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JALALABAD MEDICAL JOURNAL

Editorial

Recent Advancement in Aetiopathogenesis of Pterygia

A pterygium is a triangular fibrovascular subepthelial in growth of degenerative bulbar conjunctival tissue over the limbus onto the cornea. It is an ocular surface disease of humans attributed to chronic ultraviolet-B (UV-B) exposure. Clinically, the condition involves invasive centripetal growth with associated inflammation and neovascularization. Previous clinical studies focused primarily on the clinical characteristics and surgical management of pterygia and because of this, pathogenesis of pterygia remains incompletely understood. However considerable progress in this area has been achieved, providing additional insight into this complex disease. Pterygium is more common in people living in hot climate and doing outdoor work. In the early stage, it is asymptomatic except some cosmetic blemish. Visual disturbance occurs when it encroaches upon visual axis or induces corneal astigmatisim. Occasionally it causes diplopia due to limitation of ocular movement. Ophthalmic surgeon previously used to consider it to be simple disease and treated by simple excision but recurrence of pterygium after surgical excision was main problem (30-50%)[1] and postoperatively it may appear as more aggressive than the initial lesion. Currently in light of recent concepts about its pathogenesis it has been possible to minimize it recurrences. Old modalities of treatment by simple excision has been superceded by use of cytotoxic drug such as Mitomycin-C (MMC), Amniotic membrane graft or Conjunctival autograft. The membranes has been variously described as promoting wound healing, preventing scarring, inhibiting vascularization, facilitating re-epithelization and acting as biological bandage and thereby minimizing it recurrence[2]. The recent evidence implicate antiapoptotic mechanisms, immunological mechanism, cytokines, growth factors, extracellular matrix (ECM) modulations, genetic factors, viral infections and others possible causative factors. Attempt has been made to summarize many of recent discoveries regarding pathogenesis of pterygium[3].

UV-B → DNA mutations → a) Antiapoptotic / Cell growth related mechanism, b) Hereditary factors, c) ECM modulators, d) Immunological mechanism, e) Cytokines, f) Growth and angiogenic factors and g) Viral infections → Pterygium.

UV-B light has been attributed as a major cause of pterygium. Patient with increased UV-B exposure via hot climate, sunlight exposure especially those who living close to the equator. UV-light causes oxidative stress leading to up regulation of many potential mediators of pterygium growth. 8-Hydroxydeoxyguanosine, a marker commonly used to identify oxidative damage to DNA has been found in pterygium tissue[4]. Oxidative stress yields formation of reactive O_2 and N_2 radical which causes DNA damage. Glutathione S-transferase which enhanced UV light sensitivity is abundant in pterygial tissue. UV light exposure and resultant oxidative stress play a primary role in the pathogenesis of pterygium.

The cell cycle, especially defective regulations of apoptosis likely plays significant role in growth and formation of pterygium. Impression cytology reveals squamous metaplasia and fewer apoptotic markers. Maxia et al hypothesized UV light and resultant oxidative stress leads to increase survivin level (an inhibitor of apoptosis) and hyperproliferative state[5]. P^{53} suppressor protein (acts as a check point by preventing tissue proliferation) is defective in pterygium tissue[6].

After UV-B exposure- chemokines, cytokines and other growth factors like TNF, interleukins are released which induce inflammatory reactions and neovascularization in pterygium tissue. Cyclooxygenase-2 is over expressed and yielding formation of prostaglandin products and leading to inflammatory cascades. Pterygium samples have

increased levels of cell signal and adhesion molecules which concentrate on the head of pterygium and induce proliferation of tissue[7].

Due to stimulation of fibroblast proliferation, there is increased level of HMG Co A-reductase and LDL. This association may serve as a future therapeutic target to prevent pterygium formation[8].

Human papilloma virus (HPV) and Herpes simplex virus (HSV) may promote proliferation of tissue and pterygium formation. It may also increase likelihood of genetic mutation and predispose the individual to pterygium formation.

The pathogenesis and growth of pterygium are complex in nature and future research & study in this area may unveil & contribute to elucidate mystery of growth of pterygium.

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JALALABAD MEDICAL JOURNAL

Original article

Correlation of Endogenous Creatinine Clearance with Estimated Glomerular Filtration Rate (eGFR) in Assessment of Renal Function

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ABSTRACT

To find the correlation of endogenous creatinine clearance (Ccr) with estimated glomerular filtration rate (eGFR) in assessment of renal function. This cross sectional study was carried out in the department of Biochemistry, Sylhet MAG Osmani Medical College, Sylhet during July 2007 to June 2008. Ninety seven (97) subjects with an age ranging from 18-70 years were included in this study. Fifty eight (58) patients with creatinine clearance rate (C_{cr}) <90 ml/min were considered as chronic kidney disease & patient designated as group-I and 39 (thirty nine) study subjects with $C_{cr} \geq 90$ ml/min were considered as healthy subjects & designated as group-II. GFR was estimated by using the Cockcroft-Gault (CG) and Modification of Diet in Renal Disease (MDRD) formulae and C_{cr} was measured by collection of 24 hours urine volume. In group-I, mean creatinine clearance values by C_{cr}, CG and MDRD formulas were 54.06±22.61, 61.54±34.39 and 73.51±37.42 ml/min respectively whereas in group-II the values were108.28±17.46, 100.45±29.50 and 125.39± 42.01 ml/min respectively. Significant difference between C_{cr} and MDRD methods for GFR estimation was observed and there was no significant difference between C_{cr} and CG methods in both chronic kidney disease (CKD) patients and normal subjects. This result also indicates that the CG equation correlated better than MDRD when compared with C_{cr} for assessment of renal function both in CKD and normal subjects. However both CG and MDRD formulas are useful in assessment of renal function in CKD. Therefore, it may be suggested that eGFR is a useful effort to identification of patients with renal impairment.

Key words: *Endogenous creatinine clearance, GFR, Renal function*

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INTRODUCTION

Accurate renal function assessment is important for the diagnosis and treatment of kidney diseases. The use of highly accurate filtration markers to measure renal function has traditionally been limited by cumbersome and costly techniques and the involvement of radioactivity in some methods[1]. Glomerular filtration rate (GFR) is accepted as the best overall measures of kidney function. Many organizations recommended the use of equations that estimate the GFR to facilitate the detection, evaluation, and management of chronic kidney diseases[2].

