EDITORIAL

Dialysis Adequacy - a Difficult Challenge

Hemodialysis is the most common renal replacement therapy in the world, and hemodialysis adequacy is an important and influential factor in the reduction of various complications experienced by dialysis patients. Adequacy of dialysis is a term that has been used for many years based on measurement of small solute clearance using urea and creatinine. Multiple factors influence hemodialysis adequacy eg. Economy,distance of dialysis centre,co-morbidities of patients, supervision of nephrologists etc. The concept of quality, adequacy, or appropriateness of hemodialysis which were introduced in the 1970s, implies dialysis which enables patients to have a normal quality of life as well as clinical tolerance with minimal problems during the dialysis and interdialysis periods. Quantification of the dialysis dose is an essential element in the management of chronic HD treatment because the adequacy of the dose has a profound effect on the patient morbidity and mortality.

To ensure a sufficient dialysis, the delivered dose should be measured and monitored routinely. Urea kinetic modelling (UKM)is the best method for routine measurement of the dose of haemodialysis. UKM is assessed by several indicators such as percent reduction of urea during dialysis (URR), total clearance of urea normalized for distribution volume (Kt/V), protein catabolic rate (PCR) and time average concentration of urea (TAC) and these are calculated with mathematical formulas. Adequacy of hemodialysis improves patient survival, quality of life and biochemical outcomes and minimizes disease complications and hospitalizations.

Individualizing the hemodialysis prescription based on monthly assessment of single-pool Kt/V would be a useful and practical tool to provide a safe and cost-effective hemodialysis treatment. The National Kidney Foundation Disease Outcomes Quality Initiative (KDOQI) guidelines recommend that the minimum adequate dose of hemodialysis given three times per week to patients with Kr less than 2 mL/ min/1.73 m2 should be a single-pool Kt/V of 1.2 per dialysis. For treatment times less than 5 h, an alternative minimum dose is a urea re-duction ratio (URR) of 65%.

Most of the studies adequacy of dialysis refers to biochemical outcome measures, most of which are not related with patient relevant outcomes. For patients, adequate dialysis is a dialysis that enables them to spend as much quality time in their life as possible.

In this issue of BCPS journal, Rasul et al conducted a study over 137 patients in the dialysis center of Combined Military Hospital (CMH) Dhaka to determine adequacy of hemodialysis. Only 21% had adequate dialysis in the group of 8 hours per week hemodialysis and in the group of 12 hours per week hemodialysis, 43 % had good dialysis. Patients who achieve target spKt/V also achieve target URR and was statistically significant. URR, TAC urea and nPCR was significantly better in patients with spKt/V>1.2 group. The study also found that patients who do there dialysis with blood flow more than 250 ml/min had significantly better dialysis adequacy.

This study is from a single center and the sample size was also small, as such the result may not reflect the exact picture of whole country. Further studies could be undertaken including a large number of patients from different hospitals of different districts of the country so that overall national consensus about hemodialysis prescriptions could be made.

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Mamun Mostafi[1], Masrura Jabin[2]
Gonoshasthaya Somaj Vittik Medical College and Gonoshasthaya Nogor Hospital

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Cervical Cancer - A Preventable and Potentially Curable Cancer

Cancer is predicted to be an increasingly important cause of morbidity and mortality in Bangladesh in the next few decades. The estimated incidence of 12.7 million new cancer cases will rise to 21.4 million by 2030[1].Cervical cancer is the fourth most frequent cancer in women with an estimated 570,000 new cases in 2018 representing 7.5% of all female cancers and one women dying every 2 minutes [2]. Approximately, 90% of deaths from cervical cancer occurred in low and middle-income countries. It is the 2nd most common cancer among women in Bangladesh, and every year 11,956 new cases are detected and 6582 women die[3]. Human Papilloma Virus (HPV) has now been identified as the etiological agent responsible for cervical cancer. HPV prevalence increases with high risk sexual behaviour and poor sexual hygiene[4]. About 90% of HPV clear within 2 years and a small proportion of infections can persist and progress to cervical cancer in 15 to 20 years[5].

But the truth is that almost all of these deaths could be avoided if all adolescent girls were immunized against HPV, cervical screening and treatment of pre-cancerous lesions were available to all women. There are currently vaccines available protecting against 90% of cervical cancers. A HPV vaccination trial was conducted in Bangabandhu Sheik Mujib Medical University in 2008[6]. and Govt. initiated HPV vaccination in 2016 and scaling up the programme to girls of grade V at school and 10 years at community[3].

Early diagnosis and effective treatment can significantly improve the likelihood of survival. WHO Package of essential non-communicable (PEN) disease interventions for primary health care in low-resource settings included referral of women with suspected cervical cancer[7]. A successful initiative was taken in Korail Slum, Dhaka, Bangladesh by Massachusetts General Hospital, Boston, USA and AK Khan Health Care Trust, Dhaka, Bangladesh in 2011 with both screen-and-treat precancerous lesions with visual inspection of cervix with acetic acid (VIA) and loop electrosurgical excision procedure (LEEP)[8]. According to National Cervical Cancer Strategy, Bangladesh gradually developed opportunistic screening facilities with VIA for the women above 30 years. All screen-positive women will be counseled, further evaluated by colposcopy and treated at appropriate facilities[3]. Three types of screening tests currently recommended by WHO : HPV testing for high-risk HPV types, VIA, Pap test and liquid-based cytology (LBC), for treatment of pre-cancer lesions, WHO recommends treatment for precancerous lesion of cryotherapy and LEEP. For advanced lesions, women should be referred for further investigations and adequate management[5].

There are five types of standard treatment: Surgery, Radiation therapy, Chemotherapy, Targeted therapy and Immunotherapy. Radiation therapy uses high-energy x-rays to kill cancer cells. External radiation therapy includes 3-dimensional radiation therapy, Intensity-modulated radiation therapy and Volumetric Arc Therapy, Stereotactic Radiosurgery. Internal radiation therapy (brachytherapy) uses a radioactive substance sealed in needles, seeds, wires, or catheters that are placed directly into or near the cancer. Chemotherapy is a cancer treatment that uses drugs to stop the growth of cancer cells, either by killing the cells or by stopping them from dividing. The way the chemotherapy is given depends on the type and stage of the cancer being treated.

Cancer research is vital to find new management strategies. Some research works are also going on in Bangladesh. Recently, a promising research work has performed in National Cancer Research Institute and Hospital, Dhaka, Bangladesh on prognostic impact of histopathological type of cervical cancer on disease free survival (DFS), local, loco-regional and distal recurrence after completion of treatment with radiation therapy. In multivariate analysis it was shown that histopathological type and stage of disease were found to be independently significant prognostic factors for DFS.

It is expected that prevention and cure of cervical cancer will be possible in near future.

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Prof Syed Akram Hussain
Coordinator, Square Oncology and Radiotherapy Centre
Dhaka, Bangladesh

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Assessment of Hemodialysis Adequacy in Patients with End Stage Renal Disease in a Military Hospital of Dhaka, Bangladesh

MM RASUL[a], AKMM RAHMAN[b], A NESSA[c], AS KHAN[d], T HUSSAIN[e]

Summary:

Introduction: *The burden of kidney disease patients requiring renal replacement therapy is increasing day by day. Hemodialysis (HD) constitutes the most common form of renal replacement therapy (RRT) worldwide. Determining the adequacy of hemodialysis, Urea kinetic modeling (UKM) is an important tool for this. The aim of this study was to determine hemodialysis adequacy by UKM.*

Material & Methods: *A total 137 patients were sampled in dialysis center of Combined Military Hospital (CMH) Dhaka. This was a cross sectional study. Data were collected from predialysis, postdialysis and next predialysis blood sample. Mean of adequacy parameters like single pool Kt/V (spKt/V), urea reduction ratio (URR), time average concentration of urea (TACurea) and normalized protein catabolic rate (NPCR) were calculated and compared between twice and thrice per week hemodialysis groups. Also compared adequacy variables between groups who achieved cutoff values and who did not achieve it.*

Results: *One hundred (72.99%) patients were on 8 hours/week and 37 (27%) were on 12 hours/week hemodialysis session. Only 21(21%) and 16(43%) could achieve spKt/V cut off value among 8 hour and 12 hours group respectively. Eighty (58.39%) patients had URR < 65% in this study. Blood flow e+250 ml/min group had significantly better dialysis adequacy than blood flow <250ml/min group, URR (81.31± 10.21 vs. 54.51 ± 11.52 and p-value <0.001), spKt/V (1.99 ± 0.41 vs. 1.41 ± 0.31 p-value< 0.001) Thrice weekly hemodialysis group achieved better adequacy than twice weekly group.*

Conclusion: *Frequency and blood flow of dialysis are strongly associated with adequacy of hemodialysis as evidenced by spKt/V and URR value. So to achieve hemodialysis adequacy, increasing the frequency of dialysis from two to three sessions per week is recommended.*

Key words: *Assessment, Hemodialysis adequacy, Urea Kinetic Modeling (UKM).*

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Introduction:

Chronic kidney disease (CKD) is a devastating disease. The term "end- stage renal disease" (ESRD) generally refers to CKD treated with either dialysis or transplantation. Prevalence of ESRD in Bangladesh not known but age-adjusted incidence rate of ESRD in India has been estimated to be 229/million population[1]. Diabetes is the main cause of kidney failure in most countries, accounting for 40% or more of new patients.[2] Prevalence of CKD seems to be increasing particularly in older individuals[3]. Hemodialysis is the mainstay therapy which is offered for ESRD patients who cannot undergo renal transplantation. Situation of Bangladesh is not different. A central issue in the management of patients undergoing maintenance hemodialysis (HD) is the assessment of the adequacy of dialysis[4]. Despite its dramatic success at saving lives, HD remains far from perfect therapy. More than 20% of hemodialysis patients die each year [5]. In developed countries usually hemodialysis is done thrice a week. However in India only 20% of patients are dialyzed 3 times a week[6]. Although it is well-known that increasing the frequency of dialysis improves the quality of life but it is a difficult

a. Md. Maksudur Rasul, Combined Military Hospital, Dhaka Cantonment, Dhaka, Bangladesh

b. AKM Mijanur Rahman, Combined Military Hospital, Dhaka Cantonment, Dhaka, Bangladesh

c. Azizun Nessa, Combined Military Hospital, Dhaka Cantonment, Dhaka, Bangladesh

d. Ajfar Sazid Khan, Combined Military Hospital, Dhaka Cantonment, Dhaka, Bangladesh

e. Tahmeed Hussain, Combined Military Hospital, Dhaka Cantonment, Dhaka, Bangladesh

Address of Correspondence: Md. Maksudur Rasul, Combined Military Hospital, Dhaka Cantonment, Dhaka, Bangladesh, E-mail: ahmed4994@gmail.com

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option due to pressure from too many patients and inadequate hemodialysis machines.

UKM is a method of assessing the appropriate dose of dialysis and assessed by several indicators such as percent reduction of urea during dialysis (URR), total clearance of urea normalized for distribution volume (Kt/V), protein catabolic rate (PCR) and time average concentration of urea (TAC). Most of these parameters are calculated with mathematical formulas. 'Clinical signs and symptoms alone are not reliable indicators of hemodialysis adequacy'[7].To ensure a sufficient dialysis, the delivered dose should be measured and monitored routinely. UKM was the best method for routine measurement of the dose of hemodialysis[8]. However, it is the not simple to implement. The two widely accepted measures of urea clearance are Kt/V, and URR[9]. Several parameters must be considered to provide adequate dialysis, such as control of fluid overload and electrolytes disturbance, correction of metabolic acidosis and dialysis dose .[10] National Kidney Foundation Kidney Disease Outcome Quality Initiative (NKF-KDOQI) guidelines recommend URR greater than 65% and Kt/V greater than 1.2. HD for 12 hours/week is the standard and widely accepted regime. But 'there is a tendency to shorten dialysis time to reduce cost and to increase patients' convenience[11]. The present study conducted to find out the hemodialysis adequacy by UKM among the Bangladeshi patients on maintenance hemodialysis therapy. This study will enrich our knowledge and thus help in the management of patients of end stage kidney disease.

Material and method:

This was a hospital based cross sectional study conducted among the ESRD patients on maintenance hemodialysis (MHD) at dialysis center of CMH Dhaka from July 2014 to June 2015. Only adult patients (age more than 18 years) on MHD for at least three months through arterio-venous fistula (AVF) were included and those who do infrequently (<2 sessions /week) were excluded from the study. Purposive sampling was done among patients who fulfilled the selection criteria. After obtaining relevant clinical parameter, data collected from predialysis, postdialysis and next predialysis blood sample. Haemodialysis adequacy parameters were done among the study population only once at the entry into this study. SpKt/V, URR, TACurea and nPCR were calculated. Mean of adequacy parameters were calculated and compared between twice and thrice per week hemodialysis groups. Also compared adequacy variables between groups who achieved cutoff values of spKt/V, URR, TAC urea and nPCR with who did not achieve it. The ethical approval of the study was obtained from ethical review committee of Directorate General Medical Services (DGMS) Bangladesh armed forces. Data analysis was performed by Statistical Package for Social Science (SPSS), version-17. Statistical analyses were done and level of significance was measured by using appropriate procedures like student's t- test and others where applicable. Level of significance (p value) was set at 0.05 and confidence interval at 95%. Results are presented as text and tables.

Results:

Total 137 patients were included in this study, among them 98 (71.53%) were male and 39 (28.46%) were female. Male female ratio was 2.5:1.

Forty-nine patients were in the age group of more than 60 years. The mean age of patient in this study was 53.37 ± 13.43 years. Only six patients were under 30 years of age.

One hundred patients (72.99%) were on twice per week (8 hours/week) hemodialysis session and thirty-seven (27.01%) were on thrice weekly (12 hours/week) hemodialysis session.

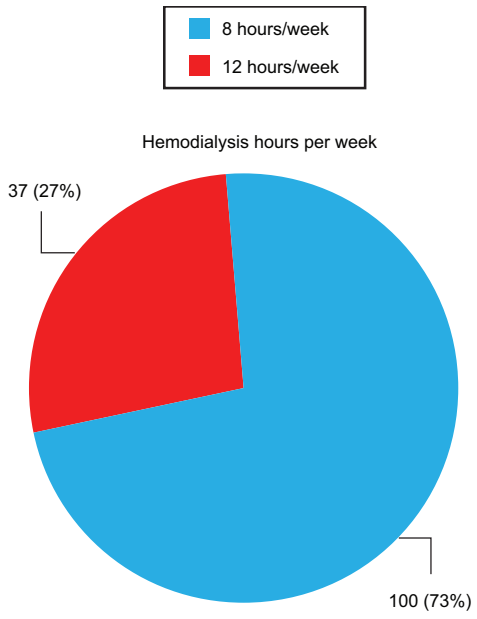

Fig.-1: *Hemodialysis hours per week*

Table-I

Adequacy parameter of all hemodialysis patients(n=137)

Variables	Mean ± SD
Urea Reduction Ratio (URR) %	64.68 ± 17.07
Single session spKt/V	1.63 ± 0.45
TAC urea (mg/dl)	76.55 ± 25.73
nPCR (gm/kg/day)	1.43 ± 0.55

Table II shows the hemodialysis adequacy parameters of different variables

Table-II

Comparison of sample mean value with target value(n=137)

Adequacy	Parameters	Sample Mean ± SD	Target Value
URR (%) (n=137)	64.68 ± 17.07	>65	
SpKt/V(n=137)	8 hours/week (n=100)	1.80 ± 0.35	>2
TACurea	12 hours/week (n=37)	1.18 ± 0.35	>1.2
nPCR		76.55 ± 25.73	< 52
		1.43 ± 0.55	>1

Mean URR of study population was lower than target value. In this study spKt/V of 8 hours per week hemodialysis group was lower than target value. Similarly in 12 hours per week hemodialysis group mean spKt/V value could not reach target value. Mean TACurea higher than target value (<52 mg/dl).

Table-III

Distribution of study population on the basis of cut off values of hemodialysis adequacy parameters (n=137)

Parameters		Cut of Values	Mean ± SD	n	%
URR (%)(N=137)		>65	81.52 ± 9.89	57	41.61
		<65	52.69 ± 9.07	80	58.39
	8 hours/week	>2	2.40 ± 0.25	21	21.00
Kt/V	(n=100)	<2	1.64 ± 0.14	79	79.00
(N=137	12 hours/week	>1.2	1.53 ± 0.25	16	43.24
	(n=37)	<1.2	0.92 ± 0.08	21	56.76

Among the 100 patients in the group of 8 hours per week hemodialysis, only 21 (21%) had Kt/V more than 2 and 79 (79%) had Kt/V less than 2. Among the 37 patients in the group of 12 hours per week hemodialysis, 16 (43.24%) had spKt/V more than 1.2 and 21 (56.76%) had spKt/V less than 1.2. Among 137 patients only 57 (41.61%) achieved URR >65%.

Table-IV

Comparisons on the basis of spKt/V cut off values of 8 hours/ week hemodialysis group (n=100)

Variables	Mean ± SD		p-value
	spKt/V >2 (n=21)	spKt/V<2 (n=79)	
URR	89.88 ± 05.30	57.01 ± 11.68	<0.001
TACurea	53.82 ± 19.71	81.83 ± 23.99	<0.001
nPCR	01.83 ± 0.71	1.48 ± 0.51	0.012

In 8 hours/week group those who achieve target spKt/V also achieve target URR and was statistically significant. And there is significant difference among the two group (spKt/V >2 Vs spKt/V <2) in relation to TACurea and nPCR(p< .05).

Table-V

Comparisons on the basis of spKt/V cut off values of 12 hours /week haemodialysis group (n=37).

Variables	Mean ± SD		p-value
	spKt/V >1.2 (n=16)	spKt/V<1.2 (n=21)	
URR	84.29 ± 6.62	53.41 ± 6.97	<0.001
TAC urea	65.16 ± 16.01	88.12 ± 27.94	0.006
nPCR	1.34 ± 0.35	0.94 ± 0.18	<0.001

URR, TAC urea and nPCR was significantly better in patients with spKt/V>1.2 group.

Table-VI

Comparisons on the basis of URR cut off values (n=137)

Variables	Mean ± SD		p-value
	URR(%) >65 (n=57)	URR(%) <65 (n=80)	
SpKt/V	1.95 ± 0.42	1.41 ± 0.31	<0.001
TAC urea	64.88 ± 21.82	84.87 ± 25.18	0.006
nPCR	1.65 ± 0.60	1.28 ± 0.46	<0.001

TAC urea, nPCR and spKt/V, significantly better in URR more than 65% groups.

Blood flow of study population:

Table-VII

Distribution of blood flow per minute of the study population (n=137)

Blood flow/minute	Frequency	Percentage
<250 ml	85	62.04
≥250 ml	52	37.96
Total	137	100

Eighty-five (62.04%) of the study population underwent hemodialysis with blood flow rate under 250ml/min. Remaining 52 (37.96%) patient's blood flow rate were above 250ml/min.

