine sample indicates infection. Colony counts of $>10^5$/mL of midstream urine are occasionally due to specimen contamination, which is especially likely when multiple species are found. The vast majority of uncomplicated UTIs are caused by the Gram negative bacillus Escherichia coli, with other pathogens including Staphylococcus aureus & Klebsiella . The extensive and inappropriate use of antimicrobial agents has invariably resulted in the development of antibiotic resistance which, in recent years, has become a major problem worldwide. In patients with suspected UTI, antibiotic treatment is usually started empirically, before urine culture results are available. To ensure appropriate treatment, knowledge of the organisms that cause UTI and their antibiotic susceptibility is mandatory. As both temporal and local variables can modify these data, they need to be constantly re-evaluated to achieve a maximal clinical response before the antibiotic susceptibility the isolate is known. The aim of the present study was to assess the changing the antimicrobial therapy against pathogens causing UTIs.

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MATERIAL AND METHODS:

A total of 135 urine culture sensitivity reports were analyzed of patients who were suspected to have urinary tract infection from Aug 2013 to January 2014 in medicine indoor, Mymensingh Medical College & Hospital, Bangladesh .Clean-catch

midstream urine specimens from patients who were diagnosed clinically to be having UTI on the basis of symptoms (fever, dysuria & increased frequency of urination) were inoculated on Blood Agar and McConkey Agar plates, which were incubated aerobically at 37°C overnight. Plates showing growth suggestive of significant bacteruria, with colony counts exceeding 10 u organism/ml were subjected to standard biochemical tests for identification and antimicrobial sensitivity . Interpretation as 'Sensitive' or 'Resistant' was done on the basis of the diameters of zones of inhibition of bacterial growth as recommended by the disc manufacturer. Antibiotics against which sensitivity was tested in the present study included Amoxycillin, Amoxiclav, Ciprofloxacin, Levofloxacin, Co-trimoxazole, Gentamicin, Amikacin, Nitro-furantoin, Ceftriaxone, meropenem, & Imipenem.

RESULT:

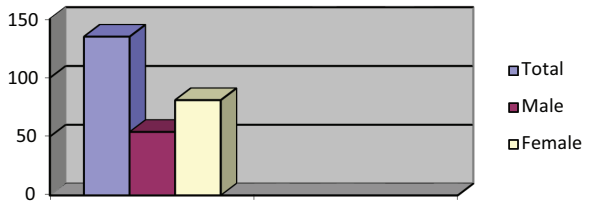
A total of 135 urine culture sensitivity reports were analyzed in this study between August 2013 and January 2014.

Sex distributions of UTI:

Total 135 urine samples showed the significant bacterial growth which were comprised of 54 (40%) samples from males and 81 (60%) from females. (Table 1) The prevalence of UTI occurred more in females than in males.

Table 1

Sex	No. of Patients (n=135)
Male	54 (40%)
Female	81 (60%)



Bar Diagram : 1

Age distributions of UTI Patients :

The highest susceptible age group of patients to UTI was ≥48 years (51.11%) followed by 15-25 years (22.22%), 26-36 y ears (11.11%), <15 years (8.89%) & 37-47 years (6.67%) (Table: 2A).

Table: 2A

Age (Years)	No. of Patients (n=135)
<15	12 (8.89%)
15-25	30 (22.22%)
26-36	15 (11.11%)
37-47	09 (6.67%)
≥48	69 (51.11%)

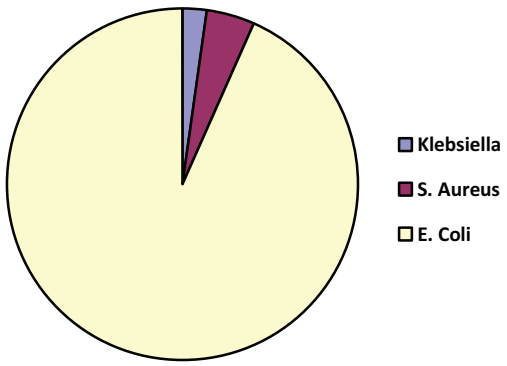
The highest prevalence of UTI in females was found in the age group of ≥48 years (37.04%) followed by age group 15-25 years (33.33%) & 26-36 years (14.81%); however in males the highest susceptible age group to UTI was also ≥48 years (72.22%).(Table : 2B)

Table: 2B

Age (Years)	No. of Male Patients (n=54)	No. of Female Patients (n=81)
<15	09 (16.67%)	03 (3.70%)
15-25	03 (5.56%)	27 (33.33%)
26-36	03 (5.56%)	12 (14.81%)
37-47	00 (00%)	09 (11.11%)
≥48	39 (72.22%)	30 (37.04%)

Patern of culture and antibiotic sensitivity pattern in UTI patients :

The predominant growth of single bacteria was seen in 135 (100%) samples. In our study , we found significant growth of Escherichia coli, Staphylococcus aureus & klebsiella. These represented 93.33%, 126; 4.44%, 6; 2.22%, 3 of isolates respectively. *(Pie Chart-1)*



Pie chart :- 1

Escherichia coli (*E. coli*) is the major aetiological agent in causing UTI, which accounts for up to 93.33% (126) of cases. In this study, the most frequent pathogens were Gram negatives which made up 95.55 % (129) of cases.