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A number of methods are used to measure the GFR. Most involve the kidney's ability to clear either an exogenous or endogenous markers. The ideal marker is one that is freely filtered at the glomerulus and neither secreted nor reabsorbed by the renal tubules and present at a stable plasma concentration. GFR is measured as the urinary or plasma clearance of ideal filtration markers such as inulin, iothalamate, ^{51}Cr-EDTA, ^{99m}Tc DTPA and iohexol[3].

Urinary clearance of an endogenous filtration marker such as creatinine and more rarely urea clearance and low molecular weight protein (for example cystatin C) can be computed from a timed urine collection (for example, a 24-hour urine collection) and blood sampling during the collection period without the need

for the administration of an exogenous marker. Creatinine is filtered by glomerulus and small negligible amount is secreted by proximal tubular cells. It is eliminated from circulation at a constant rate. Its plasma levels remaining constant, as well. In steady state conditions, creatinine excretion is equal to creatinine production, so that plasma creatinine levels vary inversely to GFR. So, a normal or slight increase in plasma creatinine does not necessarily means that glomerular filtration is normal[2,4]. In people with a relatively low muscle mass, including children, women, the elderly, malnourished patients and cancer patients, the serum creatinine is lower for a given GFR[5].

Urea is the major nitrogen-containing product of protein catabolism in humans, accounting for more than 75% of the nonprotein nitrogen eventually excreted. A significantly elevated plasma urea concentration usually indicates impaired glomerular function[6]. Serum urea is less reliable marker of GFR than creatinine because levels are more vulnerable to change for reasons unrelated to GFR. 40-50% of filtered urea may be reabsorbed by the tubules; the proportion is reduced in advanced renal failure. Thus urea clearance is not an accurate measure of GFR[3]. The concentration of urea or creatinine in blood or plasma represents the dynamic equilibrium between production and elimination. In healthy subjects, there is an enormous reserve of renal excretory function, and serum creatinine does not rise above the normal range until there is a reduction of 50-60% in the GFR. It must be re-emphasized that a normal serum urea or creatinine is not synonymous with a normal GFR[7].

Numerous equations using the serum creatinine level have been developed to calculate estimated GFR (eGFR)[8]. Automatic laboratory reporting of eGFR calculated from serum creatinine measurements help to identify the asymptomatic kidney dysfunction at an earlier stage. eGFR correlates well with complications of CKD and an increased risk of adverse outcomes such as cardiovascular morbidity and mortality. The National Kidney Foundation Dialysis Outcome Quality Initiative (KDOQl) and UK Renal Association guidelines recommend the eGFR from serum creatinine measurements[9].

Estimating equations include variables such as age, sex, race and body size, in addition to serum creatinine, as surrogates for muscle mass, and therefore, they can overcome some of the limitations of the use of serum creatinine alone. Estimating equations for GFR have been developed chiefly in study populations consisting predominantly of patients with chronic kidney disease and reduced GFR. Direct measurements of renal function, using either endogenous or exogenous filtration markers, might be the best way to consistently obtain accurate assessments of renal function[10].

The MDRD study and the Cockcroft-Gault equations have been evaluated in various populations, including blacks, whites and Asians with nondiabetic kidney disease, patients with diabetes without kidney disease, kidney transplant recipients, and potential kidney donors. The MDRD study equation is reasonably accurate in nonhospitalized patients known to have chronic kidney disease. In some studies, the MDRD study equation has been reported to be more accurate than the Cockcroft-Gault equation, whereas other studies have found that the two yield similar results. Both the MDRD study and the Cockcroft-Gault equations have been reported to be less accurate in populations without chronic kidney disease, such as in young patients with type-1 diabetes without microalbuminuria and in potential kidney donors[12]. The purpose of the present study is to evaluate the performance of the MDRD and Cockcroft-Gault equations in Bangladeshi population using creatinine clearance as standard method of GFR estimation.

MATERIALS AND METHODS

This cross-sectional study was carried out in the Department of Biochemistry, Sylhet MAG Osmani Medical College from July 2007 to June 2008. Informed written consent was taken from each study subject. Data were collected through a preformed questionnaire. Subjects with urinary tract infection, renal stone and dialysis or transplant patients were excluded from the study. A total of ninety seven (97) subjects with age ranging from 18-70 years were taken for the study and they were divided into two groups.

Group-I consists of fifty eight (58) chronic kidney disease patients. Diagnosis was made on the basis of GFR < 90 ml/min. GFR was measured by creatinine clearance by using collection of 24 hours urine volume. Group-II consists of thirty nine (39) normal study subjects. Diagnosis was made on the basis of history, physical findings, GFR ≥ 90 ml/min and other relevant parameters. All the study subjects were instructed to begin the 24 hours urine collection after completion of the first voiding in the morning thereafter collecting all the urine for 24-hours in supplied 4000 ml capacity plastic container, including the final void at the completion of 24-hours period (8 am previous morning to 8 am next morning). Preservative toluene (10 ml) was supplied to all patients and advised to mix into the container after first void and to bring the specimens as early as possible. The volume of 24-hours urine specimen was measured. After proper mixing, 5 ml of sample was taken for estimation of creatinine concentration. With all aseptic precautions, about 3 ml of venous blood were drawn from antecubital vein by

using disposable syringes. Then blood was transferred into clean, dry and plain test tubes without anticoagulant. Blood were first allowed to clot and then centrifuged at a rate of 3000 rpm for five minutes. Clear serum was taken for estimation of serum creatinine level. All the tests were done as soon as possible. When there was delay separated serum was preserved in micro centrifuge tube and stored at -20^0 C temperature in a refrigerator for subsequent assay.

Serum and urinary creatinine was measured by enzymatic method (Kinetic Jaffe method). Blood urea was measured by enzymatic method (Berthelot urease method). GFR in ml/min for clearance of creatinine were calculated by the following formula[11].

$$\text{GFR (CCr) (ml/min)} = \frac{\text{Ucr (mg/dl) X Uv (ml/min)}}{\text{Scr (mg/dl)}}$$

Cockcroft-Gault formula:

$$\text{Creatinine clearance} = \frac{(140 - \text{age}) \times \text{weight (kg)} \times \text{K}}{72 \times \text{serum creatinine(mg/dl)}}$$

Where K = 0.85 for women and 1.00 for men.