Adequacy on the basis blood flow:

Table-VIII

Adequacy on the basis blood flow of the study population (n =137)

Variables	Mean ± SD		p-value
	<250 ml (n=85)	≥250 ml (n=52)	
(URR) %	54.51 ± 11.52	81.31 ± 10.21	<0.001
SpKt/V	1.41 ± 0.31	1.99 ± 0.41	<0.001
TAC urea	83.68± 25.68	64.91 ± 21.37	<0.001
nPCR	1.27 ± 0.47	1.70 ± 0.57	<0.001

Patients who do there dialysis with blood flow more than 250 ml/min had significantly better dialysis adequacy. URR (81.31± 10.21 vs. 54.51 ± 11.52 and p-value <0.001), spKt/V (1.99 ± 0.41 vs. 1.41 ± 0.31 p-value< 0.001) .

Discussion:

The present study was conducted to observe optimum solute clearance per session of hemodialysis by applying spKt/V and URR formula. In this study mean age of patients were Mean ± SD (53.37 ± 13.43) years (Table-1). Similarly Sultania et al of Nepal in their study showed that the mean age of the patients was 49±24 years[12]. One hundred (72.99%) patients were on 2 sessions (8 hours) per week hemodialysis group (Fig. I). Anees et al in their study showed that 1, 2 and 3 sessions per week hemodialysis were 7.2%, 77.6% and 15.2% respectively [13]. 'Twice-weekly HD is prevalent in the developing countries' [14]. We also found majority of the patients were in 8 hours /week hemodialysis group. Thrice-weekly HD is regarded as a standard renal replacement therapy (RRT) for maintenance dialysis, and the KDOQI guidelines, 2006 indicates that twice-weekly hemodialysis is not appropriate for patients who have residual renal function <2 ml/min/1.73 m2 [15]. In this study mean spKt/V of all study population was 1.63 ± 0.45 (Table II). In 8 hours per week hemodialysis group, out of 100 patients, 21 (21%) patients achieved target spKt/V > 2. On the other hand in 12 hours per week hemodialysis group, out of 37 patients, 16 (43.24%) achieved target spKt/V >1.2 (table IV). Karin et al similarly showed that; mean spKt/V was 1.18 ± 0.26 for 12 hours/week group and 1.90 ± 0.35 for 8 hours/week

group of his study population [16]. Manouchehr et al in their National Multicenter Study in Iran among 4004 study population showed that spKt/V was less than 1.2 in 56.7%, of the patients[17]. In this study also most of the patients could not achieve target value. Mean URR of all study population was 64.68 ± 17.07 (table II) and only 57(41.61%) patient could achieved the cutoff value of adequacy and 80 (58.39%) patients had URR< 65% (table IV). Similar study done by Lin et al of Taiwan studied over 74 patients (23 twice weekly and 51 thrice weekly dialyzed patients) and shown no significant difference (77.77 ± 5.44 vs. 75.47 ±6.27 p-value 0.114)[18]. We also did not get any significant difference in URR (p-value 0.338) between 8 hours/week and 12 hours/week group. In 8 hours/week group those who achieve target spKt/V also achieved target URR and was statistically significant. TAC urea was significantly close to the target in spKt/V >2 group and nPCR also better maintained in patients with spKt/V >2. TAC urea, nPCR and spKt/V, significantly better in URR more than 65% groups. (Table V, VI, VII) This study showed that only 52 (37.95%) patients had blood flow rate (BFR) ≥250 ml/min during dialysis and their average URR was 81.31 ± 10.21, which is significantly higher than the URR of blood flow rate less than 250 ml/min group (p-value <0.001). Similarly other indices of adequacy of dialysis such as spKt/V shows significantly better value 1.99 ± 0.41 in BFR e"250 ml/min group (p-value <0.001). The DOPPS has shown that BFR is more than 400 ml/min account for 83.6% of the HD patients in United States [19]. In Canada and Europe, the patients with BFR >250 ml/min take about 98% of the HD patients. Comparing our data with similar studies it was clear that quality of dialysis in this center was not adequate. But by increasing the BFR it could be improved. Although dialysis facilities in Japan are concerned about the increased load on the cardiovascular system with increasing blood flow, acute changes in cardiac function was not observed in blood flow between 400 and 500 ml/min [20].

Conclusion:

We found that most of our hemodialysis patients were inadequately dialyzed which were most likely contributed by decrease dialysis frequency and low blood flow. So to achieve hemodialysis adequacy it needs to increase the frequency of dialysis from two to three sessions per week and measure should be taken to ensure the adequate blood flow (more than 250 ml/min) during dialysis.

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Prognostic Impact of Histopathology in Patients with Advanced Stage Cervical Carcinoma Treated with Radiotherapy

N HOSSAIN[a], R PERVEEN[b], MS MAHMUD[c], MK HASSAN[d]

Summary:

Introduction: Cervical cancer is the fourth most common cancer in women worldwidev . Most patients in developing countries including Bangladesh present at advanced stage. Histopathological types of cervical cancer influence the treatment outcome when treated by radiation therapy.

Objective: To determine the disease free survival (DFS) in different histopathological types in advanced stage cervical carcinoma treated with radiotherapy.

Methods: A prospective cohort study was conducted in Gynaecological oncology outpatient department (GOPD) of National institute of Cancer Research & Hospital (NICRH), Dhaka for one year from September'2016 to July'2017. Advanced stage (IIB-IVB) cervical cancer who completed radiation therapy and histopathological type either squamous cell carcinoma or adenocarcinoma of cervix were included in this study.

Results: The median follow-up time was 1.82 years; range was 8 to 24 months. Average disease free survival (DFS) was 1.53years in squamous cell carcinoma (SSC) and 1.51 years in adenocarcinoma (ADC). Local recurrences was higher in adenocarcinoma group (62.5%) than squamous cell carcinoma (30.5%) & the difference was statistically significant (p = 0.001). Loco-regional recurrence and distal recurrence were also higher in ADC than SSC but results were not statistically significant (p=.345, p=.795). In multivariate analysis it was shown that histopathological type and stage of disease were found to be independently significant prognostic factors for DFS, hazard ratio were 1.766 (p=.018) and 2.173 (p=.006).

Conclusion: Adenocarcinoma was a poor prognostic factor for patients with locally advanced cervical carcinoma. Advanced stage of disease was also significant predictor for disease free survival.

Key ward: cervical carcinoma, advanced stage, histopathological, radiotherapy.

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Introduction:

Cervical cancer is a major global public health problem and the fourth world wide leading cause of cancer death in women[1].

In Bangladesh, cervical cancer is the second common cancer in women after breast[2]. To reduce mortality from cervical cancer and improve survival, it is necessary to identify the prognostic factors.

a. Dr. Nasrin Hossain, Assistant Professor, Dept. of Gynaecological Oncology, NICRH.

b. Prof. Rahana Perveen, Former Head of Gynaecological Oncology, NICRH.

c. Dr. Lt. Col. Mohammed Sharif Mahmud, Surgical Specialist, Combined Military Hospital, Dhaka.

d. Dr. Mohammed Kabirul Hassan, Junior Consultant, Surgery, Murad Nagar UHC, Cumilla

Address of Correspondence: Dr. Nasrin Hossain, Assistant Professor, Dept. of Gynaecological Oncology, National Cancer Institute & Hospital, Dhaka. Mobile: 01711395089, E-mail: nasrinhossain23@gmail.com

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Among the gynecological malignancies, the most common cases attending GOPD of NICRH is cervical cancer[3]. Most of them are in advanced stage disease & treated with radiotherapy. Early stage of cervical cancer is defined as FIGO stages I to IIA and advanced stage in defined as stage IIB to IVBt . Several studies have reported that histopathological type is an important prognostic factor in advanced stage cervical canceru – –'v . Other factors such as clinical stage, cell differentiation, treatment modality are also prognostic factors for cervical cancerv 'w .

The present study was carried out to find out the prognostic impact of histopathological type of cervical cancer on disease free survival (DFS), local (cervical)/ loco-regional (pelvic) recurrence and distal recurrence after completion of treatment with RT.

Methods:

It was a prospective cohort study conducted in gynecological oncology outpatient department (GOPD)

of National Institute of Cancer Research &Hospital (NICRH) during the period of September 2016 to September 2017 (one year). Sampling technique was purposive. Advanced stage (IIB-IVB) cervical cancer who completed radiation therapy and histopathological type either squamous cell carcinoma or adenocarcinoma of cervical cancer were included in this study and early stage (IB-IIA) cervical cancer, patients with incomplete treatment and any malignancy other than cervical cancer were excluded from this study. Formal permission was taken from the ethical committee of the NICRH, Dhaka. Cervical cancer cases were diagnosed by history, clinical examination and histological confirmation of biopsy specimen from cervix. Inform consent was taken from each patient before enrollment. Data were collected in a pre-designed data collection sheet. Clinical and pathological data were collected from medical records, pathology reports, and cancer registry reports. Follow-up schedule was every 03 months. Every patient was evaluated by history taking, complete physical examination. If there was any suspicious of recurrence on clinical evaluation, than USG/CT scan of whole abdomen & pelvis and chest X –Ray was advised. All recurrence was confirmed by tissue diagnosis. Data were analyzed using SPSS software. A p value <0.05 was regarded as statistically significant.

Result:

One hundred and fifty biopsy proven advanced stage (IIB – IVB) cases of cervical carcinoma were included in this study. Mean age was 48 yrs (range 35-66 yrs). Mean follow-up time was 1.82(yrs) and range was (0.08-2 yrs). Table 1: showing clinicopathological characteristic of the study population. Figure 1: shows average DFS was 1.53 years in Squamous cell carcinoma and 1.51 years in Adenocarcinoma but findings was not statistically significant. Figure2: shows adenocarcinoma histopathological type was associated with shorter DFS. The differences was not statistically significant (<0.05).

Table-I

Clinicopathological characteristics (n=150)

Characteristics	SCC		ADC	
	Frequency	Percent (%)	Frequency	Percent (%)
Age				
• <50	69	46	18	12
• >50	49	32.6	14	9.3
Parity				
• <2	16	10.6	1	1
• >2	102	68	31	20.6
Menopausal Status				
• Premenopausal	53	35.3	19	12.6
• Postmenopausal	65	43.3	13	8.6
FIGO Stage				
• Stage ll B	81	54	13	8.6
• Stage lll A	4	2.6	0	0
• Stage lll B	33	22	19	12.6
Histopathological Type	118	78.7	32	21.3
Grade				
• Grade 1	33	22	5	3.3
• Grade 2	73	48.6	19	12.6
• Grade 3	12	8	8	5.3
Treatment				
• CCRT	18	12	10	6.6
• RT	96	64	22	14.6
• EBRT	4	2.4		

Table II: showing local (cervix) recurrence (62.5%) in ADC than SSC (30.5%) and found statistically significant (p=0.001). local pelvic recurrence was higher in ADC (12.5%) than SSC (8.5%). Distal recurrence was also higher in ADC than SSC which was 6.2% VS 5.1% respectively .Both of the differences were not statistically significant (> 0.05). Table III: shows univariate analysis, shorter disease-free survival in both SSC and ADC in relation to advanced stage of cervical cancer. Table IV: shows local recurrence was higher in stage IIIB (50%) and local regional recurrence was also higher in stage IIIB (57.1%). Both of the differences were statistically significant (<0.05%). Multivariate analysis revealed that histopathological type and stages of cervical cancer were independent significant predictors for DFS of the patients. Hazard ration of histopathological type and stages were being 1.76 (q= .018) and 2.17(q =.006). (Table VI)

Table-II

Relationship of different histopathological type of cervical cancer with recurrence

	SSC		ADC		p value
	No	%	No	%	
Local recurrence	36	30.5	20	62.5	0.001
Loco- recurrence (regional)	10	8.5	4	12.5	0.345
Distal recurrence	6	5.1	2	6.2	0.795

Table-III

Univariate analysis showing DFS in different stages of cervical cancer patients

	Stage IIB	Stage IIIB	P value
SCC			
Disease free survival	1.59±0.39	1.50±0.32	0.670
ADC			
Disease free survival	1.55±0.37	1.20±0.36	0.592

Table-IV

Relationship of local recurrence, local regional recurrence and metastasis according to different stages of cervical carcinoma

	Stage IIB		Stage IIIA		Stage IIIB		P value
	No	%	No	%	No	%	
Local recurrence	24	42.9	4	7.1	28	50.0	0.005
Loco- regional recurrence	6	42.9	0	00	8	57.1	0.005
Distal recurrence	4	50.0	0	00	4	50	0.163

Table-V

Multivariate analysis showing DFS in relation to different variable

DFS	HR	95% CI		P value
		Lower	Upper	
Age	1.005	0.657	1.538	0.980
Histology	1.766	1.100	2.836	0.018
Stage (II VS III)	2.173	1.256	3.760	0.006
Grade (I&II VS III)	1.453	0.855	2.467	0.167
Treatment duration	0.641	0.375	1.095	0.103

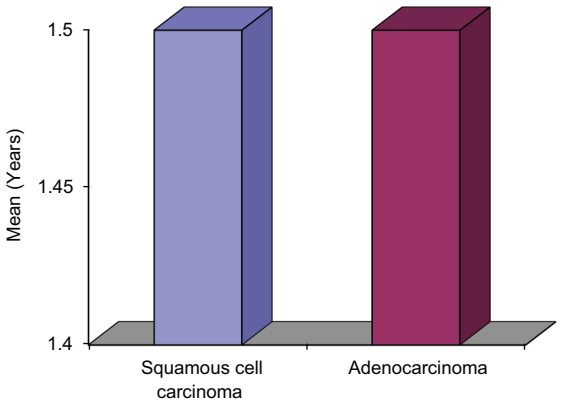

Fig.-1: *Disease free survival according to squamous cell carcinoma and adenocarcinoma*

Figure shows average disease free survival of 1.53 years in squamous cell carcinoma and 1.51 years in adenocarcinoma.

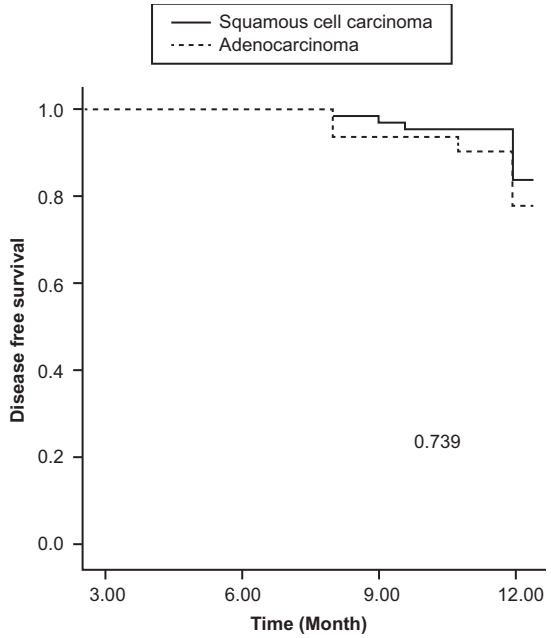

Fig.-2: *The kaplan- Meier survival curve showing graphic presentation DFS of SSC and ADC*

Discussion:

The factors, which affect the prognosis of patients with cervical cancer, are very complex and interactive and they jointly affect the prognosis of patients. This study revealed that Histopathological type was an important prognostic factor in advanced stage cervical cancer treated by radiation therapy.This study showed that, Disease free survival was longer in squamous cell carcinoma cases (1.53 years) than adenocarcinoma (1.51 years).

In case of squamous cell carcinoma, 83.9% of patients were disease free for more than 01 years and in adenocarcinoma, 75% of patients were disease free for more than one year. Similar findings were found in several other studiesv ‘w . In one studyx , patients with ADC had a poorer survival than SSC, particularly among the patients with advanced stage and indicate a strong impact of Adenocarcinoma compared with squamous cell carcinoma. Another studyy reported that the DFS and OS (overall survival) of patients with adenocarcinoma were significantly shorter than that of patients with SSC. One Japanese study[1]p reported that non-squamous histopathological type was the first independent risk factor when all relevant factors were taken into account. One Chinese study[11] reported that adenocarcinoma was an independent factor OS (HR= 7.83; 95% CI=2.23-27.4; p=0.001), LFES (Local failure free survival) (HR = 5.67; 95% CI= 1.68- 19.1; p=0.005) and DFS (disease free survival) (HR= 6.47; 95% CI= 2.26-18.5: P= 0.001). The 4 years DFS rates for ADC and SSC were 45.3% versus 71.9% (p=0.006) respectively.

In this study, among total number of SSC (118) cases, local recurrences was 36 (30.5%) and total number of ADC (32) cases, local recurrences was 20 62.5%). Local (cervical) recurrence was significantly higher in ADC than SSC (p=0.001). Local pelvic recurrence occurred in 10 patients of SSC (8.5%) and 4 patients in ADC (12.5%). Local regional recurrence is higher in ADC than SCC. Distal recurrence was also high in ADC type (6.2%) than SSC (5.1%). Several other studies have similar finding [11′13′1]t ′1v . In one study[1]v reported that in case of SCC, 25.0% case had loco regional recurrence and 36.1% had distant failure. In case of ADC, 32.7% developed loco-regional recurrence and 49.1% had distant recurrence. Eifel al[1]w analyzed 229 patients with cervical carcinoma and reported that the incidence of the pelvic recurrence was 17% for ADC and 13% for SSC. Also reported that distant metastasis were more frequent in patient with adenocarcinoma than SSC (37% VS 21% p=0.01). In this study finding ADC has higher local recurrence, pelvic recurrence, metastasis than SSC. One Taiwan study[11] reported that local failure free survival for adenocarcinoma and Squamous cell

carcinoma were 55.4% versus 83.9% (p=0.01) respectively. One study conducted in Thailand[13] included 611cervical cancer patients and reported that (6.2%) developed recurrence of disease. Among them local recurrence was 21 (55.3%), distal recurrence was 15 (39.5%) and combined 2 (5.2%). One Japanese study[1u] reported that distant failure rates of SSC and ADC cases were 36.1% and 49.1% respectively.

In present study, multivariate analysis shows that histopathological type and advanced stage cervical carcinoma were independent prognostic factors in disease free survival of SSC and ADC. Advanced stage cervical adenocarcinoma has shorter disease free survival than squamous cell carcinoma. These findings correlated with several other studiesy [´12´13]. One European study [13] reported that advanced stage cervical carcinoma tended to have poor survival. The 4 years OS, LFES(local failure free survival) and DFS were for stage I+II and stage III were 76.2% versus 70.1% (p=0.33), 80.4% versus 72.3% (p=0.59) and 70.8% versus 60.7% (p=0.52) respectively. Another study[12] reported that FIGO stage was a independent prognostic for OS & DFS. OS and DFS as a function of FIGO stage were 87.9% (95% CI 77.1%-93.8%) and 83.3% (95% CI 71.8% - 90.5%) for stage II, 59.1% (95% Cl 47.6%- 68.9%) and 66.6% (95% CL 54.6%- 76.1%) for stage III. One Thailand studyy reported that FIGO stage IIB compared with FIGO stage III +IV were associated with poor survival among patients with advanced stage ADC (HR 2.9; 95% 2.0- 4.4 and HR 4.5 95% CI 2.6- 7.9 respectively) and SSC (HR 1.7; 95% CI 1.4-2.0 and HR 3.7 95% Cl 2.8-4.9 respectively).