Table: 3A *(Antibiotics susceptibility patterns of E. coli (n=126)*

Antibiotics	No. of isolated tested(%)	No. of sensitive isolates	No. of resistant (%) isolates
Imipenem	33	100	0
Meropenem	91	100	0
Amikacin	42	85.7	14.3
Gentamicin	120	80	20
Nitrofurantoin	114	73.68	26.32
Ceftriaxone	18	41.2	58.8
Ciprofloxacin	123	36.59	63.41
Cefuroxime	15	33.3	66.7
Cotrimoxazole	15	25	75
Nalidexic acid	10	0	100
Cephradine	10	0	100

Among 135 samples E. Coli found in 126 cases. The most useful antibiotics in this study were Imipenem, Meropenem, Amikacin, Gentamicin, and Nitrofurantoin notably. On the other hand organisms were 100% of sensitive to meropenem, imipenem, next 85.7% of Amikacin, 80% gentamicin and 73.68% of nitrofurantoin.

Resistance to antimicrobial agents has been noted since the first use of these agents and is an increasing world-wide problem[10]. This study revealed that a higher prevalence rate of resistance to the commonly prescribed antibiotic agent. The finding that 100% of *E. coli* isolates were resistant to Amoxicillin, Co-amoxiclav and Cephradine, Nalidixic acid is of great importance and implies that these antibiotics cannot be used as empirical therapy for urinary tract infection particularly in the study area. Next to these,cotrimoxazole , cefuroxime, ciprofloxacin ,Ceftriaxone are also resistant in75%, 66.7%, 63.4% & 58.8% cases respectively. (Table-3A).

Table: 3B (Antibiotics susceptibility patterns of *S. aureus* (n=6)

Antibiotics	No. of isolated tested	No. of sensitive (%) isolates	No. of resistant (%) isolates
Gentamicin	6	100	0
Nitrofurantoin	3	100	0
Levofloxacin	6	100	0
Azithromycin	3	100	0
Amoxicillin	6	50	50
Ciprofloxacin	3	0	100

Among 135 samples, S. aureus was found in 6 cases. The most useful antibiotics in this study were Gentamicin, Nitrofurantoin, Levofloxacin, Azithromycin notably. 100% of *S. aureus* isolates were resistant to Ciprofloxacin. (Table-3B)

Table: 3C: (Antibiotics susceptibility patterns of Klebsiella (n=3)

Antibiotics	No. of isolated tested	No. of sensitive (%) isolates	No. resistant (%) isolates
Amikacin	3	100	0
Nitrofurantoin	3	100	0
Amoxicillin	3	0	100
Ceftriaxone	3	0	100
Gentamicin	3	0	100
Ciprofloxacin	3	0	100

Among 135 samples Klebsiella was found in 3 cases. The most useful antibiotics in this study were Amikacin, Nitrofurantoin notably. 100% of *Klebsiella* isolates were resistant to Ciprofloxacin, Amoxicillin, Ceftriaxone, Gentamicin (Table-3C).

DISCUSSION

Urinary tract infection is one of the most common types of infectious disease encountered in the practice of medicine these days.UTI is one of the most important causes of morbidity even today in the developing countries like Bangladesh[9]. This may be due to abuse of chemotherapeutic agents and most importantly ignorance of people and little or

no prevention measure. The present study had been investigating that the causative organism of UTI in adult in both sex and their pattern of culture sensitivity as well as their drug resistant pattern.

Among total 135 urine samples showed the significant bacterial growth which were comprised of 54 (40%) samples from males and 81 (60%) from females. The prevalence of UTI occurred more in females than in males. It was shown in several studies that women are at increased risk to develop UTI then men[24].These results also agree with other reports, which showed that UTIs are more frequent in females than males during adulthood[7, 8, 9].

In present study we observe that the occurrence of UTI recorded among the elderly was higher (≥48 years, 51.11%) compared to young age patients 15-25 years (22.22%), 26-36 years (11.11%), <15 years (8.89%) and middle-age patients & 37-47 years (6.67%) which differs from the other studies done in Kuwait and Nigeria[7] in which the highest incidence of UTI was recorded among the age group 20 to 50 years (63.4 and 74.7%, resp.) and lowest among the age group >50 years (13.3 and 10.3%, resp.). However, our results agree with the study done in Japan with a 20-year period in which a trend of increasing complicated UTI was reported in elderly patients. In this study it was found that the elderly males had a higher incidence of UTI (72.22%) when compared with the elderly females (37.04%). This finding is similar to a study conducted at a tertiary care hospital at Jaipur & Rajasthan in India.