Abbreviated MDRD formula = 186 x $(S_{Cr})^{-1.154}$ x $\text{age}^{-0.203}$ x 0.742 (if the subject is female) or x 1.212 (if the subject is black).

All statistical analysis was done by Statistical Package for Social Science (SPSS) version 12.0. Values were presented as mean ± SD. Unpaired t-test and Pearson's correlation test were done to see the significant difference among the groups. Comparison among the groups was done by ANOVA test and multiple comparisons between different formulas were done by Bonferroni test.

RESULTS

A total of ninety seven (97) subjects were studied. Fifty eight (58) patients with C_{Cr} <90 ml/min were considered as chronic kidney disease (CKD) patient designated as group-I and thirty nine (39) study subjects with C_{Cr} ≥ 90 ml/min were considered as healthy subjects designated as group-II. The results were expressed as mean ± SD. A level of P<0.05 was accepted as statistically significant.

There was significant difference found between the two groups in regard to age (p=0.002) and no significant difference in weight between two groups (p=0.799).

In this study, there was significant difference of serum and urinary creatinine and blood urea between two groups was found.

Table-I: *Comparisons of creatinine clearance by different methods*

Study Groups	Study Parameters			F Value	P Value
	C_{Cr} (Mean ± SD)	CG (Mean ± SD)	MDRD (Mean ± SD)		
Group-I (n=58) C_{Cr} <90 ml/min	54.06 ± 22.61	61.54 ± 34.39	73.51 ± 37.42	5.411	0.005
Group-II (n=39) C_{Cr} >90 ml/min	108.28 ± 17.46	100.45 ± 29.20	125.39 ± 42.01	6.512	0.002

ANOVA test was done

Table-II: *Multiple comparisons of creatinine clearance by C_{Cr}, Cockcroft-Gault and MDRD methods in Group-I (n=58) (C_{Cr} < 90 ml/min)*

Parameters Compared		P-value
C_{Cr} (ml/min) (mean ± SD)	54.06±22.61	0.634
CG (ml/min) (mean ± SD)	61.54±34.39	
C_{Cr} (ml/min) (mean ± SD)	54.06±22.61	0.004
MDRD (ml/min) (mean ± SD)	73.51±37.42	
MDRD (ml/min) (mean ± SD)	73.51±37.42	0.139
CG (ml/min) (mean ± SD)	61.54±34.39	

Bonferroni test was done.

Significant difference of creatinine clearance values among C_{Cr}, Cockcroft-Gault and MDRD formulas were found in both groups. [Table-I]

Table-II shown the multiple comparison of creatinine clearance by C_{Cr}, Cockcroft-Gault and MDRD formulas in group-I. There was significant difference of creatinine clearance between C_{Cr} and MDRD methods. No significant difference of creatinine clearance was found between C_{Cr} and Cockcroft-Gault, MDRD and Cockcroft-Gault methods.

Table-III shows the multiple comparison of creatinine clearance by C_{Cr}, Cockcroft-Gault and MDRD formula in group-II. There was significant difference of creatinine clearance between C_{Cr} and MDRD methods, MDRD and Cockcroft-Gault methods. There was no significant difference of creatinine clearance between C_{Cr} and Cockcroft-Gault methods.

Table-III: *Multiple comparisons of creatinine clearance by C_{Cr}, Cockcroft-Gault and MDRD methods in Group-II (n=39) (C_{Cr} > 90 ml/min)*

Parameters compared		P-value
C_{Cr} (ml/min) (mean ± SD)	108.28±17.46	0.811
CG (ml/min) (mean ± SD)	100.45±29.20	
C_{Cr} (ml/min) (mean ± SD)	108.28±17.46	0.05
MDRD (ml/min) (mean ± SD)	125.39±42.01	
MDRD (ml/min) (mean ± SD)	125.39±42.01	0.002
CG (ml/min) (mean ± SD)	100.45±29.20	

Bonferroni test was done

Table-IV: *Correlation of C_{Cr}, Cockcroft-Gault (CG) and MDRD methods in study groups*

Study Groups	Correlation parameters		F value	P value
Group-I (n=58) (C_{Cr} <90 ml/ min)	C_{Cr}	CG	0.666	<0.001
	C_{Cr}	MDRD	0.784	<0.001
	CG	MDRD	0.841	<0.001
Group-II (n=39) (C_{Cr} >90 ml/ min)	C_{Cr}	CG	0.192	NS
	C_{Cr}	MDRD	0.187	NS
	CG	MDRD	0.743	<0.001

In group I, there was significant positive correlation of C_{Cr} with Cockcroft-Gault and MDRD methods and also between Cockcroft-Gault and MDRD methods. In groups II, there was significant positive correlation between Cockcroft-Gault and MDRD methods but no correlation of C_{Cr} was found with Cockcroft-Gault or MDRD methods. [Table-IV]

DISCUSSION

Measurement of GFR is considered the standard for estimating renal function. However, standardized accurate GFR methodology is expensive and cumbersome. Therefore renal function is typically estimated by using various specifically derived prediction equations based on serum creatinine concentration[12]. Thus direct measurements of renal function using either endogenous or exogenous filtration markers might be the best way to consistently obtain accurate assessment of renal function[1].

The purpose of this cross-sectional study was to evaluate the performance of Cockcroft Gault equations and the MDRD equation in assessment of renal function. Significant difference of age distribution was observed between the study groups. No significant difference of weight between study groups was observed. This finding of no difference of body weight between study groups was important as there may be no influence of body weight on serum creatinine.

There was significant difference of serum creatinine between two groups. Also there was significantly raised urinary creatinine and blood urea in group having chronic kidney disease. This finding is expected as group I patients are grouped according to C_{Cr} <90 ml/min and considered as suffering from chronic kidney disease.

There was significant difference of creatinine clearance values among $C_{Cr,}$ Cockcroft-Gault and MDRD formulas in both groups (P= 0.005 in group–I and P=0.002 in group-II). This findings are partially similar to study conducted by Chudliegh et al[13].

In this study group-I with C_{Cr} < 90ml/min there was significant difference of creatinine clearance between C_{Cr} and MDRD methods (p=0.004) and there was no significant difference of creatinine clearance between C_{Cr} and Cockcroft-Gault methods (p=0.634). Creatinine clearance of MDRD and Cockcroft-Gault methods had no significant difference (p=1.39). Boston, Kronenberg and Ritz[1] studied the predictive performance of renal function equations for a CKD population with normal serum creatinine demonstrated that the most accurate results were obtained with the Cockroft-Gault equation.