In this study revealed that local recurrence was more common in stage IIIB (50.0%) than stage IIB (42.9%). This finding was similar to several other studies[13´1t ´1v] reported that local recurrence was more common according to advance stage cervical carcinoma.

In current study local regional recurrence is higher in stage IIIB (57.1%) than stage IIB (42.9%). Loco-regional recurrence is higher in advanced stage cervical carcinoma in following study [13´1t ´1v] .

In present study, 37% of cases with stage IIB or III had local recurrence after RT and 14.6% of cases with stage IIB or III had distant metastasis after RT. Nakano et at[1x] reported that the rate of distant failure after RT was 14% for stage II disease and 25% for stage III disease.

Conclusion:

Histopathological type of adenocarcinoma is a significant and independent prognostic factor for disease free survival and local recurrence in advanced stage cervical carcinoma patient treated with radiotherapy. Advanced stage cervical carcinoma is also significant and independent prognostic factor in DFS, local recurrence and metastasis. This finding may be useful for further tailored treatment-strategies and follow-up planning among patients in each histopathological type.

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Sciatic Nerve Block in Single Nerve Block Technique for Unilateral Foot Surgery - an Alternative to Spinal Anaesthesia

M HAQUE[a], M HUSSAIN[b], MZ FARUQUEE[c], MR ALAM[d], MZ ISLAM[e]

Summary:

Background: *In lower extremity surgeries, central neuraxial block or peripheral regional anesthesia technique can be used, mainly in elderly patients. This study investigates the efficiency of spinal anesthesia and sciatic nerve block techniques in lower extremity surgery. Spinal anesthesia may impair hemodynamic stability; peripheral nerve blocks targeting the sciatic nerve may be a useful alternative.*

Objective: *To compare Unilateral Spinal Anesthesia versus Popliteal Block in patients undergoing elective foot surgery to determine the method of better outcome.*

Patients and Methods: *This randomized comparative study was carried out on fifty co-operative patients of both sexes who were scheduled for elective foot surgeries. According to the used method of regional anesthesia, patients were divided into: (S) group unilateral intrathecal block with low-dose (7.5mg) of hyperbaric bupivacaine plus intrathecal fentanyl (25 mcg) and (P) group in which the sciatic nerve at the popliteal fossa was blocked via posterior approach by injecting 20ml 0.5% bupivacaine (100mg). The difficulty of the block performance, level of patient discomfort, block performance time, onset of sensory and motor blocks, time in hours to the first request for supplemental systemic analgesia postoperatively, its total consumption for 24 hours postoperatively and associated side effects were recorded in each group.*

Results: *Statistically, it was found no significant differences between the demographic characteristics as well as the duration of surgery between the groups. The groups did differ significantly in the difficulty of the block performance. However, a longer duration for performing the block was observed in the P group. The level of patient discomfort was significantly lesser in the P group. The onset of complete sensory block was significantly longer in the P group. Hemodynamic profiles of our patients were found to be remarkably stable throughout the intraoperative period. In the P group, the time to first pain medication was significant longer. Moreover, the total dosage of analgesics during the first 24 hours postoperatively in group P was highly significant lesser compared to the other groups.*

Conclusion: *Sciatic nerve block at the popliteal fossa is an ideal alternative where it is preferable to avoid spinal anesthesia for foot surgeries in haemodynamicaly unstable patients.*

Key Words: *Sciatic nerve block, spinal anesthesia, foot surgery.*

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Introduction:

Lower limb surgery under neuraxial block is a popular choice of technique. But many a time patients present with the conditions that preclude neuraxial anaesthesia relatively or absolutely. For example spinal anaesthesia in patients with severe aortic or mitral stenosis and cardiomyopathy with low ejection fraction is likely to cause profound hypotension. Neuraxial block is also relatively contraindicated in patients taking oral anticoagulant like warfarin and antiplatelet drug like clopidogrel. Other conditions that preclude neuraxial block are local sepsis, anatomical deformity of the spine and critically ill patient. So when patients present with this condition for lower limb surgery the next safer option is peripheral nerve block technique. Peripheral nerve block with a long acting local anaesthetic agent like bupivacaine not only provides surgical anaesthesia but also produces prolonged post-operative analgesia[1]. This avoids the adverse effects of opioids and NSAIDs when administered for postoperative analgesia. On the basis of the anatomical distribution of the sciatic nerve,

a. Prof. (Brigadier General) Mozibul Haque, Head of the department of Anaesthesiology, Combined Military Hospital, Dhaka
b. Colonel Muhammad Delwar Hussain, Classified specialist in Anaesthesia, Combined Military Hospital, Dhaka.
c. Dr. Md. Zulfiker Ali Faruquee, Consultant & Associate Professor Cardiac Anaesthesia, Ibrahim Cardiac Hospital & Research Institute, Shahbag, Dhaka
d. Lieutenant Colonel Md. Rabiul Alam, Classified specialist in Anaesthesia, Combined Military Hospital, Dhaka.
e. Major Md. Zahedul Islam Classified Anaesthesiologist, Combined Military Hospital, Dhaka.

Address of Correspondence: Professor (Brigadier General) Mozibul Haque, Head of the department of Anaesthesiology, Combined Military Hospital, Dhaka. Mobile: +8801769014756, Email: colmhaque@yahoo.com

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block anywhere above its division into tibial and common peroneal nerve should produce complete surgical anaesthesia of the foot below the ankle. Although a significant mass of local anaesthetic is required to block sciatic nerve, there have been few reports of systemic drug disposition[2]. We therefore, designed a prospective study to assess the clinical effectiveness of sciatic nerve block alone for unilateral foot surgery below the ankle in comparison to spinal anaesthesia.

Patients and methods:

After getting ethical clearance fifty adult patients of ASA 1-3 presenting for different types of foot surgery below ankle were selected for the study. Informed consent was taken from each patient explaining the procedure of either spinal anaesthesia or sciatic nerve block in details. This study was conducted at the department of Anaesthesia, Combined Military Hospital, Dhaka over a period of 8-months. Patients who were willing to go for surgery whilst awake under sciatic nerve block were included for the study. No premedication was given to any patient before coming to operation theatre. On arrival in the anaesthetic room a 20G cannula was placed in the peripheral vein for the administration of fluid and drugs. On the operating table, fentanyl 50 microgram was administered intravenously before the placement of the block. Patients were divided into a spinal anesthesia (S) group and sciatic nerve block (P) group consisting of 25 patients in each group. Base line recording of heart rate, blood pressure and SpO_2 were done non-invasively using standard monitoring technique, and then continued at 10 min intervals till the end of surgery. In the (S) group, the patients were positioned in lateral decubitus. The region was aseptically cleaned and draped. In the selected intervertebral space (L4-L5 or L3-L4) injection site, 2-3 ml of 1% lidocaine was injected into the skin and subcutaneous tissue. After ensuring that dura was passed and the spinal space was entered, the plunger of a 25G Quincke spinal needle was drawn back and the free flow of the spinal fluid was observed. 1.5 ml of 0.5% hyperbaric bupivacaine was injected to the subarachnoid space. When this procedure was completed, the patient was kept in the lateral position for 5 minutes to ensure unilateral neuraxial block. In the (P) group, after infiltration of skin and subcutaneous tissue with 1% lignocaine, the sciatic nerve injection was performed at the popliteal fossa of the affected lower extremity. Confirmation of the needle placement was achieved by eliciting parasthesia and numbness along the course of the sciatic nerve. After careful intermittent aspiration, 20ml of 0.5% bupivacaine was injected over a period of 2 min. All the blocks were performed by the same investigator.

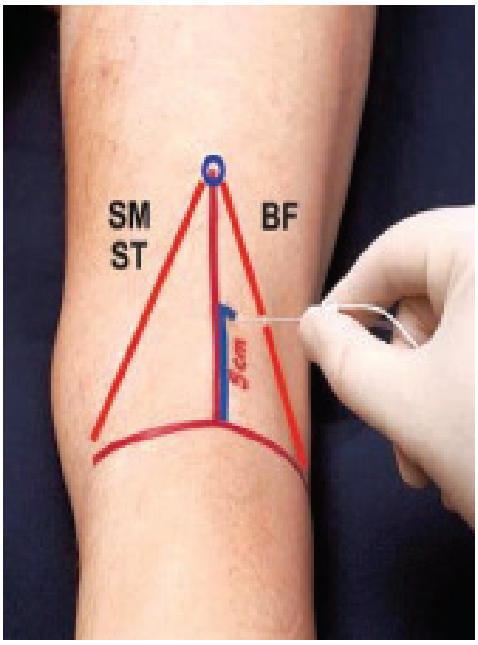

Fig.-1: *Diagramatic presentation of Sciatic Nerve Block at the level of the popliteal fossa (SM – Semimembranosus muscle, ST – Semitendenosus muscle, BF – Tendon of Biceps femoris)*

Development of the sensory nerve block was assessed by the response to pin-prick on dorsal and planter aspects of the foot using a short-beveled 27G dental needle before and 5, 10, 15, 25, and 30 min after injection . Sensation was categorized as 'sharp' (same as the contra-lateral foot), 'dull' (pin-prick perceived as pressure) or 'absent' (complete loss of awareness of pinprick). Onset of sensory block was defined as the time taken to achieve complete loss of sensation ('dull'/ 'absent') on both dorsal and planter aspects of the foot. Once the sensory block was completed an arterial tourniquet was applied to the calf, a one hand's breadth below the tibial tuberosity to avoid proximal compression of the peroneal nerve. The foot was exanguinated using an Esmarch bandage, and the arterial tourniquet was inflated. The clinical efficiency of the

sensory block was assessed by the use of Bromage Grading:

Excellent- complete surgical anaesthesia without use of i.v. supplementation

Good- surgery was possible with the use of i.v. opioids/ ketamine & sedatives

Fair- inhalational anaesthetic was required in addition to i.v. supplementation.

The duration of sensory block was indicated as the onset of complete sensory block to the time that the patient first requesting for the post-operative analgesia. The patient's satisfaction was categorized on verbal rating as 'excellent' (very happy in all respect), 'good' (happy, no complain), 'fair' (not unhappy, it's OK) & 'poor' (unhappy, could have been better). Each patient was observed for any untoward effect like nausea, vomiting, arrhythmia or seizure during the operation and in the postoperative period.

Statistical analysis was done using Statistical Software, SPSS (Statistical Package for Social Science) version 19. Data was presented as mean (standard deviation), median (interquartile range) and percentage values. Comparison of mean values was done using the t-test, with comparison of median values was performed using Kruskal-Wallis test. Percentage comparison of 'positive' and 'negative' values (response) was done using Pearson's Chi-squared test or by Fisher's Exact test as appropriate. Statistical comparison for the characteristics of the nerve block was performed using the Mann-Whitney *U* test. Time to onset and duration of sensory block was compared by Wilcoxon signed rank test. The level of significance was set at ±=0.05 ($p < 0.05$).

Results:

Statistically, there were no significant differences between the demographic characteristics (age, sex, weight and height) as well as ASA grading between the groups (Table 1). Statistically, the groups did not differ significantly in the difficulty of the block performance. But the mean block performance time in the P group was highly significantly longer than that of the other group (Table 2). The majority of the patients in the groups needed only one or two attempts for either subarachnoid space identification or sciatic nerve localization while, the number of those who needed three attempts were 1 and 3 patients in group S and P respectively. Patient's discomfort, like shivering, nausea and vomiting were more common with spinal (S) group than sciatic (P). While technical difficulties like, vessel puncture and multiple attempts were more with sciatic nerve block (P) group than spinal (S) (Table III).

Statistically, there were no significant differences found between the demographic characteristics of the two groups like age, sex, weight, height and ASA grading (Table 1).

Table-I

The demographic characteristics of the patients

	Spinal (S) group	Sciatic nerve block (P) group	P Value
Age	64.59±9.1	62.59±8.7	0.61
Sex (F/M)	7/18	5/20	0.74
Weight (kg)	74.02±6.18	73.67±7.66	0.47
Height (cm)	167.78±6.78	171.31±5.32	0.81
ASA Grading (II/III)	11/14	8/17	0.15

Table-II

Onset of anaethesia, duration of surgery and duration of analgesia in both the groups

	Spinal (S) group (min)	Sciatic nerve block (P) group (min)	P Value
Onset of anaesthesia	5.3±1.3	8.9±1.8	Â0.001
Duration of surgery	69.84±15.37	70.13±13.67	1
Duration of analgesia	185.20±37.65	327.56±43.32	Â0.001

Data expressed as mean±SD

Differences are statistically significant when P value Â0.05

Both onset and duration of anaesthesia were significantly longer in sciatic nerve block group than spinal group.

Table-III

Complications during the procedure

	Spinal (S) group (n=25)	Sciatic nerve block (P) group (n=25)
Vessel puncture	1 (4%)	3(12%)
Shivering	8 (32%)	1 (4%)
Multiple attempt	1 (4%)	3 (12%)
Nausea, Vomiting	2 (8%)	0 (0%)

The majority of the patients in the groups needed only one or two attempts for either subarachnoid space identification or sciatic nerve localization while, the number of those who needed three attempts were 1 and 3 patients in group S and P respectively.

Discussion:

This study was designed to assess the clinical efficiency of sciatic nerve block alone as the primary anaesthesia for the foot surgery in comparison with traditional unilateral subarachnoid block. In our present study we found that the sciatic nerve block is a useful technique for unilateral foot surgery in terms of effective surgical anaesthesia and haemodynamic stability. In a prospective study on 100 patients, Davies et al showed that sciatic nerve block had an acceptable success rate of 89% and is a suitable technique for vascular surgical patients undergoing procedures distal to the knee joint[3]. The attractiveness of the sciatic nerve block lies in its potential ability to minimize haemodynamic disturbances and improve regional blood flow to the lower limb[4,5]. Fanelli et al compared the haemodynamic changes induced by combined sciatic-femoral nerve block and unilateral spinal anaesthesia. They found that the mean arterial pressure did not change in patients in nerve block group whereas in spinal group mean arterial pressure was reduced with a mean 15% reduction. Cardiac index was decreased by 15-20% in group spinal anaesthesia while no changes were observed in group nerve block[6].

In this study we used 20 ml of 0.5% bupivacaine and observed that mean duration of analgesia including effective surgical anaesthesia was 12 hours 30 minutes. In another study Tharwat used similar volume of 0.5% bupivacaine in combined femoral-obturator-sciatic nerve block for ACL reconstruction and found that the mean duration of analgesia was 14 hours and ranged up to 24 hours[9] which is comparable to our study. To produce effective sciatic nerve block for surgical anaesthesia we used 20 ml of bupivacaine in a concentration of 5.0 mg/ml. We did not notice any adverse systemic toxicity of bupivacaine such as seizure, arrhythmia, or cardiovascular collapse. Connolly et al used similar volume and concentration of bupivacaine to see the plasma concentration after sciatic nerve block and observed mean plasma and individual highest plasma concentration of 0.6 and 1.1 mg/liter respectively[8]. Moore and colleagues observed a peak plasma concentration of 1.6 mg/liter after 400 mg bupivacaine with epinephrine for combined sciatic, femoral, and lateral cutaneous nerve of the thigh block[9]. The foregoing reviews attest the fact that even after use of significantly large mass of bupivacaine for peripheral nerve block its plasma concentration always remains well below its toxic level.

Adverse effects of the sciatic nerve block are rare, but our present study included some technical complications like multiple attempts and a few vessel punctures. We observed some minor complications like nausea, vomiting and shivering, due to the effect of spinal anaestesia.

Conclusion:

Sciatic nerve block alone provides good surgical anaesthesia and prolongs satisfactory postoperative analgesia. With the added advantages of stable haemodynamics and improved regional blood flow, sciatic nerve block should be considered more often in high risk patients undergoing foot surgery who are otherwise relatively contraindicate for spinal anaesthesia. Moreover sciatic block technique is suitable for day-stay surgery and meets the discharge criteria within several hours of surgery.

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Role of Routine Histopathology of Gallbladder Specimen from Gallstone Disease to Detect Unsuspected Carcinoma

MJ ISLAM[a], S AKTER[b], AR TALUKDER[c], MS HAQUE[d]

Summary:

Introduction: *Carcinoma of the gallbladder is a malignancy with very high mortality rate. Unfortunately, our common practice to discard gallbladder specimens after cholecystectomy in unsuspected malignancy. This results in missing some premalignant conditions and early carcinomas. This study was conducted to find out the incidence of unsuspected gallbladder carcinoma from cholecystectomy patients in routine histopathology of specimens and analyze their clinico-pathological features.*

Methods: *This was a two years cross sectional study included 542 patients with acute or chronic cholecystitis secondary to cholelithiasis operated by cholecystectomy. All cases of carcinoma gallbladder, on clinical grounds or confirmed by radiology were excluded. Gallbladders showing gross abnormalities suggestive of localized or infiltrative malignancy during surgery were also excluded. All gallbladder specimens were send for histopathology examination.*

Results: *Over a period of two years, five hundred and forty-two patients with symptomatic gallstones were admitted for cholecystectomy. The male to female ratio was 1:3. Most of the patients (26.49%) were found in fourth decade of life. Majority of patients (93.54%) presented with upper abdominal pain of varying duration. All the specimens were sent for histopathology. Four hundred sixty cases (84.87%) showed chronic cholecystitis (including intestinal metaplasia and dysplasia). Seventy of the cases (12.92%) showed evidence of acute cholecystitis (including empyema and mucocele). Twelve gallbladders (2.21%) showed evidence of adenocarcinoma of varying differentiation along with cholelithiasis.*

Conclusion: *Incidental diagnosis of carcinoma gallbladder is not rare. We strongly recommend to submit all cholecystectomy specimens routinely to histopathology laboratory, as this is the only means by which subclinical malignancies can be detected at an early stage.*

Key word: *Gallstone, Unsuspected carcinoma, Routine histopathology.*

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Introduction:

Carcinoma gallbladder is one of the worst cancer for its morbidity and mortality. It is a frequent underlying pathology in patients undergoing surgical intervention for chronic cholecystitis with cholelithiasis.[1] Long standing chronic inflammation by gallstones is considered an important etiological role in carcinogenesis. The incidence of carcinoma gallbladder associated with gallstones varies from 0.3 to 12 percent. Histopathological analysis is therefore mandatory for diagnosis of early carcinomas. Good prognosis and prolong survival is anticipated in patients with gallbladder carcinoma discovered as an incidental finding in early stage disease.[2] Bangladesh is a highly populated country with a major fraction of population of lower socioeconomic status having less access to proper health facilities, a reason why early stage malignancy may escape detection leading to poor survival.