According to our study, we have found that the most common organisms isolated were Escherichia coli, klebsiella and Staphylococcus aureus which represented 93.33%, (126); 4.44%, (6); 2.22%, (3) of isolates respectively *E. coli* is by far the most common bacteria isolated from urine samples in both sexes and this finding is in agreement with others finding too[1,2,3,4 25.]. In this study the second reported isolates was Staphylococcus species which is similar to other studies [2, 4, 5, 6,25].

On this study, we have found that 100% of isolated E. coli were sensitive to meropenem, imipenem, next 85.7% of Amikacin, 80% gentamicin and 73.68% of nitrofurantoin and a comparable rate of sensitivity has been reported for these drugs in previous studies done in Ethiopia[16, 17, 20, 21, 22] in Kosovo [19], in Iran [12]and in South Croatia [2].This study also revealed that a higher prevalence rate of resistance to the commonly prescribed antibiotic agent. The finding that 100% of *E. coli* isolates were resistant to Amoxicillin, Co-amoxiclav and Cephradine, Nalidixic acid is of great importance and implies that these antibiotics cannot be used as empirical therapy for urinary tract infection particularly in the study area. Next to these, cefuroxime, ciprofloxacin, Ceftriaxone are also resistant in 66.7%, 63.4% & 58.8% cases respectively. Similar findings were observed by many workers around the world.[12-18,2627]. Apart from these, 63.4% isolates were found resistant against ciprofloxacin. A study in Taiwan found that prior exposure to ciprofloxacin raises the risk of resistance[26].

In 6 cases , S. aureus was found Among 135 samples. The most useful antibiotics in this study were Gentamicin, Nitrofurantoin, Levofloxacin, Azithromycin notably. 100% of *S. aureus* isolates were resistant to Ciprofloxacin. In 3 cases among 135 samples, Klebsiella was found and the most useful antibiotics were Amikacin, Nitrofurantoin notably. 100% of *Klebsiella* isolates were resistant to Ciprofloxacin, Amoxicillin, Ceftriaxone & Gentamicin.

The possible explanation behind the resistance showed to these antibiotics, may be because these antibiotics have been in use for a long period and must have been abused and as a result the organisms must have developed mechanisms of circumventing their mode of action. Two alarming findings seen in the study were that, the substantial resistance shown to Amoxicillin, Co-amoxiclav, cephradine & nalidixic acid by almost all important gram negative isolates and resistance to third generation cephalosporin, Ceftriaxone.

CONCLUSION

In conclusion one can truly affirm that the choice of drugs in the treatment of UTI is quite narrow today due to the wide scale resistance that the common UTI pathogens show to drugs which have been used previously. Drugs like Amoxicillin, Cotrimoxazole, Cephradine, Co-amoxiclav, Nalidixic acid which were considered as effective against uropathogens, are now rarely prescribed as empirical therapy in areas where resistance rate to

theses antibiotics is high. But it is clear that Meropenem, Imipenem, Nitrofurantoin, Gentamicin & Amikacin are good choices for the treatment of indoor patients.

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Original Article

Histopathological Review of Uterine Leiomyoma

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Abstract

Background: *Leiomyomas are benign tumors of smooth muscle cells commonly encountered in women of reproductive age group. Their gross appearances are often altered by various secondary changes. Subtypes of leiomyomas are chiefly of interest as they may mimic malignancy in some cases.*

Objective: *This study was done to analyze clinical and histopathological changes of uterine leiomyomas.*

Materials and Methods: *It was a retrospective cross-sectional study conducted in the Department of Pathology, Enam Medical College & Hospital, Savar, Dhaka during the period from January 2014 to December 2017. A total of 229 hysterectomy specimens diagnosed as uterine leiomyoma and 36 myomectomy specimens were subjected to clinicopathological evaluation.*

Results: *The age of the patients ranged from 20 to 80 years with a mean age 42.5 years. Majority of the patients were between 41-50 years (58.5% cases). Menorrhagia was the commonest symptom occurring in 45% of cases, followed by mass in abdomen (25%) and pain in abdomen (20%). Most of the cases showed a single fibroid (64.5%) and mainly occured in parous women (97%). Majority of the fibroids were intramural in location (57.7%). Leiomyoma variants were seen in 13 cases (4.9%), amongst which cellular leiomyoma (1.5%) was the commonest. Secondary degenerative changes were observed in 12.1% of cases, amongst which hyaline change was the most common (6.8%).*