In group-II with C_{Cr} >90ml/min there was significant difference of creatinine clearance between C_{Cr} and MDRD methods (p=0.05) and there was no significant difference between C_{Cr} and Cockcroft-Gault methods (p=0.811) and creatinine clearance of MDRD and Cockcroft-Gault methods had significant difference (p=0.002). This finding is similar to study conducted by Lin et al[14]. The MDRD equation performed much more poorly in subjects without kidney disease than in those with chronic kidney disease, as compared with Cockcroft-Gault equation.

Multiple comparisons show that creatinine clearance by Cockcroft-Gault formula has no significant difference with C_{Cr}. But by MDRD equation shows significant difference with C_{Cr}. So the difference among C_{Cr}, Cockcroft-Gault and MDRD equation is due to MDRD formula. According to Mathew et al[15] eGFR estimation using MDRD formula is not validated for Asian people.

This study has significant correlation of C_{Cr} with Cockcroft-Gault and MDRD methods in Group-I. But no significant correlation of C_{Cr} found with Cockcroft-Gault or MDRD methods in Group-II. Cockcroft-Gault

and MDRD methods correlated significantly in both groups. This finding is consistent with Ibrahim et al[16] and Jabary et al[4] who found a linear correlation among three methods. The results of our study shows that Cockcroft-Gault formula correlated batter than MDRD formula when compared with C_{Cr} in both CKD and normal subjects but both Cockcroft-Gault and MDRD formulas are useful in assessment of renal function in CKD.

The limitation of our study was the small sample size. Moreover we did not use a gold standard method for GFR estimation e.g. isotopic GFR estimation due to lack of proper facility.

CONCLUSION

It may be concluded that eGFR is a useful effort to improve the identification of patients with renal impairment and Cockcroft-Gault formula is correlated with C_{Cr} (using 24 hours urine volume) in both normal and CKD patients. Both Cockcroft-Gault and MDRD can be used in clinical practice for assessment of CKD. Further studies are recommended to confirm the generalized ability of our findings with large sample size and categorizing the patients with renal impairment.

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JALALABAD MEDICAL JOURNAL

Original article

Copper Status in Iron Deficient Anemic Adolescents

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ABSTRACT

Changes in serum copper level have important contribution in the development of iron deficiency in adolescence. An observational study has been carried out in the department of Physiology, Bangabandhu Sheikh Mujib Medical University (BSMMU) from January to December, 2007 to observe copper status in iron deficient anemic adolescents. For this purpose, a total number of 60 subjects of both sexes with age ranged from 11-18 years were selected of whom 30 were iron deficient adolescents and 30 were apparently healthy. Iron status was lower and copper status was higher in iron deficient adolescents of both sexes. The present study revealed that deficiency of iron is associated with hypercupremia in adolescents.

Key words: *Copper, Iron deficiency anemia, Adolescence*

[Jalalabad Med J 2010; 7 (2): 44-46]

INTRODUCTION

Physiological processes during puberty are particularly linked to increased requirements for iron to meet the increased demand for erythropoiesis as well as high growth rate[1,2]. During adolescence requirement of iron is increased in boys for increase in blood volume, muscle mass and myoglobin, whereas increased demands for growth and loss of iron due to onset of menstruation in female[3,4]. Iron status influences serum levels of some other trace elements like copper [5].

Changes in serum copper level have important role in the development of iron deficiency[6]. An increased concentration of copper is associated with iron deficiency anemia. This increased copper concentration may occur due to excessive gastrointestinal copper absorption as grain products are major source of dietary copper [7].

In Bangladesh, many people are suffering from anemia. Along with iron, copper have some role in contributing deficiency of iron, where copper overload has been observed. In our country there is a few data regarding iron and copper status are available in anemic patients. It is expected that the results would give a guideline to the physicians to adopt appropriate measure for the management of iron deficiency anemic patients.

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MATERIALS AND METHODS

The present observational study was carried out in department of Physiology, BSMMU, Dhaka from 1st January to 31st December, 2007. In this study, a total number of 60 subjects with the age range of 11 to 18 years of both sexes were included, of whom 30 were apparently healthy and 30 were iron deficient anemic adolescents. All the subjects were selected randomly from resident of different area of Dhaka city and belonged to lower middle socioeconomic status. On the basis of Hb concentration[8] and serum ferritin level (SF)[9] the subjects were divided into control A and study group B. They were further subdivided into A_1=15 male (Hb>13g/dl, SF>30μg/L), A_2=15 female (Hb>11.5g/dl, SF>22μg/L) and B_1 =15 male (Hb<13g/dl, SF<30μg/L), B_2 =15 female (Hb<11.5g/dl, SF<22μg/L). The subjects with history of blood transfusion and iron therapy during the last

three month, any history of kidney diseases, liver diseases were excluded from the study. Iron status was assessed by measuring serum ferritin, serum iron, TIBC and also by calculating transferrin saturation. Copper status was assessed by measuring serum copper level by spectrophotometric method. The statistical analysis was done by using SPSS programme, version-12. p value <0.05 was considered as significant. The comparison between the groups were calculated by unpaired Student's 't' test.

RESULTS

Mean (±SD) serum ferritin, serum iron, total iron binding capacity (TIBC) and transferrin saturation (TS) are presented in Table-I. Mean serum ferritin, serum iron level and transferrin saturation were significantly ($p<0.001$) lower in both the iron deficient group B_1 and B_2 in comparison to those of healthy control group A_1 and A_2. Mean total iron binding capacity was significantly ($p<0.001$) higher in both iron deficient group B_1 and B_2 than those of control group A_1 vs A_2.

Mean (±SD) serum copper level of different groups are presented in Figure-1. Mean serum copper level in iron deficient group B_1 was significantly ($p<0.01$) higher in comparison to those of healthy group A_1 and A_2. Again, this level was significantly higher in iron deficient group B_2 than those of group A_1($p<0.001$) and A_2 ($p<0.01$).