Discarding gallbladder specimens without histopathological analysis may results in missing discrete pathologies like premalignant lesions such as porcelain gallbladder, dysplasia, carcinoma-in-situ and early carcinomas. Our common practice is to do histopathology of only those gallbladder specimens which shows gross abnormality. This practice is based on the assumption that gallbladder carcinoma is always associated with macroscopic abnormalities. At the same time, this selective approach is justified by claiming that it reduces patient's financial liabilities and pathologist's workload. This contradicts to the worldwide practice where gallbladder specimen is routinely sent for histological analysis for the sole purpose of identifying discrete carcinoma in early stage. Gallbladder carcinoma

a. Dr. Md. Jahidul Islam, Assistant Professor of Surgery, Shaheed M. Monsur Ali Medical College, Sirajganj.
b. Dr. Shaheen Akter, Associate Professor of Pathology, North Bengal Medical College, Sirajganj.
c. Dr. Abdur Rabban Talukder, Associate Professor of Surgery, Shaheed M. Monsur Ali Medical College, Sirajganj.
d. Dr. Md Shariful Haque, Assistant Professor of Nephrology, Shaheed M. Monsur Ali Medical College, Sirajganj.

Address of Correspondence: Dr. Md. Jahidul Islam, Assistant Professor, Surgery, Shaheed M Monsur Ali Medical College, Sirajganj. Mobile: 01712053831, E mail: drjahidul@gmail.com

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is usually not suspected clinically nor detected by preoperative imaging. Indeed, when diagnosed by imaging, gallbladder cancer is usually advanced stage. Grossly, gallbladder carcinoma may present as a diffusely growing (70%) or polypoid (30%) mass. When diffuse, the gross distinction from chronic cholecystitis may be difficult. The fact that some gallbladder carcinomas are not obvious on gross examination indicates the need for microscopic examination of every excised gallbladder. Sometimes unexpected metastatic tumor can be found in the liver after the removal of a gallbladder thought to have only lithiasis and inflammation on gross examination by the surgeon and therefore discarded.[3]

With this background, we carried out this study with the following objectives: i) To find out the incidence of unsuspected gall bladder carcinoma with their clinicopathological analysis in routine histopathology of cholecystectomy specimens. ii) to assess the feasibility of performing histopathology in every specimen of gallbladder. This would ensure picking of unsuspected carcinoma of gallbladder, which in turn will assist in decreasing mortality rate.

Methods:

This was a two years cross sectional study, conducted in the Department of Surgery, Shaheed M Monsur Ali Medical College and 250 bed General Hospital, Sirajganj from 1st July 2015 to 30th June 2017. Study population were patients with acute or chronic cholecystitis secondary to cholelithiasis admitted and operated in General Hospital Sirajganj, North Bengal Medical College hospital and other hospitals in Sirajganj during the mentioned period. Five hundred and forty-two patients of cholelithiasis which were selected conveniently. Written informed consent was taken from all the patients.

Patients with evidence of carcinoma gallbladder, on clinical grounds and confirmed on ultrasonography and/ or CT scan were excluded. Gallbladders showing gross abnormalities suggestive of localized or infiltrative malignancy during surgery were excluded. Detailed history and thorough clinical examination of the patients was done with special attention to the right hypochondrium for preoperative assessment of palpable mass. Systemic review was done to see any co-morbidity. Baseline and specific investigations especially ultrasonography of abdomen and liver function tests were done in all patients. Clinical presentations, investigations, preoperative diagnosis and intraoperative findings were recorded in data sheet. All gallbladder specimens, were sent for histopathology. Gross findings and histological diagnosis were noted from histopathology report. A predesigned proforma was used to put down the information gathered.

Results:

Over a period of two years, five hundred and forty-two patients with symptomatic gallstones were admitted for cholecystectomy. There were130 males and 412 females with a male to female ratio of 1:3. The age ranged from 20 to 75 years with the mean age of 34 years (Table I). Most of the patients were found in fourth decade of life (146/ 542 cases, 26.94%). Majority of patients (93.54%) presented with upper abdominal pain of varying duration. Other symptoms are depicted in Table II.

Table-I

Age distribution of the patients

Age of patients (years)	No. of patients	%
≤20	08	1.47
21-30	124	22.88
31-40	146	26.94
41-50	112	20.66
51-60	108	19.93
61-70	40	7.38
71-80	04	0.74
Total	542	100

Table-II

Common presenting symptoms of the patients

Symptoms	No. of patients	%
Upper abdominal pain	507	93.54
Flatulence and/ or dyspepsia	323	59.59
Intolerance to fatty food	70	12.91
Nausea and/ or vomiting	66	12.17

All 542 gallbladders were palpated and were opened per-operatively for any focal or diffuse thickening of the gallbladder wall, a raised mucosal plaque, polypoid growth or an infiltrating mass. The specimens were then sent for histopathology. Seventy of the cases (12.92%) showed evidence of acute cholecystitis (including empyema and mucocele). Four hundred sixty cases (84.87%) showed chronic cholecystitis (including intestinal metaplasia & dysplasia). Twelve gallbladders (2.21%) showed evidence of adenocarcinoma of varying differentiation along with cholelithiasis, (Table III).

Table-III

Histopathological findings of the cases

Histopathology	Male	Female	Total	%
Acute cholecystitis (including empyema, mucocele)	32	38	70	12.92
Chronic cholecystitis (including intestinal metaplasia & dysplasia)	96	364	460	84.87
Adenocarcinoma	2	10	12	2.21
Total	130	412	542	100

There were twelve incidental or non-suspected carcinomas with no gross abnormalities in this series. Subsequent staging revealed nine adenocarcinomas in stage T1 and three in stages T2, none with distant metastasis. Nine patients with T1 tumors did not undergo any further procedure; three patients with stage T2 referred to hepatobiliary surgeons for revision surgery.

Discussion:

Gall bladder carcinoma has a high mortality rate because of its late presentation, high propensity to metastasize and lack of effective therapy. In the United states, it continues to be a rare cancer and it is thought to be disease of elderly.[4] The scenario is, however, different in this study. Most of the patients of this study were found in fourth decade of life.

In this study, male to female ratio is 1:3. Female predominance is also reported by similar study (Channa et al., 2007).[5] The mean age 34 years ranging from 20 to 75 years. This is slightly earlier than that reported in other studies from India (Pandey et al., 2001; Kapoor et al., 2003).[6,7] Increasing detection rate at early age may be due to increasing awareness, accessibility to health care facilities and also may due to geographical distribution.

Over ninety-three per cent patients presented with pain in upper abdomen, a number significantly lower than that reported by Laghari et al, where all patients had upper abdominal pain.[8] That may be due to routine use of proton pump inhibitors in our practice. We exclude the patients had any evidence of malignancy either clinically or on ultrasound examination.

Chronic cholecystitis was the most common histopathological finding in this study. Specimen of 460 (84.87%) patients were reported as chronic inflammation with mucosal ulceration, denudation, metaplasia to dysplasia and wall infiltration by chronic inflammatory cells. A similar study by Memon also reports chronic cholecystitis as major histopathological finding, identified in 64.8% cases. In this study, 70 (12.92%) cases were reported as acute cholecystitis including empyema and mucocele of gallbladder. In contrast Memon reported 31.5% as acute cholecystitis.[9]

In this series, incidental carcinoma of gallbladder was found in 12 cases (2.21%). These gallbladders showed no gross abnormality per-operatively. Whereas its incidence was less i.e. 0.3% and 1.1% in the series according to Daphna et al[10] and Morere et al [11] respectively. It was even higher, as shown by Shigeki et al, 4.7% of incidental gallbladder carcinoma. [12] Wide range of variation in incidence in different studies, might be due to difference in total number of study population of cholecystectomy cases carried out for the study purpose. Incidence of primary gallbladder carcinoma itself is low and finding of incidental carcinoma would be low too.

In this study all patients presented with history of chronic cholecystitis or acute cholecystitis. We exclude patients with any clinical features or investigation findings on favor of carcinoma gallbladder. Gallbladder malignancy usually does not have any characteristic clinical features. Over 90 per cent of patients presenting with symptoms of acute or chronic cholecystitis.[13] Ultrasound has a high diagnostic accuracy for both advanced and early gallbladder cancer. None of the twelve carcinomas in this series were picked on preoperative ultrasound. In addition, all these twelve gallbladder specimens showed no macroscopic evidence of malignancy when they were opened during surgery. This is in contrast to the study by De Zoyasa et al. in whom all four cancers were suspected either on preoperative ultrasound or grossly during surgery; they suggest a more selective approach to gallbladder histology which may have saved both time and cost

without having any unfavorable effects on patients well-being.[14] Similar observations and recommendations are made by other studies.[15,16] The issue of routine histopathology of all gallbladder specimen therefore remains unresolved; the need to send every specimen for histopathology or otherwise therefore depends on the expertise of the ultrasonologist as it depends on the skill of the operating surgeon. There is widespread variation in the practice of general surgeons regarding intra operative examination as well as submission of specimens for histopathology, in developing countries.[17] We, however, advocate routine histopathology of all gallbladders removed at surgery since the subsequent report would provide evidence of incidental malignancy on solid grounds.

Chronic inflammation, infection and gall stones – are currently believed to be the factors leading to malignant transformation of gall bladder epithelium.[18] Carcinoma gallbladder has a strong association with gallstones.[19] The strong association between the two warrants attention paid to histopathology of specimen in all cases undergoing cholecystectomy for cholelithiasis, irrespective of presence or otherwise of any gross abnormalities. It is widely reported that long standing mucosal irritation by the stones cause atypical cellular changes and increased cellular proliferation. It has been hypothesized that in long standing cases, these areas of hyperplasia progress to metaplasia and carcinoma-in- situ. Studies confirm presence of such changes in the vicinity of gallbladder carcinoma.[20]

In this study the incidental carcinomas (3/4) were at very early T1 stage(9 of 12 carcinomas) and not a single case was found with distant metastasis. Tantia et al and Vincenzo et al found the majority of incidental carcinomas at early stage.[21,22] Most of the incidentally detected carcinomas are surgically resectable, with a good survival rate.[23] This study revealed all of them in pathological T1 and T2 stage and none with distant metastasis. Though simple cholecystectomy is said to be sufficient in stages T1 carcinomas, radical re-resection is strongly recommended in stages beyond that. Yi et al. (2013) suggested that the reoperation should be performed as soon as possible, preferably within 10 days after the initial operation.[24] This reflects the importance of histopathological study of all cholecystectomy specimens, irrespective of clinical impression.

All twelve cases of incidentally detected carcinoma had associated gallstones, thereby strongly supporting the role of chronic irritation by long standing gallstones as etiological factor for carcinoma gall bladder. All the cases are adenocarcinoma, no case of squamous cell carcinoma, or other variant of cancerous histopathology seen.

Conclusion:

Incidental diagnosis of carcinoma gallbladder is not rare. We showed evidence of malignancy in twelve (2.21%) cases on subsequent histopathological examination of gallbladder specimen, which had no gross features of cancer. These cases had neither symptom suggestive of underlying malignancy nor was cancer reported on any of the preoperative investigations. We therefore recommend, each and every cholecystectomy specimen should be routinely submitted to histopathology laboratory, as gall bladder cancer can be detected at an early, potentially curable stage and unsuspected carcinoma can be detect only by histopathological examination.

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Caesarean Scar Pregnancy: A Case Series

L CHOWDHURY[a], ANJANA[b], I JAHAN[c]

Summary:

Caesarean section rate is increasing day by day. Incidence of caesarean scar pregnancy (CSP) is also increasing. Prompt and multidisciplinary approach towards diagnosis of the condition is required to reduce associated morbidity. Major haemorrhage and hysterectomy are the main risks associated with CSP. Therefore, adequate counseling and availability of surgical expertise and blood transfusion should be part of a comprehensive management strategy. There are many single reports in literature but only few case series. In this paper, 10 cases of caesarean scar pregnancy treated in Obstetrics and Gynaecology department of CMH Dhaka, CMH Jashore and Hightech Multicare Hospital Private Limited over 10 years are analyzed. Three of 10 patients had mild pain in their lower abdomen and vaginal bleeding. Seven of them had profuse bleeding during D&C for miscarriage as they were not diagnosed at the time of admission. All patients had 1 or 2 caesarean sections. Gestational age of the pregnancy was estimated from 8 to 12 weeks by the last menstrual period. 9 patients were treated surgically. Eight of them had local resection of ectopic pregnancy mass with conservation of the uterus. One patient was treated with D&C followed by intrauterine balloon catheter insertion to control excessive bleeding. There was no total or subtotal hysterectomy. One patient was treated with Inj. Methotrexate. Common symptoms of caesarean scar pregnancy are pain in the lower abdomen and variable degree of vaginal bleeding. The treatment depends on severity of symptoms, gestational age and experience of the obstetrician dealing these cases.

Keywords: Caesarean section, Scar ectopic pregnancy, Maternal morbidity.

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Introduction:

Rate of caesarean section is increasing day by day. Along with this surgery its complications are also increasing with emergence of newer ones. Caesarean Scar Pregnancy (CSP) is one of those. It is a rare form of ectopic pregnancy where by the gestational sac is fully or partially implanted within the scar of previous caesarean section (CS). The first case was reported in 1978.[1]Its incidence ranges from 1/1800 to 1/2500 of all pregnancies.[2,3] 6.1% of pregnancies in women with at least one previous CS, a diagnosis of ectopic pregnancy will be CSP.[4] Only 19 cases of CSP were reported in the literature up to 2001 and by 2007, 161 cases had been reported.[5,6] This is attributable partly to the increasing number of CS performed and also to increasing awareness and better ultrasound diagnosis.

a. Brig Gen Liza Chowdhury, Dept. of Obstetrics and Gynecology, Combined Military Hospital (CMH), Dhaka.

b. Maj Anjana, Graded Specialist, Dept. of Obstetrics and Gynecology, Combined Military Hospital (CMH), Dhaka.

c. Maj Ishrat Jahan, Classified Specialist, Dept. of Obstetrics and Gynecology, Combined Military Hospital (CMH), Dhaka.

Address of Correspondence: Brig Gen Liza Chowdhury, Dept. of Obstetrics and Gynecology, CMH Dhaka. Mobile: 01769014814, E-mail: dr.lizachy@gmail.com

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This study presents 10 cases of caesarean scar pregnancy treated over 10 years in department of Obstetrics and Gynaecology of CMH Dhaka, CMH Jashore and Hightech Multicare Hospital Private Limited, Dhaka.

Case Series

This is a retrospective case series of 10 patients with caesarean scar pregnancy who reported to department of Obstetrics and Gynaecology for diagnosis and treatment between 2008 to 2018. The diagnosis was confirmed by both transabdominal, transvaginal ultrasound scan and MRI. Patients underwent both medical and surgical treatment. Clinical data and findings are presented in the Table 1.

Over 10 years, there were 10 patients with confirmed caesarean scar pregnancy in our gynecological departments. The maternal age was from 29 to 36 years. Presenting symptoms were amenorrhoea with per vaginal bleeding or pain abdomen or both. Duration of pregnancy was estimated to be from 8 to 12 weeks by the last menstrual period. Estimated gestational age by USG was from 6 to 10 weeks; no embryos had cardiac activity. Five patients had 1 previous caesarean section and five patients had 2. Almost all patients, except one, had previous abortions in their history.

Table-I

Characteristics of the ten patients with CSP

SL.	Maternal Age (Years)	Presenting Symptoms	Gestational Age in Weeks (by LMP)	Gestational Age in Weeks (by USG)	No. of Caesarean Section and Indication	Diagnosis on Admission	Treatment	β -hCGmIU/ml Pretreatment	Days in Hospital
1	36	Vaginal bleeding and mild pain in abdomen	8	7	1 (CPD)	CSP	D & C with intra uterine balloon catheter	7,650	7
2	32	Profuse vaginal bleeding during D,E& C	8	6	2	Incomplete abortion	Laparotomy followed by excision of scar pregnancy	8,300	8
3	30	Profuse vaginal bleeding during D,E&C	9	7	1 (foetal distress)	Missed abortion	Laparotomy followed by excision of scar pregnancy	20,608	10
4	31	Profuse vaginal bleeding during D,E& C	11	8	1 (breech presentation)	Incomplete abortion	Laparotomy followed by excision of scar pregnancy	19,780	9
5	33	Profuse vaginal bleeding during D,E& C	10	9	1(placenta praevia)	Missed abortion	Laparotomy followed by excision of scar pregnancy	20,580	9
6	32	Profuse vaginal bleeding during D,E& C	9	8	2	Incomplete abortion	Laparotomy followed by excision of scar pregnancy	15,756	8
7	33	Profuse vaginal bleeding during D,E&C	8	7	2	Incomplete abortion	Laparotomy followed by excision of scar pregnancy	9,159	7
8	30	Profuse vaginal bleeding during D,E& C	12	10	2	Missed abortion	Laparotomy followed by excision of scar pregnancy with myometrial flap	20,570	9
9	31	Vaginal spoting and mild lower abdominal pain	10	9	2	CSP	Laparotomy followed by excision of scar pregnancy with myometrial flap	18,203	10
10	29	Vaginal bleeding and pain in lower abdomen	8	6	1 (Breech presentation)	CSP	Inj. Methotrexate (50 mg) and Inj. Folinic acid 2 doses	16,427	8

3 of 10 patients had scanty P/V bleeding at presentation. 7 patients were urgently hospitalized with profuse vaginal bleeding after attempt to curettage with initial diagnosis of either incomplete or missed miscarriages.

In 3 cases the diagnosis - caesarean scar pregnancy was mentioned at the first examination in the emergency room. In 3 cases missed abortion and in 4 cases incomplete abortion were suspected.

Eight patients were treated by emergency laparotomy. One patient underwent D&C and intrauterine balloon catheter insertion (case-1). This patient had recurrence of CSP in her next pregnancy that was treated by laparotomy. One patient was treated with 2 doses of Inj. Methotrexate (MTX, 50 mg) and Inj. Folinic acid at 7 days apart. In eight cases laparotomy was followed by excision of scar pregnancy (Fig-1) with conservation of uterus. In two patients, myometrial flap (case-8,case-9) was used to cover the gap created by excision.No total or subtotal hysterectomy was required.

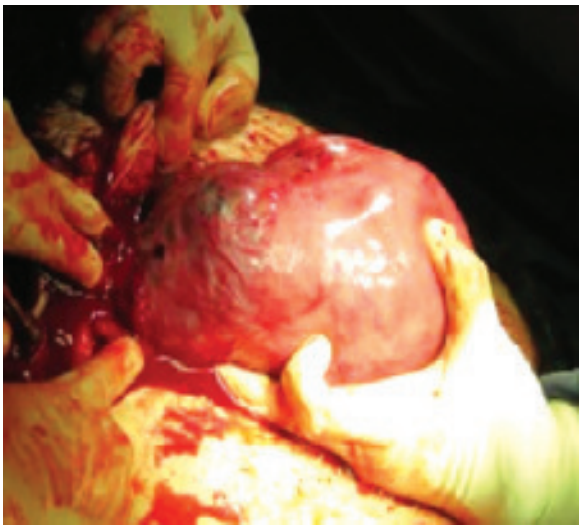

Fig.-1: *Peroperative finding of CSP*

On the day of admission, levels of beta-human chorionic gonadotropin (²-hCG) ranged from 7650 to 20608 mIU/ml. Average stay in hospital was 9 days, ranged from 7 to 10 days.