Conclusion: *Hysterectomy is a commonly performed procedure in the management of uterine leiomyomas. The ultimate diagnosis and prognosis depends on the histopathological examination; therefore, every operated specimen must be subjected to histopathology.*

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Keywords:
Leiomyoma, Hysterectomy, Menorrhagia

INTRODUCTION

Leiomyoma is synonymously called as "fibroid," "fibromyoma," "myoma" or "fibroleiomyoma." It is the most common solid tumor in women and the most frequently occurring among smooth muscle tumors, with an estimated incidence of 70% in hysterectomy specimens for noncancer-related conditions. Fibroids are also a common reason for hysterectomy, accounting for at least 200,000 such procedures annually in the US. They are present in 20–30% of women over 30 years of age, rising to > 40% in women older than 40 years. The prevalence of uterine leiomyomas varies among ethnic groups; black women tend to have leiomyomas at a younger age that are more often multiple and typically larger than those in white women, indicating the presence of a genetic predisposition or other influences[1, 2].

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Most patients with uterine leiomyomas are asymptomatic. When symptoms occur, they usually correlate with location of the leiomyomas, their size, or associated degenerative changes. Abnormal uterine bleeding is the most common presenting symptom, either in the form of menorrhagia or hypermenorrhea, which may lead to severe anemia. Abdominal pain secondary to acute hemorrhage may occur. Patients may have a history of infertility, increased rates of spontaneous abortion, and pregnancy-related problems when there is a submucosal myoma. Rarely, the myoma is large and the patient may present with a pelvic mass and secondary gastrointestinal or urinary symptoms due to compression. Symptomatic leiomyomas need urgent attention either by myomectomy in younger women desirous of retaining the childbearing function. In elderly women hysterectomy still remains the traditional modality of treatment. The clinical diagnosis of myoma is usually based on the finding of an enlarged, mobile uterus with an irregular contour on bi manual examination or an incidental finding on transabdominal sonography. But ultrasonographics are also only suggestive; the final diagnosis is confirmed by gross and microscopic examination of the surgically removed fibroids. Only a few studies have elaborated on the clinicopathological changes seen in uterine leiomyoma. This study is undertaken to analyze clinical and histopathological changes of uterine leiomyoma[2].

MATERIALS AND METHODS

This is a retrospective cross-sectional study of uterine leiomyoma, reported from the Department of Pathology of Enam Medical College & Hospital, during a period of 4 years, from January 2014 to December 2017. A total of 229 hysterectomy specimens histologically diagnosed as leiomyoma and 36 myomectomy specimens were included in the study. The clinical information and the relevant investigations of the patients were obtained from the histopathological requisition forms and clinical record files. The specimens received in the department of pathology were properly labeled, numbered and fixed in 10% buffered formalin. After a detailed gross examination of the specimens, multiple sections were taken from representative sites, processed and paraffin blocks were made. The blocks were then sectioned and stained routinely with hematoxylin and eosin. Special stains were used wherever required.

RESULTS

We received 816 hysterectomy specimens done for various indications and 36 were myomectomy specimens. Among the hysterectomy specimens, 229 specimens were found to have fibroids. Patients who underwent myomectomy were in their reproductive age and found to have fundal fibroid, thus hysterectomy was deferred. The age of the patients ranged from 20 to 80 years with a mean age of 42.5 years. The highest proportion of cases of uterine leiomyoma occurred in the age range of 41-50 years that accounted for 155 cases (58.5%). This is followed by 31-40 years age (Table-1). Maximum cases of leiomyoma were seen in the age group 31-50 years (212 cases, 80%). Out of 265 patients studied, 257 patients (97%) were parous, which included 16 cases of uniparous patients. Parity of the patients ranged from 0-5. Eight patients were nulliparous.

Table-1: *Age wise distribution of patients with leiomyoma.*

Age range (in years)	No of cases	Percentage
20	1	0.4
21-30	27	10.2
31-40	57	21.5
41-50	155	58.5
51-60	21	7.9
61-70	1	0.4
>71	13	1.1

Most fibroids were diagnosed clinically and some were incidental findings. Most of the patients presented with multiple features. The commonest complaint was menstrual disturbance, followed by abdominal swelling and abdominal pain (Table-2). Size of the fibroids varied from few mm to maximum 13 cm in diameter. Highest dimension of the lesion measured was 13x10x9 cm found in a female of 35 years. Most of the uteri showed a single fibroid accounting for 64.5% cases (n=172). The number varied from 2 to 10 in the remaining. The commonest site where the fibroids were located was intramural (153 cases, 57.7%), followed by subserous (37 cases, 14%), submucous (8 cases, 3%) and 25.3% of the cases (67 cases) had leiomyomas in more than one location.