Table-I: *Serum ferritin, serum iron, Total iron binding capacity (TIBC) and Transferrin saturation in different groups (n = 60)*

Sub groups	Serum ferritin (µg/L)	Serum iron (µg/dl)	TIBC (µg/dl)	Transferrin saturation (%)
A_1 (n=15)	64.76 ± 25.52 (38.52-128.00)	81.33 ± 12.94 (61-104)	285.73±34.45 (253-367)	28.01±5.51 (19.52-6.07)
A_2 (n=15)	56.43±27.74 (24.86-114.30)	67.73±13.32 (48-97)	298.26±33.72 (251-367)	23.11±5.99 (17.44-8.64)
B_1 (n=15)	14.76±5.96*** (5.69-24.30)	38.86±9.28*** (21-51)	449.13±26.87*** (407-501)	8.69±2.19*** (4.36-1.72)
B_2 (n=15)	13.66±3.66*** (6.96-19.27)	28.93±4.90*** (18-36)	456.13±30.64*** (415-520)	6.37±1.18*** (3.72-7.92)

Figures in parentheses indicate ranges. n = Total number of subjects. *** Significant at $p<0.001$

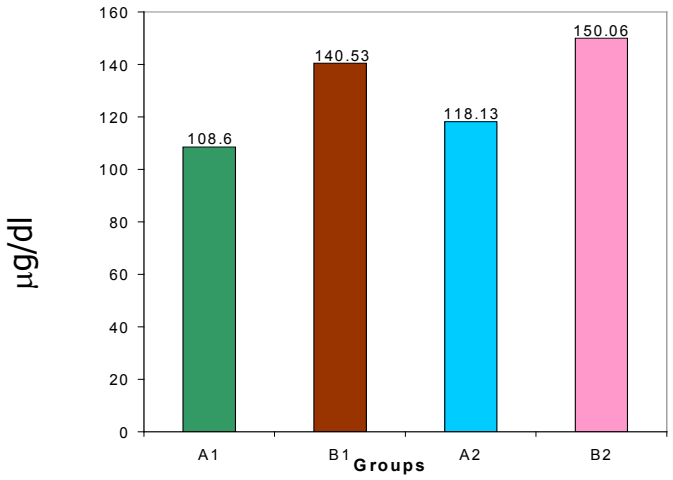

Figure-1: *Mean serum copper level in different groups (n=60)*

DISCUSSION

In this study, iron status was lower and copper status was higher in iron deficient adolescents. Lower iron status is determined by reduced values of serum ferritin, serum iron, transferrin saturation and increased value of TIBC. In this study, serum ferritin, serum iron level and transferrin saturation were significantly ($p<0.001$) lower in both the groups of iron deficient adolescents in comparison to their respective healthy control (non deficient group) These findings are consistent to other investigators of different countries[7,10,11]. On the other hand, serum TIBC was

significantly (p<0.001) higher in iron deficient adolescents of both sexes in comparison to their respective healthy control. Similar findings are observed by others[7]. It has been suggested that decreased iron absorption may result from dietary iron deficiency or from high fiber content of diet[7]. Moreover, selection of food may be a major factor on the bioavailability of iron. Flesh foods are rich source of readily available haem iron, whereas cereals are strong inhibitor of iron absorption[2]. In adolescence increase in body need due to rapid growth may lead to iron deficiency[12]. Again, hookworm infestation usually causes chronic blood loss which may lead to iron deficiency [13].

Serum copper level was significantly (p<0.01) higher in both sexes of iron deficient adolescents in comparison to their respective healthy control. Similar observations were also made by others[7,11,14]. Grain products are a major source of dietary copper which may lead to increased copper absorption and thereby may results in higher copper concentration in blood [7]. Some researchers suggested that iron and copper shares with the same metal transporter. Therefore, copper exhibits competitive antagonism with iron for uptake into enterocyte during iron deficiency [5,15].

In the present study, as all the subjects were belonged to poor socioeconomic class, deficiency of iron with decreased tissue store is most likely due to inadequate food intake and low dietary protein as suggested by various investigators of different countries[2,7]. Again, high fiber content of the diet with low dietary flesh foods may also have some role in the contribution of iron deficiency in this group of subjects. On the other hand, increased dietary intake of grain is most likely to be the cause of hypercupremia as all the subjects of the present study had history of high dietary intake of cereals. Therefore, this study revealed that deficiency of iron is an important cause of hypercupremia which may occur in adolescents.

From this study, it may be concluded that deficiency of iron is associated with hypercupremia due to complex kinetic interaction between iron and copper for uptake into enterocyte during iron deficiency.

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JALALABAD MEDICAL JOURNAL

Original article

Transplacental Transfer of Measles Antibody

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ABSTRACT

Transplacental transfer of measles antibody gives protection to newborn against measles from few weeks to few months depending on the amount of antibody transfer. The transferred antibody gradually decays from fetal blood and finally disappears from baby's blood within few months when the baby becomes vulnerable to the attack of measles. To evaluate the transplacental transfer of measles antibody this cross sectional comparative study was done on pregnant women admitted for delivery in Sylhet MAG Osmani Medical College Hospital and their newborn babies from July 2008 to June 2009. 94 maternal venous blood samples and their corresponding 94 cord blood samples of their newborn babies were collected and processed as per work schedules. All the samples were tested by Quantitative ELISA method for measles IgG. Out of 94 pregnant women, 35.1% were naturally immune to measles and 33.3% acquired immunity through artificial vaccination. The baby of naturally immune mother had higher level of protective antibody against measles than vaccinated mother.

Key words: *Measles antibody, Vaccine, Maternal, Neonatal.*

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INTRODUCTION

Measles is a highly contagious, infectious disease which has a major impact on child survival particularly in developing countries[1]. No animal reservoir for measles virus exists. No vector is involved in its spread and vaccination with the currently used live attenuated vaccine proved to be highly effective in preventing the diseases[2]. There is only one antigenic type of measles virus infection. Immunity after natural infection confers life long immunity[3].

Maternal antibody passes the placenta and infants are protected during the first 6-9 months of life. Placental transfer of measles antibody occurs more in 3rd trimester (after 36 wks) which can give protection against measles[4]. Premature and many preterm infants may fail to reach the detectable antibody level at birth, leaving them more susceptible to infection than full term infants[5]. About 20 million cases of measles occur in India alone and responsible for 2- 3% of all deaths occurring at age of 1- 4 years[6]. It has been noted that death rate of acute measles infection is higher in malnourished population[7].

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Malnutrition including anaemia diminishes the immune response to virus allowing great proliferation of the virus and subsequent damages to the host and causes prolonged immune suppression. Secondary bacterial infection like *Streptococcus pneumoniae* and other bacterial infection follow in the wake of this intense immune suppression often killing the child[8].