During follow up of the patients they found in good health. Only one patient developed CSP in her next pregnancy.

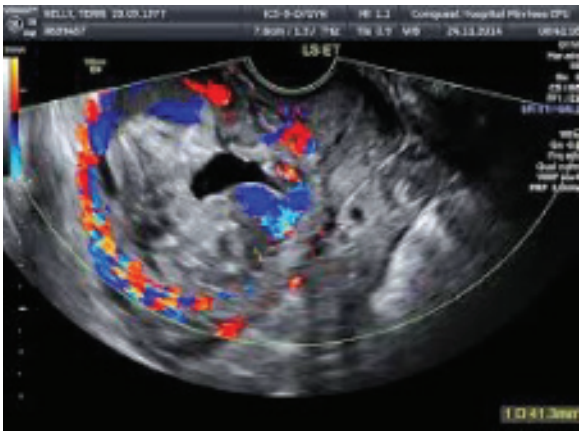

Fig.-2: *Transvaginal image of caesarean scar pregnancy.*

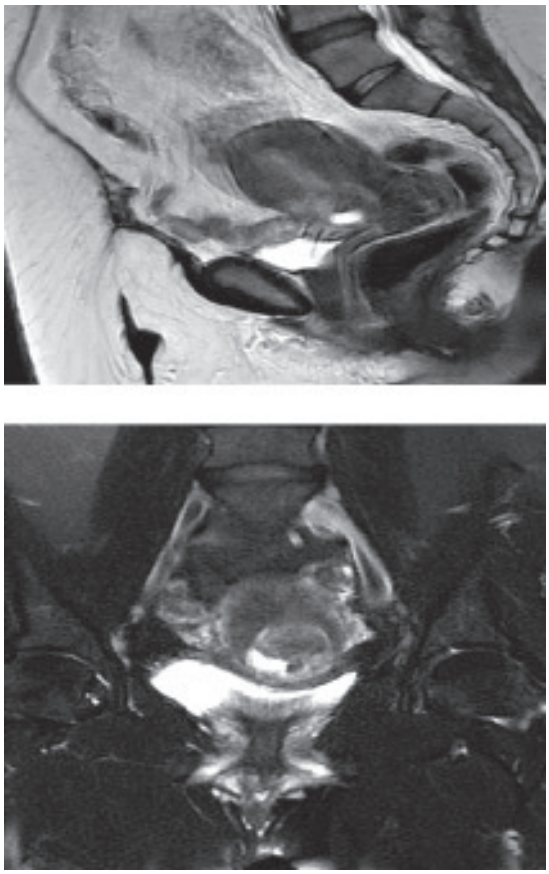

Fig.-3: *MRI Image of CSP*

Discussion:

Little is known about the etiopathology and mechanism of CSP. The most common mechanism is invasion by the implanting blastocyst through a microscopic tract

that develops from the trauma of an earlier caesarean section.[7]CS because of breech presentation in a previous pregnancy appears to be most frequently at risk of future CSP.[8]Risk of recurrence is 3.2% - 5.0% in women with previous CSP.[9,10] In our study one patient had recurrence. Common symptoms are slight vaginal bleeding and/or abdominal discomfort.[11]Rarely acute pain and profuse vaginal bleeding may occur. It is not uncommon to diagnose CSP during or after attempted surgical evacuation for miscarriage which has happened with 7 of 10 presented cases in this series. Heamodynamic instability and collapse in a suspected CSP strongly indicates rupture of caesarean scar with intra-abdominal bleeding.

In our study only three patients presented with slight P/V bleeding and abdominal discomfort. Seven patients presented with profuse P/V bleeding following attempt of D,E&C as they were diagnosed as miscarriage, either missed or incomplete and referred to tertiary centers in haemodynamically unstable condition.

A combined transabdominal and transvaginal ultrasound scan has a high accuracy rate in the diagnosis of CSP[12]. MRI is also a useful adjunct for the diagnosis of CSP.[13]

Ultrasound criteria for diagnosis of CSP are-(1) empty uterine cavity and closed and empty cervical canal;(2) placenta and/or a gestational sac embedded in the scar of a previous CS;(3) a triangular or round or oval shaped gestational sac that fills the niche of the scar;(4) a thin or absent myometrial layer between the gestational sac and the bladder;(5) evidence of functional trophoblastic or placental circulation on color flow on Doppler examination characterized by high velocity and low impedance blood flow; (9) negative sliding organs sign.

In principle pregnancy should be ended as soon as possible. It can be done both by medical and surgical methods. The medical methods are– (1) systemic MTX, (2) local administration of embryocides. Methotrexate is the commonest drug used for local administration as well. Potassium chloride, etoposide and hyperosmolar glucose have also been used for local administration in different studies. In a series of 11 cases treated by MTX injection, 54% women required further doses of systemic MTX with eventual complete resolution of the CSP mass[14]. In our series only one patient has been treated with 2 doses of intramuscular injection of MTX. For intrasac application of embryocides transvaginal approach is the most suitable one. Combined local and systemic MTX, uterine artery chemoembolization, bilateral uterine artery chemoembolization with gel foams and MTX have also been used as treatment option.

Surgical management options are –(1) cervical dilatation and curettage; (2) abdominal or laparoscopic resection – preferred in cases of exogenous CSP with a thin overlying myometrium; (3) Hysteroscopic management– can be combined with laparoscopic excision for complete removal of the mass, particularly in exogenous CSP; (4) transvaginal resection – offers the advantage of removing the products of conception and scar tissue; (5) combined and sequential management – Uterine artery embolization/chemoembolization followed by D&C or surgical resection in 24 – 48 hours or MTX followed by surgical evacuation or resection after an interval.

Expectant management is used very rarely in selected cases, only endogenous type of CSP progressing towards the uterine cavity in patient who declines termination remaining asymptomatic with non-viable CSP and declining hCG level.

In our series one patient has been treated by D&C and intrauterine balloon catheter and eight patients have been treated with laparotomy with satisfactory outcomes. There is no specific guideline for treatment of CSP. Each particular patient is unique.

Conclusion:

Diagnosis and management of CSP needs expertise and multidisciplinary approach. Increase CS rate will increase CSP from time to time. CSP can be prevented by reducing the number of primary CS. Prompt and accurate diagnosis of CSP and individualized treatment plan and follow up are required to reduce overall morbidity. The risk of CSP and placenta accreta should be specifically emphasized when counseling woman requesting CS for nonmedical reasons.

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REVIEW ARTICLE

Clinical Practice Guidance for Management of Anti HBc Positive Patients

S ALAM[a], S ISLAM[b], AH KHAN[c], M ALAM[d], G AZAM[e], G MUSTAFA[f], M HOSSAIN[g], M KHAN[h]

Summary:

Hepatitis B core antibody (Anti HBc) is currently considered the most sensitive serological marker for a patient's history of hepatitis B virus (HBV) infection given its long-term persistence in the bloodstream. The serological pattern of isolated Anti HBc (IAHBc) has been of clinical interest over the past several years.,Thegrowing data of IAHBcsuggestingit as a marker for occult HBV infection (OBI). Occult HBV infection defined as HBV DNA detection in serum or the liver by sensitive diagnostic tests in HBsAg negative individuals with or without serologic markers of previous viral exposure. OBI is especially concerned in blood transfusion (BT), organ donation and reactivation of HBV infection following immunosuppressive therapy. HBV reactivation depends on viral and host factors. The important clinical implications of IAHBcis in the setting of co-infection with hepatitis C virus (HCV), reactivation risk of HBV during directly acting anti viral (DAA) therapy in HCV infection which may lead to progression of liver disease and hepatocellular carcinoma (HCC). Antiviral prophylaxis has been recommended in moderate to high risk of reactivation prior to immunosuppressive and biologics. The main goal of therapy is to improve survival and quality of life by preventing disease progression and to prevent consequent development of HCC. It is proposed to perform Anti-HBc test as a screening test prior to blood transfusion, HBVvaccination, DAA and immunosuppressive therapy in addition to HBsAg screening test.

Keywords: Hepatitis B Virus; Hepatitis B virus DNA; Occult hepatitis B virus infection; Hepatocellular carcinoma; Hepatitis B surface antigen,;AntiHBc total; Bangladesh

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Introduction:

Hepatitis B Virus (HBV) is a major global public health concern. Over 2 billion people worldwide had been infected and 250 million people in world are chronically infectedwith HBV[1].Regional prevalence of HBV is highest in sub Saharan Africa and South East Asia between 5-10%[1]. Bangladesh belongs to an intermediate prevalent region, which is about 4.2%[2]. Another study conducted atSavar, a suburban area of Bangladeshrevealed prevalence of HBsAg is 5.5%[3]. Hepatitis B core antibody (AntiHBc) is one of the most important serological markers of HBV infection. In HBV endemic area prevalence of Anti HBc is high.In Bangladesh prevalence of AntiHBcamong general population is 31%[2],among chronic kidney disease patient is 39.3%[4]. Another study conducted in Kallyanpur, a densely populated community in Dhaka, Bangladesh explored its prevalence is 47.7% among 384 healthy subjects[5]. General populations as well as physicians arevery much worried about Anti HBc positivity.: in special situation likeco infectionofHCV and HBV, immunosuppression, blood transfusion, organ donation.No local guide line exists from any professional . So a local guidancefor management recommendation is needed for proper handling of AntiHBc positive cases.

a. Dr. Shahinul Alam, Associate Professor, Department of Hepatology, Bangabandhu Sheikh Mujib Medical University, Shahbag, Dhaka- 1000
b. Dr. Saiful Islam, Research Assistant. Department of Hepatology, Bangabandhu Sheikh Mujib Medical University, Shahbag, Dhaka- 1000, Bangladesh.
c. Dr. Asma Helen Khan, Medical Officer. Department of Hepatology, Bangabandhu Sheikh Mujib Medical University, Shahbag, Dhaka- 1000, Bangladesh.
d. Dr. Mahabubul Alam, Department of Hepatology, Bangabandhu Sheikh Mujib Medical University, Shahbag, Dhaka- 1000, Bangladesh.
e. Dr. Golam Azam, Associate Professor. Department of Gastrointestinal Hepatobiliary and Pancreatic disorders (GHPD). BIRDEM. Dhaka, Bangladesh.
f. Dr. Golam Mustafa, Associate Professor Department of Hepatology, Bangabandhu Sheikh Mujib Medical University, Shahbag, Dhaka- 1000, Bangladesh.
g. Dr. Motahar Hossain, Hepatology Society. House 64. Road 8A. Dhanmondi R/A. Dhaka.
h. Prof. Mobin Khan, Professor of Hepatology (Rtd). Hepatology Society. House 64. Road 8A. Dhanmondi R/A. Dhaka.

Address of Correspondence: Shahinul Alam, Associate Professor, Department of Hepatology, Bangabandhu Sheikh Mujib Medical University, Shahbag, Dhaka- 1000, Bangladesh. Phone: +8801973007173, Email: shahinul67@yahoo.com

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Methodology:

We have explored all the online publications available on HVB of Bangladesh from beginning to 2018. We have reviewed the guide lines and recommendations published on HBV and or Anti HBcby professional bodies of Asia Pacific region, European association and United states from 2010 to 2018.Here anti HBc and Anti HBc totalconsidered as clinically synonymous.

Discussion:

Anti HBc as a serological marker

AntiHBc is recognized as an important serological marker forhepatitis B virus infection identifying patients infected with hepatitis B virus infectionand persists for life.,Regardless of whether the HBV resolves or remains chronic. AntiHBc is found in different phases of HBV infection:acute, chronic, resolved HBV infection, occult HBV infection (OBI), as well as false positive cases. Anti HBc positive with HBsAg positive indicates ongoing infection. High degree of suspicion with persistently raised transaminases and or chronic liver disease where other causes were excluded would direct for further evaluation.Occult, HBV infection, where low viraemia is detected by HBV DNA in serum or liver. Very rarely hepatitis B virus core (HBc) antigen may persist in the nucleus of hepatocyte. Immunosupression may cause reactivation (reappearance) of HBV infection.

Spectrum of clinical conditions with Isolated Anti HBc(IAHBc)

Current literature has used the IAHBcspecifically to HBsAg-negative, antiHBc-positive patients, often stratifying this population into antiHBs-positive and Anti HBs-negative subgroup[6].IAHBc can occur for variety of phases.

a. Previous exposure to HBV:It is the most common reason for Anti HBc positivity. These persons recovered from acute HBV in past and Anti HBs has waned to undetected level, but some had been chronically infected with HBV for decades (with DNA 20 -200IU/ml) before clearing HBsAg. They are still in minor risk of developing HCC like inactive chronic HBV with undetectable DNA[7,8] .If IAHBc is confirmed, consideration of subsequent testing should be pursued to evaluate for OBI[9].

b. False positive: less commonly antiHBc may be a false-positive test result, particularly in lowprevalence areas[10].

c. Window phase: AntiHBc may be the only marker of HBV infection during the window phase of acute hepatitis B; these persons should be tested for anti HBc immunoglobulin M.

d. False Negative HBsAg: In case ofHBsAg mutations that leads to false-negative HBsAg with ongoing HBV infection[11].In this rare condition Anti HBc will be positive and HBsAg will be negative.

Occult HBV infection (OBI)

OBI refers to the presence of HBV DNA in the absence of detectable hepatitis B surface antigen [12]. OBI can be defined by the presence HBV DNA in the serum or liver tissue with either seropositive or seronegativestatus[13].High risk group for OBI:Blood donors,transplant recipients, patients co-infected with HCV, HIV immunosuppressive therapy or hemodialysis, cryptogenic liver disease, intravenous drug abuser andhealthcare workers[15].

Types of OBI

Seropositive OBI: Seropositive OBI is characterized by detection of anti HBc with or without Anti HBs antibody with detectable HBV DNA[12].

Seronegative OBI: Seronegative OBI is described by undetectable both Anti HBc and Anti HBs with detectable HBV DNA[12].

Most OBI is seropositive butaround 20% of OBI are seronegative representing a population negative for all serum markerof HBV infection but detectable HBV DNA[14].

Prevalence:OBI varies worldwide.Prevalence rates of OBI are influenced by several factors as follows: (1) geographic differences (endemicity); (2) Co morbid diseases such as chronic hepatitis C; and (3) and the different diagnostic techniques[15].OBI was reported higher in HBV endemic area, where 41-90% people had previous exposure to HBV[16].

If IAHBc is confirmed, consideration of subsequent testing should be pursued to evaluate for OBI. Kanget al.[17] described rates of occult infection ranging from 0% to 22.5%.They also provided an updated range of 1.7% to 41%, reporting on subjects who are HBsAg negative, anti-HBc positive, and HBV DNA positive among a sample of studies from 2001 to 2015 around the

globe. OBI is primarily been associated with the suppression of viral replication and gene expression.However, it has also been seen in patients with mutant forms of HBV with undetectable HBsAg. OBI is significant in various clinical contexts including viral transmission with blood transfusion and organ donation, reactivation after biologics, chemotherapy, and antiviral and progression of liver disease including HCC.

IAHBc total positivity with or without HBV DNA positive around the world is 7.7% in Germany[18], 3.7% in USA[19], 4% in UK[20], 8.2% in Mexico[21], 22.8% in India[22], 3 % in Australia[23], 1.7% in Korea[17], 30 % in Iran[24], 18.5 % in Egypt[25] and 16 % in Laos[26].

Indication of screening HBV DNA

IAHBc cases with regard to the consequence of OBI, for improving the treatment and management, the screening of HBV DNA by real-time PCR should be implemented in the following groups: (1) patients with a previous history of chronic HBV infection; (2) Co infection with HCV or HIV; (3) patients undergoing chemotherapy with anti-CD20 therapy; (4) any recipients of organ transplantation; (5) organ transplant donors; (6) thalassemia or hemophilia patients; 7) health care workers; (8) patients with cryptogenic hepatitis or cryptogenic liver related disease:cirrhosis and HCC and (9) haemodialysis patients [13].

IAHBc with HCV Co Infection

Chronic HBV infection along with HCV co infection accelerates liver diseases progression and HCC. Treatment with DAAs may cause reactivation of HBV. Patients with HBsAg negative AntiHBc positive are at very low risk of reactivation with HCV DAA therapy[27]. For Anti HBcpositive, HBsAg negative patient monitoring of ALT is reasonable, HBsAg and HBV DNA is recommended if ALT fail to normalize or increase despite declining or undetectable HCV RNA level[27]. Joint American Association for the Study of Liver Diseases and Infectious Diseases Society of America guidelines recommend all patients undergoing HCV DAA therapy be evaluated for HBV co infection by measuring HBsAg, antiHBs, and antiHBc[28].

Immunosuppressed conditions

HBV reactivation is a key consideration when initiating immunosuppressive therapy. The 2015 American Gastroenterological Association guidelines summarized the prevention and treatment of HBV reactivation during immunosuppressive therapy[29]. When considering IAHBc positive patients, the use of antiviral prophylaxis/ preemptive therapy is categorized by level of risk of reactivation, with types of immunosuppression categorized into low,moderateand highrisk groups depending on perceived intensity of therapy and associated risk[12].

Low risk: Isolated Anti HBc positive patient treated with Azathioprine, 6 merceptopurine, MTX,Intraarticular steroid, Oral corticosteroid < 1 week of any dose.

Moderate risk: Isolated Anti HBc positive patient treated with TNF Alfa I (Infliximab, etanercept, adalimumab, cerolizumab), Cytokine and Integrin inhibitor(abatacept, ustekinumab, natalizumab), tyrosine kinase inhibitor(imatinib, nilotinib), prednisolone <10mg >4 weeks and with Anthracyclinewith HBsAg Negative(Doxorubicin)

High Risk: Isolated Anti HBc positive patient withB cell depleting agent (Rituximab, Ofatumumab), Anthracycline with HBsAg positive (Doxorubicin, Epirubicin) and with patient treated with 10-20mg Prednisolone >4 weeks.

HCC risk with IAHBc:

A meta-analysis was conducted on 10 observational studies in 2010 evaluate role of anti-HBc positivity for the risk of HCC in HBsAg-negative subjects with chronic liver disease[30]. Serum antiHBc, an indirect serological marker of occult HBV infection and may be associated with HCC. Study demonstrates that occult HBV patients have a significantly higher risk of HCC than the antiHBs/antiHBc negative. IAHBc was found to have a significantly higher risk of HCC than with antiHBs positive.