Table-2: *Clinical presentation of the patients.*

Clinical Presentation	No of patients	Percentage
Menstrual abnormalities		
Menorrhagia	119	45
Irregular menses	40	15
Dysmenorrhea	13	5
Mass abdomen	66	25
Pain abdomen	53	20
Primary infertility	8	3.1
Recurrent abortion	5	1.9
Bladder disturbance	3	1.2
Asymptomatic/Incidental	42	15.8

Histologically, 252 cases (95.1%) were typical lesion characterized by interlacing bundles of smooth muscle cells separated by a greater or lesser amount of well-vascularized connective tissue. The individual muscle cells were uniform in size and shape and had the characteristic oval nucleus and long, slender bipolar cytoplasmic processes. Variants of leiomyomas were seen in 13 cases (4.9%). Of these, 4 cases were cellular, 3 were lipoleiomyoma, 2 were myxoid and 2 were atypical leiomyoma, 1 was mitotically active and 1 was red degenerative. Most of these are the result of secondary changes in the leiomyoma. Secondary changes were seen in 32 cases (12.1%). Hyaline degeneration was found to be the commonest degeneration, constituting 6.8% of cases. Other secondary changes include hydropic degeneration, cystic change, myxoid change, calcification and hemorrhage (Table-3).

Table-3: Secondary changes within leiomyoma

Secondary change	No of cases	Percentage
Hyaline degeneration	18	6.8
Hydropic degeneration	06	2.3
Cystic change	04	1.5
Calcification	02	0.8
Hemorrhage	02	0.8

DISCUSSION

The age of the patients ranged from 20-80 years with a mean age of 42.5 years. Lahori et al. in a similar study found age range 18-62 years with a mean age of 45.82 years.[3] Owolabi et al. found mean age 35 years in their study and highest proportion of cases occured in the age range 30-39 years (40.31%).[4] Dayal et al.[5] and Pakesh et al.[6] also found highest number of cases in age group 31-40 years (42.1% and 48.57% respectively). However in this study, maximum number of cases were seen in 41-50 years age range (58.5%) and 80% of cases were seen in age range 31-50 years. This is comparable to the studies conducted by Gowri et al.[7] (49%), Priayadarshini et al.[8] (51%) and Ksheera et al.[9] (56%).

In this study, patients with fibroids presented with multiple features, the commonest complaint was menstrual disturbance (65% cases) and menorrhagia was the commonest presenting symptom (45% cases). Priayadarshini et al.[8] , Gowri et al.[7], Kaur et al.[10] and Dayal et al.[5] also found menorrhagia as the commonest complaint (38%, 49.03%, 51.4% and 55.6% respectively). Dysregulation of the vascular channels along with a number of growth factors in the myomatous uterus is said to be responsible for this symptom[11].

In the present study, majority of the fibroids were intramural in location constituting 57.7%, followed by subserosal (14%) and submucosal (3%) location. Priayadarshini et al. observed intramural fibroids in 67% cases, subserous in 20% and submucosal in 11% cases[8]. Intramural lesions were also the most common type in studies by Gowri et al.[7] (48%) and Pakesh et al[6] (70%). Studies have reported the risk of uterine leiomyoma to be 20-50% lower among women who have ever given birth compared to nulliparous women, and the risk appears to decrease with increasing parity. This explains that pregnancy reduces the time of exposure to unopposed estrogens, whereas nulliparity or reduced fertility may be associated with anovulatory cycles characterized by long term unopposed estrogens.[12] However, in the present study, the majority of the patients were multiparous (97%), which is similar to studies by Pakesh et al[6] (97.14%) and Kaur et al[10] (97.69%).

In this study, most of the uteri showed a single fibroid accounting for 64.5% which is in accordance with the studies of Lahori et al.[3] (56.96%),

Priayadarshini et al.[8] (59%) and Gowri et al.[7] (71%). Ksheera et al. observed solitary fibroid in 45% cases and multiple fibroid in 55% cases[9].

In this study, usual leiomyoma was the commonest accounting for 95.1% cases. Variants of leiomyoma were seen in 13 cases constituting 4.9%. Of these, 4 cases were cellular, 3 were lipoleiomyoma, 2 were myxoid, 2 were atypical, one was mitotically active and one red degenerative leiomyoma. Most of these are the result of secondary changes in the leiomyoma. Lipoleiomyoma contains an admixture of smooth muscles and mature adipose tissues. Cellular leiomyoma have increased cellularity without any necrosis, atypia, or an excessive number of mitotic figures. Atypical leiomyoma contains bizarre tumor cells with variation in size and shape, hyperchromatic nuclei, and multinucleated forms but no necrosis or increased mitotic activity. Mitotically active leiomyoma contains 5 to 15 mitotic figures per 10 HPF without any necrosis or cytological atypia. Red degeneration is characterized grossly by a bulging surface and a homogeneous dark red appearance, and microscopically by extensive coagulative necrosis.[1] Lahori et al. in their study encountered leiomyoma variants in 30.38% cases, which included cellular leiomyoma (6.33%), diffuse leiomyomatosis (5.05%), apoplectic (3.8%), cotyledonoid (3.8%), palisaded (2.53%), vascular (3.8%), intravascular (2.53%), mitotically active (1.27%) and atypical leiomyoma (1.27%).[3] Pakesh et al. found leiomyoma variants in 8.57% cases, of these 3 cases were cellular, 2 cases atypical and one case was epithelioid leiomyoma[6].