Infants born to vaccinated mother acquire a lower level of measles antibody that disappears at an earlier age than the infants born to mothers who have natural measles[9]. Therefore in determining the age of vaccination, countries must balance the consequences of an older age (lack of protection in the early months of life) and a younger age (reduce effectiveness). Many countries, where morbidity and mortality due to measles are uncommon in infants, choose an older age for vaccination such as 12 to 15 months[10].

Decay of antibody starts from the first week of life and it completes within 9-12 months but if the antibody level is lower during birth, occurs at earlier times. In case of high antibody level measles vaccination can be

delayed up to usual schedule at 9 months or even 15 months to receive a dose of MMR vaccine[11].

MATERIALS AND METHODS

This comparative cross-sectional study was conducted in Department of Microbiology, MAG Osmani Medical College, Sylhet from 1st July 2008 to 30th June 2009. Immunized (natural or vaccinated) and not immunized healthy pregnant mothers admitted in Obstetrics and Gynecology Department of Sylhet MAG Osmani Medical College hospitals and their newborn babies were the study population.

Detailed history was taken from mother and was recorded. Two ml venous and 2 ml cord blood was collected from 94 mothers and their corresponding newborns respectively in two properly labeled test tubes. The samples were allowed to clot at room temperature and then centrifuged at a rate of 2000 rpm for 10 min. Serum were separated and stored at -20^{0}C. Quantitive Enzyme Linked Immunosorbant Assay (ELISA) was done to measure measles IgG antibody in both maternal and cord blood. The ELISA test kits used for detection of measles antibody were purchased from Human, Weisbaden, Germany. Measles IgG level was recorded mIU/ml. Analysis of the test result was carried out by using SPSS 12.0 version software package and the statistical method like geometric mean, SD, unpaired Student's t-test were applied. Informed consent was taken from all the participants. Ethical clearance was obtained from ethical review committee of Sylhet MAG Osmani Medical College, Sylhet.

RESULTS

Out of 94 mothers, more than 53% of mothers could not recognize whether they had suffered from measles or not. Naturally immune mothers were 35.1%, non-immune 11.7%. There were 33.3% vaccinated mothers, non-vaccinated 44.7%, not known 22.3%. Non-vaccinated means naturally immune mother also. [Table-I]

Geometric mean IgG level of mother suffered from measles was found significantly higher than the mothers who did not suffered from measles. The IgG level of vaccinated mother was also found lower than naturally immune mother. [Table- II & III]

In this study, measles antibody level in mother and baby determined by ELISA method. Highly protective level is 200mIU/ml or above. Moderately protective level is 120-200mIU/ml and below 120 is not protective. [11]

Among 94 mothers, 30.9% had highly significant titre, 47.9% had moderately significant and 21.3% had not significant titre of measles IgG. Among 94 babies, 39.4% had highly protective titre, 48.9% had moderately protective and 11.7% had low protective titre of antibody. [Table- IV]

Table-I: *Distribution of mothers according to history of measles and vaccination status*

	History of measles		Measles vaccination	
	Frequency (n)	**Percentage (%)**	**Frequency (n)**	**Percentage (%)**
Yes	33	35.1	31	33.3
No	11	11.7	42	44.7
Not known	50	53.2	21	22.3
Total	**94**	**100**	**94**	**100**

Table-II: *Geometric means of maternal and cord measles antibody level in relation to maternal history of measles*

Maternal history of measles	Measles antibody level (mIU/ml) Geometric Means± SD (95% CI)	t-value	Measles antibody level (mIU/ml) Geometric Means± SD (95% CI)	t-value
	Maternal		Neonatal	
Suffered	198.68±11.27	5.581***	209.47±8.67	6.254***
Not suffered	122.50±26.83		126.62±31.21	
Not sure	149.04±12.5	5.044***	160.25±9.16	6.994***
Suffered	198.68±11.27		209.47±8.67	
Not suffered	122.50±26.83	-1.635	126.62±31.21	-2.146*
Not sure	149.04±12.5		160.25±9.16	

*** indicates p<0.001, * indicates p<0.05

Table-III: *Geometric means of maternal and neonatal measles antibody level in relation to maternal history of vaccination*

Maternal history of vaccination	Measles antibody level (mIU/ml) Geometric Means± SD (95% CI)	t-value	Measles antibody level (mIU/ml) Geometric Means± SD (95% CI)	t-value
	Maternal		Neonatal	
Vaccinated **Not vaccinated**	149.93±15.26 171.55±14.83	-2.085***	158.64±13.86 183.17±12.71	-2.502***
Not sure **Vaccinated**	158.05±21.57 149.93±15.26	-0.732	167.62±18.5 158.64±13.86	-0.839
Not vaccinated **Not sure**	171.55±14.83 158.05±21.57	1.019	183.17±12.71 167.62±18.5	1.281

*** indicates p<0.05

Table-IV: *Measles IgG antibody status of mother and neonate*

Titre level	Mother		Baby	
	(n)	%	(n)	%
Highly protective titre (>200mIU/ml)	29	30.9	37	39.4
Moderately protective titre (120-200mIU/ml)	45	47.9	46	48.9
Not protective titre (<120 mIU/ml)	20	21.3	11	11.7
Total	**94**	**100.0**	**94**	**100.0**

This study revealed significant positive relationship (r^2 = 0.1024) between measles antibody level of mother and measles IgG antibody level of baby. Linear Regression model shows a positive trend (regression coefficient, B=0.5) of measles antibody level of babies on measles antibody level of mother. [Figure-1]

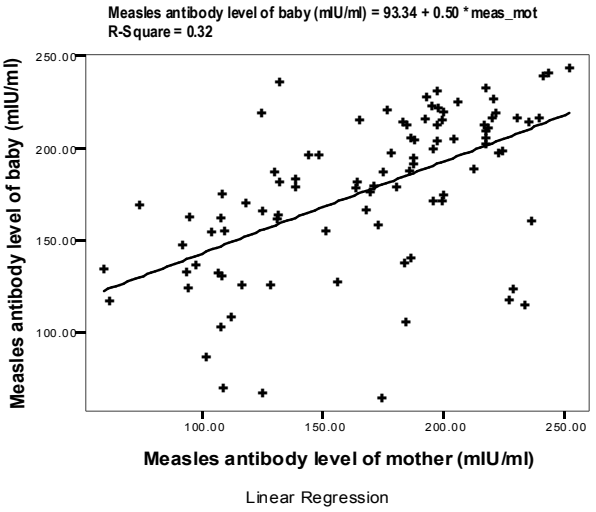

Figure-1: *Fitted Linear Regression between neonatal and maternal measles antibody level.*