Here it may also be hypothesized that circulating antiHBs may prevent the risk of HCC, most probably by controlling HBV replication. Meta-analysis indicates that, at least for HBsAg-negative/antiHBc-positive patients with chronic liver disease, a more accurate monitoring for HCC is hypothesized. This is evident for both Asian and non-Asian populations, in different stages of chronic hepatitis, in HCV etiology, and in patients with or without circulating anti-HBs. The risk of HCC seems to be lower in anti-HBs/anti-HBc-positive patients than in those with “isolated” anti-HBc,

suggesting some inhibitory effect of anti-HBs on occult HBV replication.[30]

Blood transfusion

Unsafe blood transfusion is one of the routes of transmission for HBV infection. Despite, all blood donations being tested routinely for HBsAg as a marker of transmissible HBV. HBV is transmitted by blood transfusion more frequently than HCV & HIV. In low prevalent area such as Europe and North America,< 5% of blood donors are characterized as having occult hepatitis B. On the contrary, occult HBV may be the major cause of transfusion transmitted HBV infection in high prevalence areas. Iranian study demonstratesHBV infection among anti HBc positive donor in range between 11.3% and 28.6 %[31].FDA recommends testing of HBsAg and Anti HBc for blood transfusion and organ donation[32].

Non liver solid organ transplant recipients

All patients of non liver solid organ transplantation should be tested for HBsAg, antiHBc, &antiHBs.HBsAg positivenonliver transplant recipient have a higher mortality rate with liver related complication. All HBsAg positive organ transplant recipients should receive lifelong antiviral therapy tenofovir alafenamide, tenofovir disoproxil fumerate or entacavir. HBsAg negative antiHBc positive non liver transplant recipients should be monitored for reactivation, alternatively antiviral therapy for the first 6-12 months .The period of maximum immunosuppressant, may be considered[27].Monitoring should be with ALT 3 monthly & by HBV DNA if ALT rise[33].

Vaccination of HBV in Anti HBc positive person: Clinicians should screen HBsAg,Anti HBc, and Anti HBs for HBV in high-risk persons,including persons born in countries with 2% orhigher HBVprevalence (Table I). Low prevalent countries recommend HBV vaccination in presence of Anti HBcin absence Anti HBs and HBsAg. All Asian countries including Bangladesh have> 2% HBV prevalence[27].

4. Guidance:

As per present status of information and evidence to generate guide line is not sufficient for the country. But the following guidance may upgrade the reasoning and decision making in clinical practice.

a. Guidance is required for management of Anti HBc positive person.

Table -I

HBV serological test, interpretation and vaccination [34]?(REF)

Test	Result	Interpretation	Vaccination needed
HBsAg	negative	susceptible	Yes
anti-HBc	negative		
anti-HBs	negative		
HBsAg	negative	Immunedue to	no
anti-HBc	negative	vaccination	
anti-HBs	positivewith ≥10mIU/mL		
HBsAg	negative	immune dueto natural	no
anti-HBc	positive	infection	
anti-HBs	positive		
HBsAg	positive	chronically	no
anti-HBc	positive	infected	
IgM anti-HBc	negative		
anti-HBs	negative		
HBsAg	negative	five	???
anti-HBc	positive	interpretations	
anti-HBs	negative	possible†	

b. Anti HBc positive indicates HBV infection of a person; it may be ongoing or previous infection or resolved infection.

c. Anti HBc positive with HBsAg positive indicates ongoing infection.

d. HBsAg negative and Anti HBc positive indicate previous infection or resolved HBV infection. High degree of suspicion of chronic liver disease, co infection with other viruses (HCV) and immunosuppressive condition necessitates further evaluation.

e. HBV DNA screening may be required some special populations with Anti HBc positive condition.

f. Isolated Anti HBc positive chronic hepatitis C patient on DAA should be monitor for ALT. If ALT is raised despite undetectable HCV RNA; HBV DNA is recommended.

g. Monitor for reactivation by HBsAg and HBV DNA and treat if clinically evident positivity.

h. Anti viral prophylaxis is recommended over monitoring. Treatment should be continued for 6 months after discontinuation of immunosuppressive therapy

j. Prophylactic antiviral therapy is recommended for Isolated Anti HBc total positive (HBsAg negative and anti-HBc positive) patients to prevent reactivation of HBV in moderate to high risk group who are on immunosupressive therapy. Anti viral therapy should be tTAFTDF or entecavir

k. Screening for HCC should be strengthened in Anti HBc positive patient with cirrhosis or with Anti HBc and HCV co infection.

l. Anti HBc is not yet recommended as screening test for HBV in Bangladesh for blood transfusion. It may be included for prevention of transmission of HBV with blood transfusion.

m. Solid organ transplant recipient with anti HBc positive should continue anti-viral prophylaxis according to their immunosuppressive condition.

n. Anti HBc testing may be proposed in addition to HBsAg before vaccination of HBV. HBsAg negative, Anti HBs negative necessitates HBV vaccination. HBsAg negative, Anti HBcpositive and Anti HBs positive does not require vaccination. But in case of HBsAg negative, Anti HBcpositive and Anti HBs negative may not require vaccination.

Conclusion:

Anti HBc positivity is very common in Bangladesh. It includes several spectrums of clinical conditions and related with major issues those have clinical significance. Screening for Anti HBc is mandatory for HBV evaluation, organ transplantation and HCV therapy. Anti HBc is found in different phase of HBV infection, acute, chronic, resolved HBV infection, occult HBV infection.High degree of suspicion of HBV infection with ongoing chronic liver disease in absence HBsAg requires further evaluation. HBV DNA testing and anti viral therapy for HBV is necessary during immunosuppressive therapy. Anti HBc screening should be included for blood transfusion and HBV vaccination.

Acknowledgements:
Hepatology Society. Dhaka. Bangladesh

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A Case of Granulosa Cell Tumour with Atypical Presentation

S KABIR[a], A MAJUMDER[b],S SHARMIN[c]

Summary:

Introduction: Granulosa cell tumour is one of the rare variations of ovarian tumour. As the Granulosa cells secrets Estradiol, the patient with granulosa cell tumour usually present with features of precautious puberty. But our patient present with androgenic features, which inspires us to report this atypical case.

Materials and methods: This young patient admitted in BBMH, as a diagnosed case of ovarian tumour with features of virilisation. Evaluation of patient with history taking, clinical examination and investigations are done, and information is noted accordingly.

Conclusion: Features of virilisation are a nightmare for a lady of 16 years old. So during management of this patient proper counselling is very crucial and during surgery ovarian reserve should be maintained as far as possible considering her future quality of life and obstetric outcome.

Keywords: Granulosa cell tumour, virilization.

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Introduction:

Granulosa Cell tumour [GCT] is one of the rare varieties of sex cord stromal tumours. It contributes 5% of ovarian tumors[1]. Mean age of presentation is 13 years. Most patients present with sexual precocity due to excessive estrogen production and rarely produce Androgen[2]. Our patient presented with these rare features of tumour. Granulosa cell tumour was first described by Scully in 1977[3]. In contrast to adult type juvenile one is more aggressive with high mitotic index.

Case Report :

Miss X, a 16-year-old unmarried girl of middle class family got admitted with the complaints of secondary amenorrhoea and abnormal facial hair growth for last 1 year. According to the patient, she had history of spontaneous menarche at the age of 12 years and of regular cycle. She developed amenorrhoea for last one year and feeling heaviness in lower abdomen for last 6 months. On general examination, she had average body built, height 5 feet 3 inches, weight 52 kgs, hirsutism with male pattern and excessive course hairs on upper arms and lower limbs. On mons pubis the hair distribution is of normal female pattern. Other features of virilisation were absent except mild regression of breast. On abdominal examination mild tenderness was present over lower abdomen. Vaginal inspection revealed clitoromegaly [2.5cm]. On digital rectal examination, there was a lump 8x 8cm size, mobile, non-tender, firm on posterior fornix. Ultrasono scan revealed a solido -cystic mass 10x7 cm at left adnexal area with small pelvic collection. Enocrinological studies of serum FSH, LH, ACTH were normal except serum Testosterone level, which was raised [15.6nmol/l]. On laparotomy, small amount of peritoneal fluid was found, aspirated and sent for cytology. A mass 10x8cm, party cystic partly solid, well capsulated was identified in left adnexal area. Opposite ovary and tube were healthy. There were no peritoneal seedlings or palpable pelvic or para aortic lymph nodes. Left sided salpingo-oophorectomy was done. Histopathogy revealed Granulosa cell tumour. Cytology of peritoneal fluid failed to identify any malignant cell. For abnormal hair growth she was advised dermatological consultation. Following surgery from next cycle, she resumed menstruation. Serum testosterone level regressed to normal within two months. After one year follow up she is having regular menstruations and has not developed any unwanted symptom.

a. Dr. Shanjida Kabir, Assistant Professor, Dept of Obs and Gynae, USTC, Chittagong.

b. Dr. Afroza Mojumder, Associate Professor, Dept of Obs and Gynae, USTC, Chittagong

c. Dr. Shahanaj Sharmin, Associate Professor, Dept of Obs and Gynae, CMSOGH, Chittagong

Address of Correspondence: Dr. Shanjida Kabir, Assistant Professor, Department of obstetrics and gynaecology, USTC, Chittagong. Mobile: 01815070717, E-mail: dr.shanjida.kabir@gmail.com

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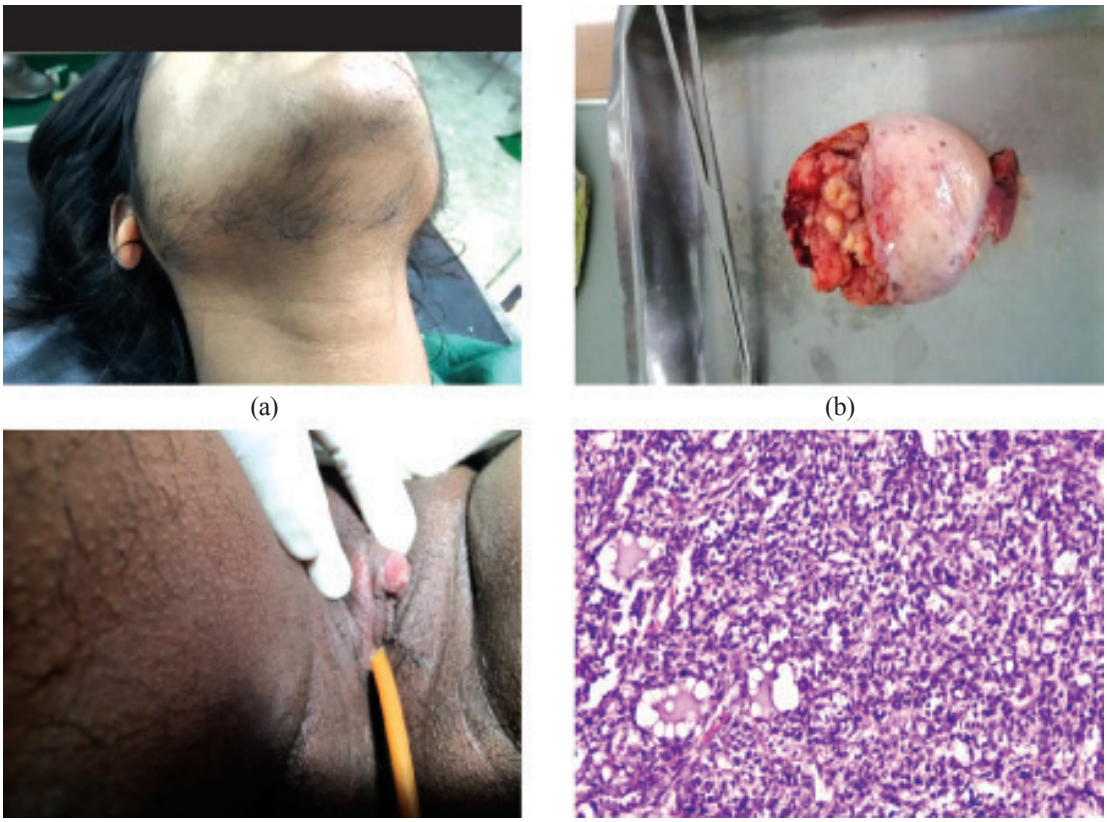

(a) (b) (c) (d)

Fig.-1: *a. Excessive facial hair growth, b. Clitoromegaly, c. Gross anatomy of tumour, d. Histopathological picture of tumour*

Discussion:

Though ovarian tumours present late stage, hormonally active ovarian neoplasm like GCT are diagnosed early due to the effect of hormones on target tissues. This is a rare ovarian tumour with two distinct clinico-pathological sub-type like Adult and Juvenile. Adult variety is common accounts to 95%.[4]

Generally the adult variety occurs in peri [40-45years] and post menopausal women with peak incidence at 50-55 years. The Juvenile one occurs in pre-pubertal age group.[5] GCT as a hormone producing tumour [Estrogen] commonly present with sexual precaucity. Other presenting features are – pain abdomen, abdominal distension, menstrual abnormalities like- menorrhagia, inter-menstrual bleeding, post-menopausal bleeding. Endocrine manifestation are related with hyper-secretion of Estrogen from granulosa cells.[6] 15% of the tumours are hormonally inert[7].

One of the rare presentation of GCT is amenorrhoea with features of virilization. The luteinizing form produces androgen leading to virilisation. To date less than 50 cases of virilizing GCT have been reported in literature[8]. Our patient presented with this feature, the unique point which drew our attention to report the case.

Sunil kumarkota et al reported one case in which a 16-year-old girl presented with primary amenorrhoea and virilization over 3years period.[9] Another case report by Arunnayak at el in which a 19 years old unmarried girl presented with secondary amenorrhoea and virilizing features like our patient.[10] She was stage 1A and unilateral salpingo-oophorectomy was done. Another patient of 17 years, was reported by Reddy et al in the year 2014, presented with secondary amenorrhoea with pelvic mass[11]. During reproductive age the typical picture of Androgen secretion is oligo-menorrhoea followed by amenorrhoea, defeminisation and progressive masculinization.

On physical examination, mass in lower abdomen could be palpable, usually unilateral upto 12 cm. On cut section the tumour is multi loculated, cystic with yellow white solid area. On histo-pathological examination, there are five histological patterns like – micro, macro-follicular, insular, trabecular and spindle/sarcomatoid. Call Exner

bodies are infrequently seen in GCT.[12] Diffuse or multi-follicular pattern with microcytes containing eosinophilic secretion and coffee bean nuclei are the commonest diagnostic point. In our case the gross and histology revealed these described features.

The serum tumour markers raised in GCT are Estradiol, Inhibin, Anti-mullerian hormone and CA-125[13]. In our patient serum Testostereone level was elevated.

General management depends on stage of tumour and age of patient. Although there are no prospective, controlled and randomized studies, fertility sparing surgery is recommended because patients are commonly young adults and tumour is uni-lateral. Unilateral salpingo-oophorectomy is the treatment of choice. Total abdominal hysterectomy with bilateral salpingo-oophorectomy for patients who has completed family. As our patient was young unilateral salpingo-oophorectomy was done.

Ascitic fluid cytology positive for malignant cell were found in few cases in some studies. In our patient it was negative. As because LN- metastasis is rarely observed in patients with sex-cord stromal tumour, pelvic and para-aortic lymphadenectomy may not be included in the staging surgery of the patient. Ultimate diagnosis is done by histopathological examination. Due to Estrogen stimulation, there is chance of development of Endometrial carcinoma in 5-13% of cases[14]. Thus endometrial histopathology must be included in management protocol. The prognostic factors in GCT includes – staging, intra-peritoneal disease, tumour size, patient age, histologic grade of differentiation, mitotic activity and nuclear atypia[15]. Survival rate after 10 years for stage 1,2,3 and 4 are 87%, 75%, 20% and 0% respectively.[7]

The role of adjuvant therapy is controversial. But it is recommended in advanced stage disease. Limited data are available regarding the chemotherapeutic agents in stage 3 and 4 disease. BEP therapy have been tried successfully. Radiotherapy is reserved for recurrent disease in selected group of patients. As these tumours are known for relapse, long term follow-up is necessary for early detection.

Conclusion:

Our patient presented with some unusual characteristics of GCT. She did not present with precautious puberty, rather presented with secondary amenorrhoea. Abnormal hormonal secretion consisted mainly of Androgen, with sign of virilisation, which is a nightmare for any young adult female. But medical science is magic at some point; it removes all her agony by a simple incision and changes her life.

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Subacute Sclerosing Panencephalitis

GC BANIK[a], S AMAN[b], F SULTANA[c], SM ARIF[d]

Summary:

Subacute sclerosing panencephalitis (SSPE) is chronic progressive encephalitis of childhood and young adoloscent due to persistent measles virus infection. This case illustrates a 14 year old girl presented with short history of intellectual decline, abnormal behavior, myoclonus and altered consciousness with suggestive neuroimaging mimicking metachromatic leucodystrophy. Subsequently she was diagnosed to be a case of Subacute sclerosing panencephalitis (SSPE) on the basis of Electroencephalography (EEG) and Cerebrospinal fluid(CSF) measles antibody titer.

KeyWords: Subacute sclerosing panencephalitis, Measles, Metachromatic leucodystrophy.

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Background:

Subacute sclerosing panencephalitis (SSPE) was first described by Dawson in 1933-1934 as sub acute inclusion encephalitis. It is a rare progressive, invariably fatal long term complication of measles infection. The latency period between acute measles and first symptoms of SSPE is usually

4 to 10 years but ranges from 1 month to 27 years.[1] It is characterized by myoclonic jerks, cognitive decline and typical EEG findings. Children with SSPE had natural infection with the measles virus at an early age, half before age of 2 years.[2] Although SSPE affects mostly children younger than 12 years, interestingly, there is a considerable increase in the number of adult cases of SSPE.[3,4] It has a progressive and fulminant course that results in death within 5 years of onset.[5] Usually it is not difficult in a child presenting with intellectual decline or behavioural issue followed by myoclonic jerks, which become generalised involving axial body parts. Diagnosis becomes a challenge when there is atypical presentation along with nonspecific laboratory or lectrophysiological values. We describe a young girl with short history of intellectual decline, myoclonic jerks , altered consciousness with neuroradiological findings mimicking metachromatic leucodystrophy the unusual association of SSPE.

Case Presentation:

14 year old girl, born of consanguinity with normal birth and development, was a student of class IV, hailing from Norshingdhi, presenting with the complaints of abnormal behaviour for three months, involuntary movements of limbs for one and half months and altered consciousness for 14 days. She had low grade fever for 2 months which was never documented. At first ,her behavioral disturbances started with irrelevant talk, gradually became aggressive and violent, deteriorating in academic performance, she left schooling due to inattentiveness, inability to remember her studies and reduced activities in her daily life. Few days later, she began to have cognitive impairment; she could not recognize her family members except her mother. She then developed rapid, sudden myoclonic jerks of all limbs persisting for few seconds, increased in frequency for one and half months. There was no history of generalized seizures, limb weakness, gait abnormalities, behavioural problems or altered sensorium. It was not associated with tongue bite, bowel bladder incontinence, loss of consciousness, post ictal confusion or headache and vomiting. The patient developed altered consciousness for last 14 days and became bed ridden. There was no history of cough, hemoptysis, jaundice and contact with tuberculosis patient. Also no previous event of birth trauma or head injury. Family history was unremarkable. There was no previous history of measles infection. Vaccination status of measles was doubtful.