Secondary degenerative changes were seen in 12.1% cases in this study. Among these, 6.8% showed hyaline degeneration which constituted the most common degenerative change observed, followed by hydropic degeneration, cystic change, calcification and hemorrhage. Gowri et al. reported secondary changes in 22.6% cases and hyalinization being the commonest change (16.9%), followed by cystic and myxoid change[7]. Lahori et al. found degenerative changes in 16.46% cases and the most common change was hyaline degeneration (6.33%)[3]. Ksheera et al. found degenerative changes in 25% of leiomyoma; the commonest change encountered on microscopic examination was hyaline change accounting 18%, followed by calcification and fatty change[9]. Degeneration in fibroids occurs secondary to inadequate blood supply, which may result commonly in hyalinization, followed by myxomatous, hydropic or calcification and very rarely malignant degeneration. The type of degenerative change depends on the degree and rapidity of the onset of vascular insufficiency[13].

In conclusion, leiomyomas are the most common benign tumors of the pelvis. These are found frequently in multiparous women in reproductive and perimenopausal age groups and present commonly with menorrhagia. Intramural site is the most common location, hyaline change is the most common secondary degeneration and cellular variant is the most common subtype seen in this study.

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Case Report

Primary Amenorrhoea (Cryptomenorrhoea) : A Mullerian Agenesis

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ABSTRACT

A case of mullerian agenesis, Mayer-Rokitansky-Kuster-Hauser(MRKH) syndrome in a 17 years old girl with primary amenorrhoea (Cryptomenorrhoea) is reported. This patient exhibited normal female external physical characteristics with a shallow, blind vaginal pouch on examination. MRKH syndrome has a prevalence of 1 in 4000 to 10000 females. Treatment is multifactorial and should non surgical vaginal dialator therapy, surgical neovaginal options, as well as psychosocial support and counseling on future reproductive options.

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INTRODUCTION

Evaluation of primary amenorrhoea is always challenging for a clinician. Either a stuctural or a numerical anomaly in the two X chromosomes of the female complement results in the failure of commencement of menstruation and the development of the secondary sexual characters, a condition referred to clinically as primary amenorrhoea. Primary amenorrhoea is usually defined as failure of the onset of menstruation by age 18 regardless of normal growth and development. Primary amenorrhoea could be physiological or anatomical. It is with reference to the physiology the defect would be related to the hypothalamic-pituitary-ovarian-endometrial pathway. The cause of primary amenorrhoea lies somewhere along this complex chain of hormonal events. When the menstrual flow is obstructed by congenital lesions such as cervical vaginal atresia, transverse vaginal septum, imperforate hymens then primary amenorrhoea would be the resultant of an anatomical defect. In this study, cryptomenorrhea was diagnosed two years back and hysterotomy was done for drainage of menstrual blood. Also tried for vaginal reconstruction but failed. This time she again diagnosed as cryptomenorrhea and severe lower abdominal pain. At first we tried vaginal reconstruction but failed. Then hysterotomy was done for drainage of menstrual blood. For preservation of uterus tried vaginal reconstruction through abdomino-vaginal route but not possible due to absent of cervix and presence of a tough intervening tissue. Then proper counseling was done about present situation, future reproductive life and also about hysterectomy for her life saving. Then hysterectomy was done.

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CASE PRESENTATION:

A 17 years old unmarried female with thelarche at 11 years old and puberche at 12 years old presented on 2/12/2017 with primary amenorrhea, history of hysterotomy with vaginoplasty and severe lower abdominal pain for 10 days. She stated that she had lower abdominal cramping, backache every 28 days, lasting 1-2 days without vaginal spotting or bleeding. She also complaints severe lower abdominal pain for last 7-10 days. On physical exam...she was

moderately anaemic, lower abdomen bulge upto umbilicus and severe tender. Per vaginal exam vulva, labia majora and minora normal, vagina-blind vaginal pouch just admitted tip of finger. Per rectal exam- A soft mass felt.

She had a past history, 2 years ago she was diagnosed as a case of haematometra.Then abdominovaginal approach was done. Hysterotomy was done and drainage of menstrual blood and attempted to vaginoplasty but failed. Last 2 years she experienced cyclical lower abdominal pain and backache. For last 7-10 days which was severe in nature and admitted in hospital.