DISCUSSION

In Bangladesh, like many other third world countries measles immunization starts at the age of 9 months because prevalence of measles among infants is high. In this study, measles antibody level in mother and baby determined by ELISA method. Plaque reduction neutralization (PRN) assay is considered as the gold standard for measuring concentration of measles antibody. In plaque neutralization test antibodies level above 200 mIU/ml is protective. Antibodies level between 120-200 mIU/ml is moderately protective required for classic measles illness protection. In such cases, vaccination is recommended at 6 months and below 120mIU/ml is not protective. In this study, measles antibody level in mother and baby were determined simultaneously by ELISA method. In this study, protective level is 200 mIU/ml or above. 120 mIU/ml to 200 mIU/ml is moderately protective and below 120 mIU/ml is not protective. So the results obtained by ELISA correlates well with the PRN assay results. The antibody level can also be determined by the haemagglutination inhibition (HI) test. But the test is relatively insensitive[11,12].

In this study, out of 94 mothers only 35.1% were naturally immune. Only 33% mothers received measles vaccination and about half of the mothers did not sure about their history of measles. These findings more or less similar with vaccination status of mother in Oman (2008) which was conducted by Patel et al[13].

This study also shows geometric mean level of measles antibody titre higher in naturally immune mother (198.86 mIU/ml) than non-immune (122.5 mIU/ml) and mother with unreliable history (149.04 mIU/ml). The IgG level for mothers suffered from measles was found significantly (P < 0.001) higher than the other groups.

Geometric mean titres were significantly higher in naturally immune than vaccinated group. A study conducted by Abassy et al[14] in 2009 showed that measles antibody level among infant born to mothers

with history of infection was significantly higher than vaccinated mothers.

It is also observed that a higher concentration of measles IgG has been shown in cord blood compare to their mothers blood which is due to haemodilution effect of pregnancy[4,15]. The present study indicates among 94 mothers, 78.8% had protective antibody level in mother with history of measles exposure and with measles vaccination history and 21.3% had no protective antibody level. Among 94 babies 88.3% had protective titre and 11.7% had no protective antibody.
This study is carried out to find out measles antibody level in mother and transplacental transfer to baby. Now a day, by EPI programme prevention of measles is successful in Bangladesh and there is dramatic fall of measles cases and also death due to measles in our country[16].

CONCLUSION

It is observed that baby of mother with history of measles have good protective level of antibody and can give protection against measles up to 9-12 months. In case of baby of vaccinated mother have lower protective titre and give protection against measles up to 5-6 months. In such cases vaccination will be given at 5-6 months. Mother with no history of measles and vaccination, the baby antibody titre is below protective level; vaccination is required to be given within few weeks. Results from this study indicate towards undertaking large scale study, so as to evaluate more cases and to find out the appropriate time for immunization against measles.

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JALALABAD MEDICAL JOURNAL

Original article

Fine Needle Aspiration Cytology in the Diagnosis of Ulcerative Oral Lesions

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ABSTRACT
The purpose of this study was to evaluate the role of fine needle aspiration cytology (FNAC) in the diagnosis of oral lesions. This study was carried out during the period of July 2006 to June 2007 in the department of Pathology in active collaboration with the department Otorhinolarygology and Head Neck Surgery, Sylhet MAG Osmani Medical College, Sylhet and a total of sixty one (61) cases were selected who had ulcerative oral lesion on the basis of clinical findings. Fine needle aspiration cytology showed the effective role in the diagnosis of ulcerative oral lesions. The sensitivity, specificity, positive predictive value, negative predictive value and accuracy of FNAC were 95.4%, 78.5%, 93.3%, 84.6% and 91.3% respectively. This study was mostly consistent with other published literature. FNAC provides a major role for early diagnosis of ulcerative oral lesions.

Key words: *Ulcerative oral lesion, FNAC.*

[Jalalabad Med J 2010; 7 (2): 51-55]

INTRODUCTION

Globally, oral cancer is the 6th most common malignancy and in the western world, it accounts for only 2-4% of all malignant tumors[1]. In contrast, in Asia, oral malignancy is the most common malignant tumor accounting in parts of India not less than 40% of all malignancy[2]. Bangladesh cancer registry showed that 3.9% cancers are oral cancer in both sexes in the year of 2005. This registry also showed oral cancer is the 8th rank cancer in Bangladesh[3].

Fine Needle Aspiration Cytology (FNAC) plays an important role in obtaining diagnostic materials from deeper parts of lesions. Though it has been widely used in assessment of various superficial lesions for many years but its use in diagnosis of oral lesions was started only for few years. FNAC is reliable, rapid and minimally invasive than surgical biopsy[4,5]. It is found that FNAC played an important role in differentiating inflammatory from neoplastic lesion and also benign from malignant neoplasm[6].

It deals with study of cell in smear prepared from material obtained by FNAC[7]. Some authors carried out research works with FNAC of oral lesions and results were varied from 80.6%-100(%) sensitivity and 94.3%-100(%) specificity [8-13].

Biopsy followed by histopathological study is the best method for diagnosis of oral lesion but it is an invasive procedure and time consuming. For biopsy sometime hospitalization and anesthesia are required. Biopsy may lead to complication like delayed wound healing and fibrosis. In this respect, FNAC is suitable because of it's acceptability by the patient, minimal morbidity and ease of performance.

As FNAC is safe, reliable diagnostic method and results of different authors varies so it has grown an interest to carry out a further study of FNAC of oral lesions.

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MATERIALS AND METHODS

This comparative, cross-sectional study was carried out in the Department of Pathology, Sylhet MAG Osmani Medical College, during the period from July 2006 to June 2007. Sixty one patients aged above 18 years of both sexes with the diagnosis of ulcerative oral lesions were selected consecutively from the out patient and in patient, Department of Otorhinolaryngology and Head Neck Surgery, SOMCH. The patients were selected on the basis of history, physical examination and willingness to undergo biopsy. Patients with bleeding diathesis already diagnosed oral lesions by histopathology and with mental retardation were excluded from the study.