General physical examinations revealed that patient was ill-looking, disoriented and unable to co-operate. She had repeated myoclonic jerks involving all four limbs. Her vital parameters were normal.

a. Dr. Gobinda Chandra Banik, Associate Professor, Dept. Medicine, Dhaka Medical College, Dhaka.
b. Dr. Sakib Aman, Indoor Medical Officer, Dept. Medicine, Dhaka Medical College, Dhaka.
c. Dr. Farhana Sultana, Retgistrar, Dept. Medicine, Dhaka Medical College, Dhaka.
d. Dr. Syed Mohammad Arif, Associate Professor, Dept. Medicine, Dhaka Medical College, Dhaka.

Address of Correspondence: Dr. Gobinda Chandra Banik, Associate Professor, Dept. Medicine, Dhaka Medical College, Dhaka. E-mail: gobinda_0171@yahoo.com

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On neurological examination, her state of consciousness according to Glasgow Coma Scale is E3+V3+M4=10/15, disoriented with irrelevant talks and there were no signs of meningeal irritation. Her cranial nerves could not be evaluated properly, fundoscopy was normal.Motor system examination showed increased tone, exaggerated tendon reflexes with bilateral planter extensor. Sensory and cerebellar functions could not be elicited.Slit lamp examination of eyes revealed no KF ring.Examination of other systems revealed no abnormality.

Investigations:

The routine blood examinations revealed no abnormality. Liver Function Test is normal. 24 hour Urinary copper<20.0mcg/l (>100 mcg/l in Wilson's disease), concentration of ceruloplasmin 29 mg/dl (20-35 mg/dl). MRI brain revealed T1Wl iso, T2WI and FLAIR hyperintense irregular lesions in both frontal and periventricular region. No restricted diffusion was seen in DWI. Lesions were suggestive of metachromatic leucodystrophy at both frontal and periventricular region.(Figure-1)

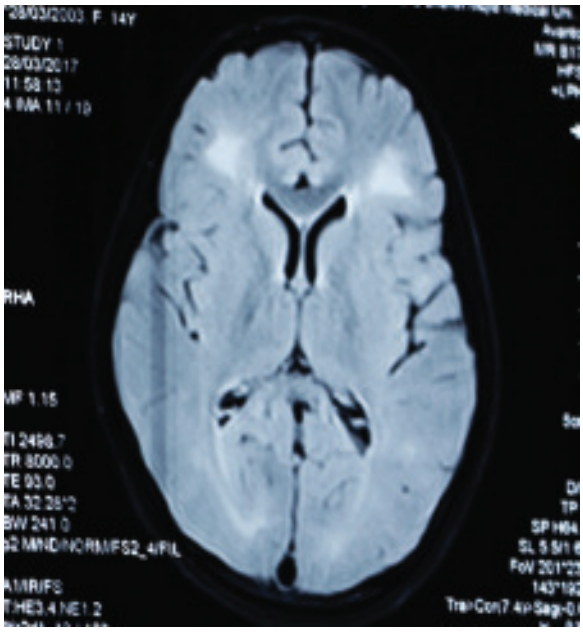

Fig.-1: *MRI of Brain with contrast showing metachromatic leucodystrophy at both frontal and periventricular region.*

EEG revealed frequent periodic bursts of spikes and slow waves from the background at regular intervals, suggestive of Subacute Sclerosing Panencephalitis. (Figure-2)

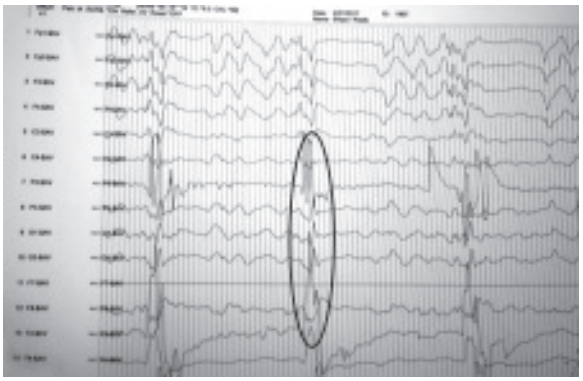

Fig.-2: *EEG showing periodic outbursts of slow waves, suggestive of Subacute Sclerosing Panencephalitis.*

Cerebrospinal fluid(CSF) studies showed that colour is watery and clear, CSF sugar was 89 mg/dL; protein was 75.10 mg/dL with acellular back ground. CSF Gram stain, Ziehl-Neelsen stain, and culture for pyogenic, tubercular and fungal organisms were negative. Gene Xpert for detection of Mycobacterium tuberculosis was negative. CSF measles immunoglobulin G antibody was positive in high titre. Screening for HIV, neurosyphilis, hepatitis B and C were negative. Brain biopsy was not done as they denied such invasive investigations.

Treatment

No specific treatment was given. Only supportive treatment as airway support, maintenance of circulation by intravenous fluid, hydration and nutrition maintenance by nasogastric tube feeding. Care of bladder-by catheterization, care of bowel by laxative for constipation, care of skin and oral hygiene.Anticonvulsant: Sodium valporate was given for her involuntary movement and Clonazepam was used for sedation.

Outcome And Follow-Up

The patient's condition remained unchanged on symptomatic treatment and patient was discharged on request. Eventually, her condition was progressively deteriorated.

Discussion:

Diagnostic criteria of SSPE are

1. Clinical Progressive, subacute mental deterioration with typical signs like myoclonus
2. EEG Periodic, stereotyped, high voltage discharges
3. Cerebrospinal fluid :Increased gammaglobulin or oligoclonal pattern
4. Measles antibodies: Increased titre in serum (>1:256) and/or cerebrospinal fluid (>1:4)
5. Brain biopsy suggestive of panencephalitis

Definitive: criteria 5 with three more criteria; probable: three of the five criteria.[6]

The initial symptoms are usually subtle and include mild intellectual deterioration and behavioral changes without any apparent neurological signs or findings. Parents and teachers may notice progressive deterioration in scholastic performance. As disease advances non-specific manifestations evolve into disturbances in motor function and development of periodic stereotyped myoclonic jerks. It initially involve the head and subsequently trunk and limbs may not be obvious early in the disease but can be elicited by the patient standing with feet together and arms held forward and then watching for periodic dropping of the head, neck, trunk, or arm; these are often concomitant with contraction of facial musculature and slow eye blinks, it does not interfere with consciousness. Patients may, frequently, develop pyramidal and extrapyramidal signs. Myoclonus can present as a difficulty in gait, periodic dropping of the head, and falling. Few patients may develop ataxia, dystonia, and dyskinesia. Generalized tonic-clonic seizures and partial seizures may also occur.[6-8] In advanced stages of the disease, patients become quadriparetic, spasticity increases, and myoclonus may decrease or disappear. There is autonomic failure with loss of thermoregulation leading to marked temperature fluctuations. There is progressive deterioration of sensorium to a comatose state and ultimately the patient becomes vegetative. Decerebrate and decorticate rigidity appear, breathing becomes noisy and irregular. At this stage, patients frequently die due to hyperpyrexia, cardiovascular collapse, or hypothalamic disturbances.[9] CSF examination is usually normal. Frequently, it is acellular with normal or a mildly raised protein concentration. The most remarkable feature of CSF examination is a markedly raised gammaglobulin level, which is usually greater than 20% of total cerebrospinal fluid protein. Because of the large increase of intrathecal synthesis of IgG, CSF IgG concentration ranges from 10–54 ìg/dl compared with 5–10 ìg/dl in normal children.[10,11] Reverse transcriptase polymerase chain reaction technique and brain biopsy might be useful in confirming the diagnosis in SSPE with negative CSF findings.[12]

Our patient presented with the complaints of abnormal behavior, myoclonus and cognitive impairment. Once myoclonus is evident the clinical diagnosis is seldom a problem. However, subtle behavioural changes at an early stage of disease are frequently missed by relatives. Many such patients are often treated by a psychiatrist at this stage. In some cases myoclonus is not present; atonia may be present but can be overlooked.[13] MRI is more sensitive in detecting white matter abnormalities. In the early stages of the disease, cerebral MRI shows lesions usually involving parieto-occipital cortico-subcortical regions asymmetrically. In time, symmetric periventricular white matter changes become more prominent. However, more recently Aydin et al.[14] described that MRI findings could be normal with SSPE. The diagnosis is based upon typical cerebrospinal fluid changes and a characteristic electroencephalography pattern. The diagnosis of SSPE can be reliably established if patient fulfils three of the five criteria given by Dyken.[6]

Conclusion:

Subacute sclerosing panencephalitis (SSPE) may have wide clinical presentation with variable age at the onset and progression which needs to be addressed while management. In developing countries, SSPE is one of the common differential diagnoses in children with or without antecedent measles infection with intellectual disability, myoclonus and variable pyramidal, extrapyramidal and cranial nerve involvement. Diagnosis is especially problematic in adult patients with SSPE; differential diagnoses are also different. Treatments available are very costly and are available only at a few centers in the world. Moreover, these treatments are not curative and only help in buying time for these patients.

Conflict of interest: None.

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Vaginal Wall Leiomyoma: A Case Report

RABEYA AKTHER[a], MD. NOWFEL ISLAM[b], HASINA AFROZ[c]

Summary:

Vaginal wall leiomyoma is rare. They are typically located in the anterior or lateral wall of the vagina. Approximately 301 cases have been reported in the literature. Usually patients with vaginal leiomyoma present with a mass per vaginum or dyspareunia or pressure symptoms on the urinary tract. However, sometimes it is difficult to diagnose preoperatively because of an unusual presentation. History and a careful clinical examination may help to rule out malignancy. Here, we report a case of vaginal leiomyoma which was incidentally identified during routine gynecological check up of a 36-year-old multiparous lady as a large, solid, painless mass in the left vaginal wall. The overlying mucosa moved freely over the mass. The USG revealed nothing abnormal in the pelvic organs. Surgical enucleation was done vaginally and subsequent histopathology showed irregular and whorling bundles of smooth muscle cells confirming vaginal leiomyoma.

Keywords: Leiomyoma, vaginal leiomyoma, benign uterine leiomyoma.

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Introduction:

Vaginal tumors are rare and include cysts of vestigial structures, implantation dermoid, endometriotic cyst, papilloma, hemangioma, mucus polyp, adenoma and rarely leiomyoma. Approximately 301 cases have been reported in the literature. It was first detected in 1733 by Denys de Leyden[1]. Bennett and Erlich[2] found only nine cases in 50,000 surgical specimens and only one case in 15,000 autopsies reviewed at Johns Hopkins Hospital. These tumors arise most commonly from the anterior vaginal wall causing varied clinical presentations. They may or may not be associated with leiomyomas elsewhere in the body. We report a case of primary leiomyoma of vagina arising from lateral wall and it was diagnosed incidentally during vaginal examination.

Case Report:

A 36-year-old female, para 2, came to the outpatient department for routine gynecological check up. A mass was felt during per vaginal examination in the left lateral vagina wall (Figure - 1), but the upper limit of the mass could not be delineated. The mass was hard inconsistency, non tender and of restricted mobility. Vaginal mucosa moved freely over the mass. There was no history of dysperunia, dysuria, increased frequency, or any feature of urinary retention. No mass was palpable in the groin. An ultrasonogram was done which revealed no abnormality. Considering it as a case of enlarged lymph node, the mass was removed surgically by vaginal route. A 4.5 cm x 3.5x2.5 cm sized solid tumor was found. (Figure 2, 3) Vaginal wall was closed in layers. To prevent bleeding or oozing a vaginal pack was given. A Foley's catheter was introduced in the urethra for protecting the latter. The tumor was then sent for histopathological examination with a presumptive diagnosis of vaginal leiomyoma. Gross examination revealed a 4.5x3.5x2.5 cm

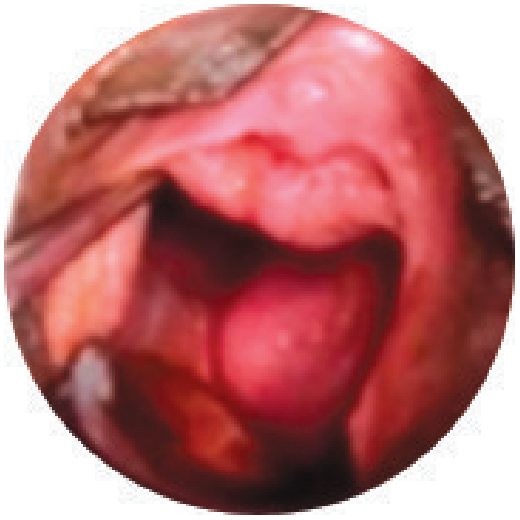

Fig.-1: *photograph showing a mass in the vagina.*

a. Dr. Rabeya Akther, Deputy Chief Medical Officer, Bangladesh Bank.

b. Prof. Md. Nowfel Islam, Professor, Pathology Department, National institute of Neurosciences & Hospital, Dhaka

c. Dr. Hasina Afroz, Consultant, Obstetrics & Gynecology Department ,United Medical College & Hospital, Dhaka.

Address of Correspondence: Dr. Rabeya Akther, Chief Consultant, Bangladesh Bank Medical Center, Motijheel, Dhaka, Mobile: 01817517100, E-mail: rabeya.akter@bb.org.bd

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solid mass with a whorling appearance in the cut section. Microscopic examination showed irregular and whorling bundles of smooth muscle cells. (Figure 4, 5, 6). No malignancy was seen. Final diagnosis was leiomyoma.

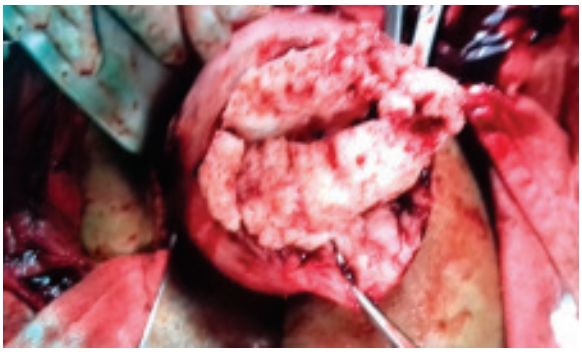

Fig.-2: *Photograph showing a mass in the vagina (during operation).*

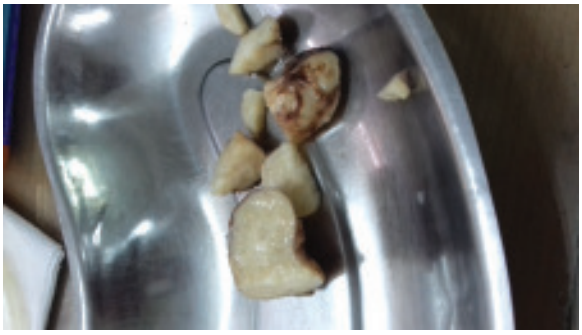

Fig.- 3: *Photograph showing the whorling pattern on cut section of the vaginal leiomyoma*

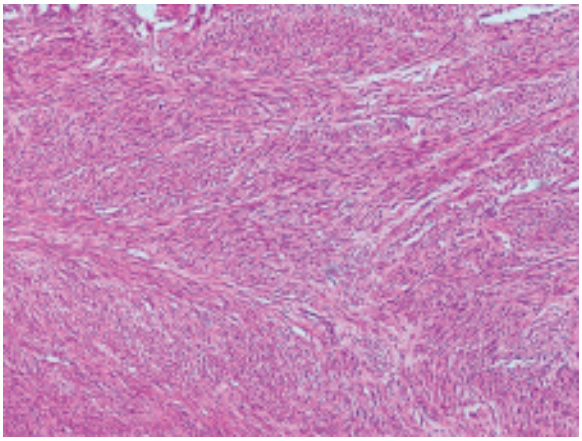

Fig.- 4: *Microphotograph showing the leiomyoma (hematoxylin and eosin stain, ×10 magnification)*

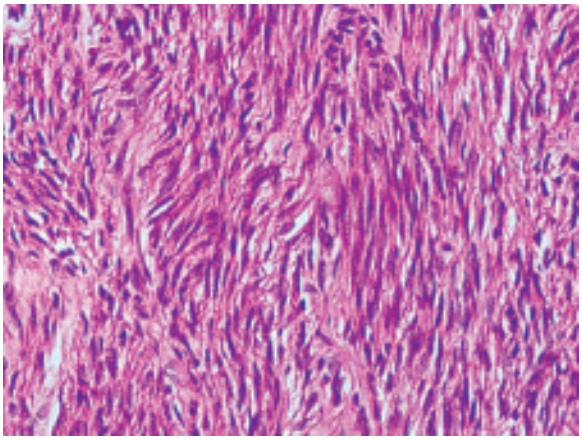

Fig.-5: *Microphotograph showing the leiomyoma (hematoxylin and eosin stain, ×40 magnification)*

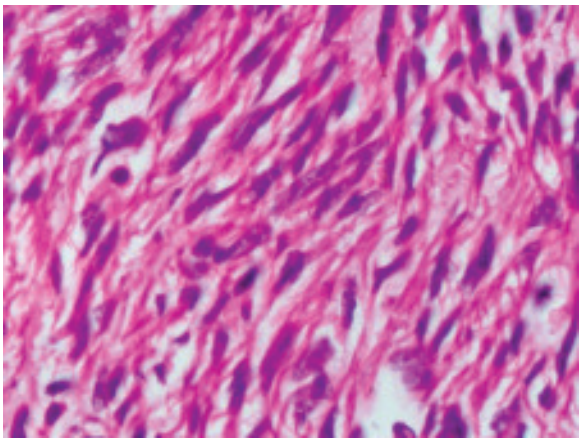

Fig.- 6: *Microphotograph showing the leiomyoma (hematoxylin and eosin stain, ×100 magnification)*

Discussion:

Tumors of vagina are rare and there are only around 301 reported cases of vaginal leiomyomas since the first described case in 1733 by Denys de Leyden[1].Leiomyomas in female genital tract are common in the uterus and to some extent in the cervix followed by the round ligament, utero-sacral ligament, ovary, and inguinal canal[1]. Occurrence in vagina is very rare. Vaginal leiomyomas are commonly seen in the age group ranging from 35 to 50 years and are reported to be more common among Caucasian women [1,2]. Usually occurs as single, well-circumscribed mass arising from the midline anterior wall and less commonly, from the posterior and lateral walls[1]. They may be asymptomatic but depending on the site of occurrence, they can give rise to varying symptoms including lower abdominal pain, low back

pain, vaginal bleeding, dyspareunia, and frequency of micturition, dysuria, or other features of urinary obstruction. These tumors can be intramural or pedunculated and solid as well as cystic. Usually these tumors are single, benign, and slow growing but sarcomatous transformation has been reported[1, 3]. Preoperatively, diagnosis by ultrasonography may be difficult, but magnetic resonance imaging usually clinches the diagnosis. In magnetic resonance imaging, they appear as well-demarcated solid masses of low signal intensity in T1 and T2 weighted images, with homogenous contrast enhancement, while leiomyosarcomas and other vaginal malignancies show characteristic high T2 signal intensity with irregular and heterogeneous areas of necrosis or hemorrhage [2, 3]. However, histopathological confirmation is the gold standard of diagnosis and also beneficial to rule out any possible focus of malignancy. Surgical removal of the tumor through vaginal approach, preferably with vaginal packing and urethral catheterization to prevent vaginal bleeding in postoperative period is recommended.