INVESTIGATION:

Hb -8.2 gm/dl ,blood group- O positive, HBsAg-negative, S.creatinine-2.15gm/dl, RBS -3.9 mmol/L

USG of whole abdomen:

1. Hematometra.

2. Non visualized right kidney.

3. Left sided moderate hydroureteronephrosis.

Nephrology consultation done. It is associated with OHVIRA syndrome.

Management: At first treated conservatively. Then decision was taken for surgical management.

Operation was done on 4/1/2018 at 12.30pm. Abdominal hysterectomy with vaginal reconstruction was done.

At first vaginal approach was done. A transverse (2cm) incision was given on posterior forchette. Then preceding towards pouch of vagina and mainly finger dissection was done. But failed to reach up to cervix (absent of cervix).Then abdominal approach was done. After opening of abdomen by pfannenstiel incision omentum was found swallowed by tarry coloured blood which was spilled through fallopian tubes. Both ovaries and fallopian tubes seem to be normal and preserved. 1.5cm incision was given on anterior wall of lower uterine segment. About 500-700 ml tarry coloured blood drainage through suction tube. Then a small sized dialator passed through uterine cavity and another passed through the vaginal route but no communication can be done due to tough intervening tissue. So decision was taken for hysterectomy. One unit of blood transfusion was given during operation. Her postoperative period was uneventful and discharged on 5th POD.

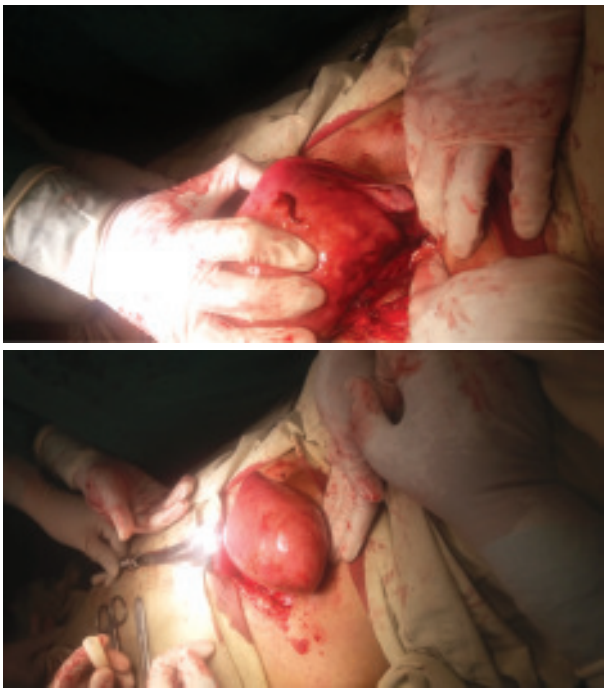

Fig.-1: *Uterus, ovary and fallopian tubes*

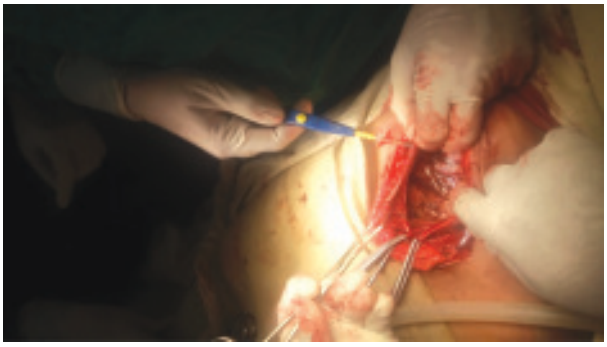

Fig.-2: *Intestines and omentum swallowed by tarry coloured blood*

DISCUSSION:

Primary amenorrhoea is defined as failure to reach menarche. Evaluation should begin if no pubertal development has occurred by the age 13, if menarche has not occured by age 15,or if menarche has not occurred with in five years of thelarche.The differential diagnosis of primary amenorrhoea encompasses that of secondary amenorrhoea and includes pregnancy, hyperprolactinemia, thyroid dysfunction,hypothalamic-pituitary dysfunction, primary ovarian insufficiency related to chromosomal abnormalities and polycystic ovarian syndrome. The differential diagnosis expands to congenital absence of the vagina, low transverse

vaginal septum, imperforate hymen and 46,XY disorders such as androgen insensitivity. A thorough history and physical examination should be the first step in the primary amenorrhoea work up[4].