Reference:

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COLLEGE NEWS

(J Bangladesh Coll Phys Surg 2019; 37: 212)
DOI: http://dx.doi.org/10.3329/jbcps.v37i4.43354

College of Examinations news: Results of **FCPS Part-I, Part-II and MCPS** examination held in July are given bellow:

3280 candidates appeared in **FCPS Part-I**, examination held in **July, 2019 of which 603** candidates came out successful.

Subject wise results are as follows:

Result of FCPS Part-I Examination (July, 2019)

SL. No.	Subject	July-2018		
		Total Candidate	Total Passed	Percentage %
1.	Anaesthesiology	127	22	17.32
2.	Biochemistry	1	0	0.00
3.	Dentistry	143	48	33.57
4.	Family Medicine	47	7	14.89
5.	Dermatology and Venereology	1	0	0.00
6.	Haematology	10	3	30.00
7.	Histopathology	15	7	46.67
8.	Medicine	1106	174	15.73
9.	Microbiology	6	1	16.67
10.	Obstetrics & Gynaecology	561	40	7.13
11.	Ophthalmology	94	23	24.47
12.	Otolaryngology	103	11	10.68
13.	Paediatrics	269	81	30.11
14.	Physical Medicine & Rehabilitation	21	5	23.81
15.	Psychiatry	26	9	34.62
16.	Radiology & Imaging	47	8	17.02
17.	Radiotherapy	19	2	10.53
18.	Surgery	677	162	23.93
19.	Transfusion Medicine	7	0	0.00
	TOTAL	3280	603	18.34

CPD Program in 2019

(J Bangladesh Coll Phys Surg 2019; 37: 213)
DOI: http://dx.doi.org/10.3329/jbcps.v37i4.43355

Sl	Date	Vanue	Topics
1.	13 Feb' 2019	Shaheed Suhrawardy Medical College Dhaka.	• Child health in the era of digital technology. • Sensitivity and specificity of integrated test for detection of fetal chromosomal abnormality at 11-13 (+6) weeks of gestation.
2.	25 June, 2019	BCPS Auditorium, Dhaka.	• End of life care-an untouched issue. • How to construct an effective training module. • Customized training module in our setting.
3.	03 Sep' 2019	Chattagram International Medical College, Chattagram	• Polycystic ovarian disease-a management dilemma. • Oxygen therapy in neonates-a vital issue.

IMPORTANT RECENT ABSTRACTS

(J Bangladesh Coll Phys Surg 2019; 37: 214-216)
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IN HEALTHY NON-OBESE MEN AND WOMEN, A 25% CALORIE RESTRICTION DIET REDUCED CARDIOMETABOLIC RISK FACTORS MORE THAN AN AD LIBITUM DIET AFTER 2 YEARS.

Kraus WE, Bhapkar M, Huffman KM, et al. *2 years of calorie restriction and cardiometabolic risk (CALERIE): exploratory outcomes of a multicentre, phase 2, randomised controlled trial.*Read full-text (not free)View on PubMedRead rater commentsRead user comments

Background: For several cardiometabolic risk factors, values considered within normal range are associated with an increased risk of cardiovascular morbidity and mortality. We aimed to investigate the short-term and long-term effects of calorie restriction with adequate nutrition on these risk factors in healthy, lean, or slightly overweight young and middle-aged individuals.

Methods: CALERIE was a phase 2, multicentre, randomised controlled trial in young and middle-aged (21-50 years), healthy non-obese (BMI 22·0-27·9 kg/m2) men and women done in three clinical centres in the USA. Participants were randomly assigned (2:1) to a 25% calorie restriction diet or an ad libitum control diet. Exploratory cardiometabolic risk factor responses to a prescribed 25% calorie restriction diet for 2 years were evaluated (systolic, diastolic, and mean blood pressure; plasma lipids; high-sensitivity C-reactive protein; metabolic syndrome score; and glucose homoeostasis measures of fasting insulin, glucose, insulin resistance, and 2-h glucose, area-under-the curve for glucose, and insulin from an oral glucose tolerance test) analysed in the intention-to-treat population. This study is registered with ClinicalTrials.gov, number NCT00427193.

Findings: From May 8, 2007, to Feb 26, 2010, of 238 participants that were assessed, 218 were randomly assigned to and started a 25% calorie restriction diet (n=143, 66%) or an ad libitum control diet (n=75, 34%). Individuals in the calorie restriction group achieved a mean reduction in calorie intake of 11·9% (SE 0·7; from 2467 kcal to 2170 kcal) versus 0·8% (1·0) in the control group, and a sustained mean weight reduction of 7·5 kg (SE 0·4) versus an increase of 0·1 kg (0·5) in the control group, of which 71% (mean change in fat mass 5·3 kg [SE 0·3] divided by mean change in weight 7·5 kg [0·4]) was fat mass loss. Calorie restriction caused a persistent and significant reduction from baseline to 2 years of all measured conventional cardiometabolic risk factors, including change scores for LDL-cholesterol ($p<0·0001$), total cholesterol to HDL-cholesterol ratio ($p<0·0001$), and systolic ($p<0·0011$) and diastolic ($p<0·0001$) blood pressure. In addition, calorie restriction resulted in a significant improvement at 2 years in C-reactive protein ($p=0·012$), insulin sensitivity index ($p<0·0001$), and metabolic syndrome score ($p<0·0001$) relative to control. A sensitivity analysis revealed the responses to be robust after controlling for relative weight loss changes.

Interpretation: 2 years of moderate calorie restriction significantly reduced multiple cardiometabolic risk factors in young, non-obese adults. These findings suggest the potential for a substantial advantage for cardiovascular health of practicing moderate calorie restriction in young and middle-aged healthy individuals, and they offer promise for pronounced long-term population health benefits.

SGLT2 INHIBITORS' INTERACTION WITH OTHER RENOACTIVE DRUGS IN TYPE 2 DIABETES PATIENTS: STILL A LOT TO LEARN.

vanBaar MJB[1], Scholtes RA[1], van Raalte DH[2].

The first cardiovascular (CV) safety trial conducted with a sodium-glucose cotransporter (SGLT)-2 inhibitor, Empagliflozin Cardiovascular Outcome Event Trial in Type 2 Diabetes Mellitus Patients-Removing Excess Glucose (EMPA-REG OUTCOME), reported not only remarkable risk reductions in CV outcome, but also impressive improvements in renal outcome. Changes in renal hemodynamics could be involved in the benefit of SGLT2 inhibitors on renal outcomes. Considering that all patients of EMPA-REG OUTCOME had established atherosclerotic CV disease at baseline, many patients were also treated with several CV drugs at baseline, including RAS blockers, diuretics, calcium-channel blockers, and nonsteroidal anti-inflammatory drugs. These drugs also impact renal physiology and possibly renal outcome, which could cause relevant drug-drug interactions. This topic is addressed in this issue of Kidney International by Mayer and colleagues. In their manuscript, the impact

of empagliflozin on kidney function, renal outcome, and renal safety is presented with stratification for background therapy. Although the beneficial effects of empagliflozin and its safety profile are consistent among all groups, we wonder, do we really understand the renal effects of all these drugs in type 2 diabetes (T2D) patients as studied in the large outcome trials?

ANALYSIS FROM THE EMPA-REG OUTCOME® TRIAL INDICATES EMPAGLIFLOZIN MAY ASSIST IN PREVENTING THE PROGRESSION OF CHRONIC KIDNEY DISEASE IN PATIENTS WITH TYPE 2 DIABETES IRRESPECTIVE OF MEDICATIONS THAT ALTER INTRARENAL HEMODYNAMICS

Gert J. Mayer[1], Christoph Wanner[2], Matthew R. Weir[3], Silvio E. Inzucchi[4], Audrey Koitka, Weber[2,5,6], Stefan Hantel[5], Maximilian von Eynatten[5], Bernard Zinman[7], David Z.I. Cherney[8,"],

In patients with type 2 diabetes mellitus (T2DM) and cardiovascular (CV) disease, empagliflozin (EMPA) decreased progression of chronic kidney disease (CKD), likely via a reduction in intraglomerular pressure. Due to prevalent comorbidities, such as hypertension and albuminuria, patients often receive other agents that alter intrarenal hemodynamics, including angiotensin converting enzyme inhibitors/angiotensin receptor blockers (ACEi/ARBs), calcium channel blockers (CCBs) and diuretics. Nonsteroidal anti-inflammatory drugs (NSAIDs) may also be used by some individuals. In this exploratory, non-prespecified analysis, we investigated whether the kidney benefits of EMPA are altered in individuals already using the medications in these categories. In the BI 10773 (Empagliflozin) Cardiovascular Outcome Event Trial in Type 2 Diabetes Mellitus Patients (EMPA-REG OUTCOME®) trial, 7020 patients were essentially equally randomized to EMPA 10 mg, 25 mg or placebo added to their standard care. Differences in risk of incident or worsening nephropathy for pooled EMPA vs placebo across subgroups by baseline background medications (to which patients were not randomized) were assessed using a Cox proportional hazards model. Risk reductions in incident or worsening nephropathy with EMPA were consistent across medication subgroups, with no heterogeneity of treatment effect. As a representative example, the risk for acute renal failure was overall slightly increased in patients using ACEi/ARBs in all groups (placebo, EMPA 10 mg or EMPA 25 mg) but incidence rates were numerically lower in those assigned to EMPA. Similar patterns were observed for other medications included in this analysis. Thus, EMPA may assist to prevent CKD progression in patients with T2DM with CV disease, irrespective of common background medications that alter intrarenal hemodynamics, and without increasing acute renal adverse events.

EFFECT OF SYSTOLIC AND DIASTOLIC BLOOD PRESSURE ON CARDIOVASCULAR OUTCOMES

Alexander C. Flint, M.D., Ph.D., Carol Conell, Ph.D., XiushuiRen, M.D., Nader M. Banki, M.D., Sheila L. Chan, M.D., Vivek A. Rao, M.D., Ronald B. Melles, M.D., and Deepak L. Bhatt, M.D., M.P.H.

Background: The relationship between outpatient systolic and diastolic blood pressure and cardiovascular outcomes remains unclear and has been complicated by recently revised guidelines with two different thresholds (e"140/90 mm Hg and e"130/80 mm Hg) for treating hypertension.

Methods: Using data from 1.3 million adults in a general outpatient population, we performed a multivariable Cox survival analysis to determine the effect of the burden of systolic and diastolic hypertension on a composite outcome of myocardial infarction, ischemic stroke, or hemorrhagic stroke over a period of 8 years. The analysis controlled for demographic characteristics and coexisting conditions.

Results: The burdens of systolic and diastolic hypertension each independently predicted adverse outcomes. In survival models, a continuous burden of systolic hypertension (e"140 mm Hg; hazard ratio per unit increase in z score, 1.18; 95% confidence interval [CI], 1.17 to 1.18) and diastolic hypertension (e"90 mm Hg; hazard ratio per unit increase in z score, 1.06; 95% CI, 1.06 to 1.07) independently predicted the composite outcome. Similar results were observed with the lower threshold of hypertension (≥130/80 mm Hg) and with systolic and diastolic blood pressures used as predictors without hypertension thresholds. A J-curve relation between diastolic blood pressure and outcomes was seen that was explained at least in part by age and other covariates and by a higher effect of systolic hypertension among persons in the lowest quartile of diastolic blood pressure.

Conclusions: Although systolic blood-pressure elevation had a greater effect on outcomes, both systolic and diastolic hypertension independently influenced the risk of adverse cardiovascular events, regardless of the definition of hypertension (e"140/90 mm Hg or e"130/80 mm Hg).

AMBIENT PARTICULATE AIR POLLUTION AND DAILY MORTALITY IN 652 CITIES

C. Liu, R. Chen, F. Sera, A.M. Vicedo Cabrera, Y. Guo, S. Tong, M.S.Z.S. Coelho, P.H.N. Saldiva, E. Lavigne, P. Matus, N. Valdes Ortega, S. Osorio Garcia, M. Pascal, M. Stafoggia, M. Scortichini, M. Hashizume, Y. Honda, M. Hurtado Diaz, J. Cruz, B. Nunes, J.P. Teixeira, H. Kim, A. Tobias, C. Íñiguez, B. Forsberg, C. Åström, M.S. Ragettli, Y.-L.Guo, B.-Y. Chen, M.L. Bell, C.Y. Wright, N. Scovronick, R.M. Garland, A. Milojevic, J. Kyselý, A. Urban, H. Orru, E. Indermitte, J.J.K. Jaakkola, N.R.I. Ryti, K. Katsouyanni, A. Analitis, A. Zanobetti, J. Schwartz, J. Chen, T. Wu, A. Cohen, A. Gasparrini, and H. Kan

Background: The systematic evaluation of the results of time-series studies of air pollution is challenged by differences in model specification and publication bias.

Methods: We evaluated the associations of inhalable particulate matter (PM) with an aerodynamic diameter of 10 ¼m or less (PM10) and fine PM with an aerodynamic diameter of 2.5 ¼m or less (PM2.5) with daily all-cause, cardiovascular, and respiratory mortality across multiple countries or regions. Daily data on mortality and air pollution were collected from 652 cities in 24 countries or regions. We used overdispersed generalized additive models with random-effects meta-analysis to investigate the associations. Two-pollutant models were fitted to test the robustness of the associations. Concentration–response curves from each city were pooled to allow global estimates to be derived.

Results: On average, an increase of 10 ¼g per cubic meter in the 2-day moving average of PM10 concentration, which represents the average over the current and previous day, was associated with increases of 0.44% (95% confidence interval [CI], 0.39 to 0.50) in daily all-cause mortality, 0.36% (95% CI, 0.30 to 0.43) in daily cardiovascular mortality, and 0.47% (95% CI, 0.35 to 0.58) in daily respiratory mortality. The corresponding increases in daily mortality for the same change in PM2.5 concentration were 0.68% (95% CI, 0.59 to 0.77), 0.55% (95% CI, 0.45 to 0.66), and 0.74% (95% CI, 0.53 to 0.95). These associations remained significant after adjustment for gaseous pollutants. Associations were stronger in locations with lower annual mean PM concentrations and higher annual mean temperatures. The pooled concentration–response curves showed a consistent increase in daily mortality with increasing PM concentration, with steeper slopes at lower PM concentrations.

Conclusions: Our data show independent associations between short-term exposure to PM10 and PM2.5 and daily all-cause, cardiovascular, and respiratory mortality in more than 600 cities across the globe. These data reinforce the evidence of a link between mortality and PM concentration established in regional and local studies.

DRUG-INDUCED LIVER INJURY — TYPES AND PHENOTYPES

Jay H. Hoofnagle, M.D., and Einar S. Björnsson, M.D.

Drug-induced liver injury is an uncommon but challenging Clinical problem with respect to both diagnosis and management.1-3 Its incidence is estimated to be 14 to 19 cases per 100,000 persons, with jaundice accompanying 30% of cases.4,5 Drug-induced liver injury is responsible for 3 to 5% of hospital admissions for jaundice6 and is the most frequent cause of acute liver failure in most Western countries, accounting for more than half of cases.7,8Advances have been made in our understanding of viral, autoimmune, and genetic liver diseases, as well as approaches to their prevention and treatment, but progress on these fronts has been modest in the case of drug-induced liver injury.

The diagnosis of drug-induced liver injury is particularly challenging, since it is based largely on exclusion of other causes. The timing of the onset of injury after the implicated agent has been started (latency), resolution after the agent is stopped ("dechallenge"), recurrence on re-exposure (rechallenge), knowledge of the agent's potential for hepatotoxicity (likelihood), and clinical features (phenotype) are the major diagnostic elements.9-11 With few exceptions, there are no specific diagnostic markers for drug-induced liver injury, and special tests (liver biopsy, imaging, and testing for serologic markers) are helpful mostly in ruling out other causes of liver injury. The large number of agents that can cause liver injury highlights these challenges. LiverTox, the National Institutes of Health–sponsored website on hepatotoxicity, has descriptions of more than 1200 agents (prescription and over-the-counter medications, herbal products, nutritional supplements, metals, and toxins), along with their potential to cause liver injury.12

Among the 971 prescription drugs described, 447 (46%) have been implicated in causing liver injury in at least one published case report.11 This brief review cannot cover all aspects of drug-induced liver injury but focuses on general principles, newer concepts, and current challenges, with frequent references to the LiverTox website for further detail.

Obituary

(J Bangladesh Coll Phys Surg 2019; 37: 217-219)
DOI: http://dx.doi.org/10.3329/jbcps.v37i4.43357

Professor Md. Sadequzzaman died on 16th March,2019. He Passed fellowship in Medicine in January 1973 from Bangladesh College of Physicians and Surgeons (BCPS).

Dr. Rajan Karmakar died on 17th March,2019. He Passed fellowship in Oral and Maxillofacial Surgery in January 2012 from Bangladesh College of Physicians and Surgeons (BCPS).

Dr. Md. Yousuf Ur Rahman died on 27th April,2019. He Passed fellowship in Medicine in January 2015 from Bangladesh College of Physicians and Surgeons (BCPS).

Dr. Dulal Abdul Jabbar Chaudhury died on 6th May,2019. He Honorary fellowship in General Practitioner in 2001 from Bangladesh College of Physicians and Surgeons (BCPS).

Professor Ahsanul Habib died on 7th May, 2019. He Passed fellowship in Anaesthesiology in July 1989 from Bangladesh College of Physicians and Surgeons (BCPS).

Professor Syeda Nurjahan Bhuiyan died on 29th August,2019. He Honorary fellowship in Obst. & Gynae in 2007 from Bangladesh College of Physicians and Surgeons (BCPS).

Journal of Bangladesh College of Physicians and Surgeons (JBCPS)

INFORMATION FOR AUTHORS

MANUSCRIPT PREPARATION AND SUBMISSION

Guide to Authors

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A manuscript number will be mailed to the corresponding author within two working days.

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Article Types:
Five types of manuscripts may be submitted:

Editorials: It will be preferably written invited only and usually covers a single topic of contemporary interest.

Original Articles: These should describe new and carefully confirmed findings, and experimental procedures should be given in sufficient detail for others to verify the work. The length of a full paper should be the minimum required to describe and interpret the work clearly.

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Reviews: Submissions of reviews and perspectives covering topics of current interest are welcome and encouraged. Reviews should be concise and no longer than 4 to 6 printed pages (about 12 to 18 manuscript pages). It should be focused and must be up to date. Reviews are also peer-reviewed.

Case Reports: This should cover uncommon and/or interesting cases with appropriate confirmation process.

Review Process:
All manuscripts are initially screened by editor and sent to selective reviewer. Decisions will be made as