Evaluation of a patient with primary amenorrhoea should include a vaginal exam, uterine assessment, follicle-stimulating hormone, luteinizing hormone, prolactin and thyroid-stimulating hormone levels. Karyotype analysis should be considered when differentiating testicular feminization and Turner syndrome(45, XO) from MRKH syndrome. Free and total testosterone, as well as dehydroepiandrosterone sulfate should be considered if signs of hyperandrogenism such as virilization or hirsuitism are present. Estradiol levels can be obtained if signs of estradiol exposure(eg. thelarche) are not present. Progesterone level can be obtained, followed by a progesterone challenge test to confirm functional anatomy if a uterus is indeed present. Transvaginal ultrasound should be first choice in imaging to assess for mullerian anomalies. A magnetic resonance imaging of the abdomen and pelvis can then be used to further describe those findings seen on screening transvaginal ultrasound. Lastly, if ultrasound and MRI are not yielding, laparoscopy can be performed to assess for degree of MRKH anomalies[5].

While MRKH syndrome physical examination reveals normal height, body hair distribution, secondary sexual characteristics, and external genitalia the patient will often have an absent vagina or shortened blind pouch without a cervix. Careful evaluation of abdominal, urinary tract and skeletal structures is recommended as upto 53% of MRKH syndrome patients will have congenital malformations. Our patient was associated with Ohvira syndrome.

MRKH syndrome was described between 1829 by physiologist Mayer (1829), Rokitansky (1938), Kuster(1910) and gynaecologist Hauser (1961)[1] and is second most common cause of primary amenorrhea, behind gonadal dysgenesis. MRKH syndrome has an incidence of 1 per 4000-10000 females and results from interrupted embryonic development of the paired mullerian ducts between the 4th and 12th week of gestation. These ducts normally fuse distally into lower two-thirds of the vagina and uterus, but remain independent proximally to form the fallopian tubes.In 2% to 7% of patients with MRKH syndrome, active endometrial tissue can be identified. Ovarian development is normal given the separate embryologic source.The molecular basis for MRKH syndrome has yet to be identified but multiple genes are being investigated. Genetic transmission is believed be an autosomal dominant fashion with incomplete penetrance and variable expressivity[2,5].

There are three forms of MRKH syndrome: typical, atypical and MURCS(Mullerian duct aplasia, renal aplasia, cervico-thoracic somite dysplasia). American Fertility Society classifications(A and B).The typical form represents 47% of MRKH syndrome and is defined as development of fallopian tubes, ovaries,,and renal system. The atypical form represents 21% of MRKH syndrome and is defined as malformations of the ovary or renal system. MURCS represents 32% of MRKH syndrome and is associated with skeletal and/or heart malformations, muscular weakness and renal malformations. The renal system seems to be most affected in MRKH syndrome due to early interaction of the mullerian(paramesonephric) and wolffian (mesonephric) ducts[3].

A comprehensive approach to the management of MRKH syndrome patients is necessary and should include psychosocial counseling (healthy sexual practice, emotional stability and fertility option such as assisted reproductive techniques and use of a surrogate). Vaginal reconstructive techniques to produce a neovagina should be considered. Progressive vaginal dilatation produces a functional in 90-95% of patients and should be attempted prior to any surgical approaches [2].

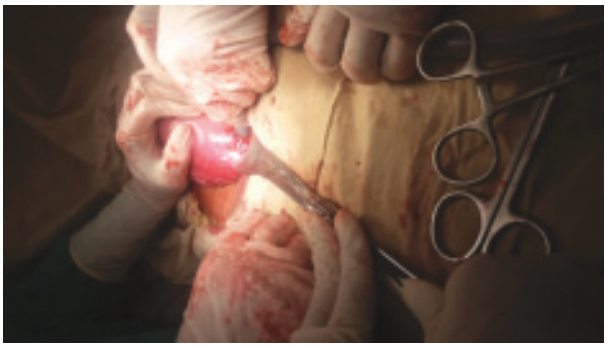

Fig.-3: *Drainage of collected menstrual blood by sucktion tube*

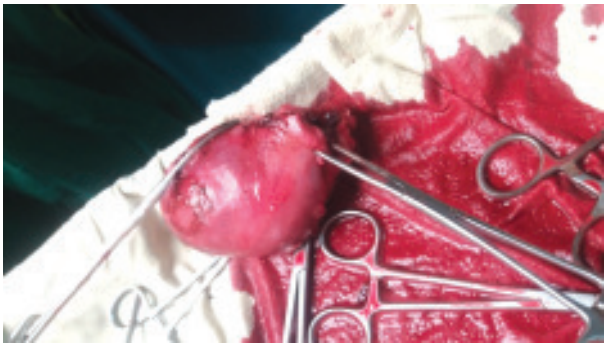

Fig.4: *Uterus after operation*

CONCLUSION

Evidence of primary amenorrhea is less than 1%. A thorough history and physical exam is critical in the evaluation of primary amenorrhea in the primary care setting. In this case, MRKH syndrome was diagnosed. A multidisciplinary and comprehensive approach done for this patient and counseling done for psychological support.

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