After taking clinical history and physical examination, FNAC was done. Smears were interpreted and results were recorded. Then punched or incisional biopsy and histopathological diagnosis of biopsy specimen were carried out subsequently. Relevant clinical history, physical findings, FNAC findings and histological findings were recorded in the predestined patient's profile.

Technique of FNAC[14, 15]

For the ulcerative lesions, both the margins and the base were aspirated. With the help of artificial light and administration of local anaesthetic spray, the site of the lesion was properly visualized. A 5 cc syringe attached with 21 gauge needle, 1.5 inches long was inserted into the determined site and advanced into the lesion. Whether the needle did hit the actual site of lesion was felt by tilting the syringe lateral wise. While the needle was inside the lesion, full suction was applied to the syringe to create negative pressure within the syringe. With full suction the needle was advanced and withdrawn in the lesion with slightly different directions in order to get adequate materials for smears. Smear was made by laying another slide on the top of the drop and pulling the slides apart quickly allowing the drop to spread. 2-4 slides were prepared in this way. The smeared slides were promptly dropped into 95% ethyl alcohol for fixation and kept for at least 30 minutes. Then the smear was stained according to Papanicolaou method.

RESULTS

FNAC's were performed in all 61 cases and histopathological examination was done in 58 cases. Among the remaining 3 cases, FNA cytology findings revealed inflammatory lesion and were not recommended for biopsy.

The age of the patients ranged from 27 to 73 years with the mean ± SD age was 48.84 ± 11.43 yrs. Patients were divided into 6 groups considering each decade as a single group. Out of 61 patients maximum number 24 (39.3%) of patients belongs to the age group 41-50 years. 62.29% of the patients were male and 37.71% were female and ratio is 1.6:1. [Figure-1]

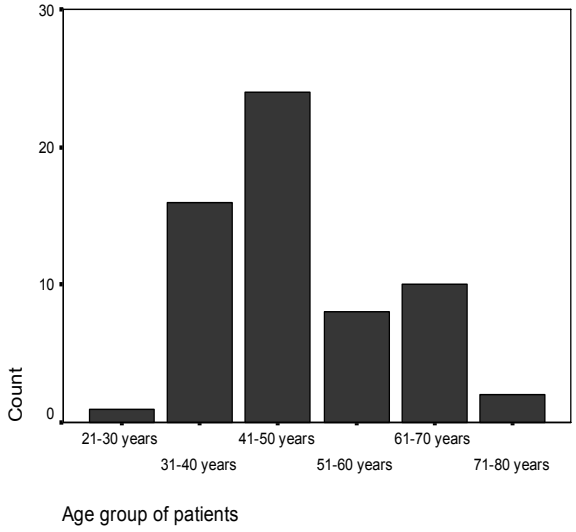

Figure-1: *Age distribution of study subjects in six stage groups.*

Sites of ulcerative oral lesions:

The maximum number of patients examined in the present study had lesions of the buccal mucosa 19(31.1 %) and tongue 17(27.9%). It was followed by 9(14.8 %) patients with lesions of the palate. Lowest number patient was found lesion in the lip. [Table-I]

Table-I: *Sites of ulcerative oral lesions*

Site of lesions	*Frequency*	*Percentage (%)*
Buccal mucosa	19	31.1
Tongue	17	27.9
Palate	9	14.8
Tonsil	6	9.8
Lip	1	1.6
Gum	2	3.3
Angle of mouth	4	6.6
Floor of mouth	3	4.9
Total	**61**	**100.0**

FNAC was done in all cases and satisfactory smears were found in 58(95.08%) cases and 3(4.92%) cases were unsatisfactory or inadequate. On cytological examination 5(8.2%) cases were found to be acute suppurative inflammation, 8(13.1%) cases were chronic non specific inflammation, 2(3.3%) cases were found to be pleomorphic adenoma, 38(62.3%) cases were found to be squamous cell carcinoma and 5(8.2%) cases were suspicious for malignancy. [Table-II]

Table-II: *FNAC findings of ulcerative oral lesions*

Type of lesion	No's of FNAC (%)
Acute suppurative inflammation	5(8.2)
Chrinic non specific inflammation	8(13.1)
Pleomorphic adenoma	2(3.3)
Squamous cell carcinoma	38(62.3)
Inadequate smear	3(4.9)
Suspicious for malignancy	5(8.2)
Total	**61(100)**

Histopathological findings of ulcerative oral lesions were shown in Table-III.

Table-III: *Histopathologic findings of ulcerative oral lesions*

Name of lesion	*Frequency*	*Percent*
Benign		
Acute suppurative inflammation	3	4.9
Chronic non specific inflammation	9	14.8
Pleomorphic adenoma	2	3.3
Malignant		
Squamous cell carcinoma-I	37	60.7
Squamous cell carcinoma-II	4	6.6
Squamous cell carcinoma-III	1	1.6
Adenoid cystic carcinoma	1	1.6
Mucoepidermoid carcinoma	1	1.6
Not done	3	4.9
Total	**61**	**100.0**

Comparison of FNAC and histopathological findings of ulcerative oral lesions:

FNAC results showed that 38 squamous cell carcinoma, 5 acute suppurative inflammation, 8 chronic nonspecific inflammation, 2 pleomorphic adenoma, 3 inadequate smear and 5 suspicious for malignancy. Among 5 suspicious reports, 1 acute suppurative inflammation, 2 chronic nonspecific inflammation, 1 adenoid cystic carcinoma and 1 was diagnosed as mucoepidermoid carcinoma. Out of 3 inadequate smear, 1 chronic non specific inflammation and 2 cases were diagnosed subsequently by histopathology as squamous cell carcinoma grade-I. Among 2 cases of pleomorphic adenoma, all were diagnosed as pleomorphic adenoma by histopathology. In case of 8 chronic non specific inflammation, 6 as chronic non specific inflammation and remaining 2 were diagnosed by histopathology as squamous cell carcinoma. Out of 5 acute suppurative inflammation, 2 cases were diagnosed as acute suppurative inflammation and in remaining 3 cases histopathological diagnosis were not recommended. Among 38 cases of squamous cell carcinoma, 33 as squamous cell carcinoma grade-I, 4 as squamous cell carcinoma grade-II and 1 was diagnosed by histopathology as squamous cell carcinoma grade-III. [Table-IV]

Fine needle aspiration cytology showed that sensitivity 95.4%, specificity 78.5%, positive predictive value 93.2%, negative predictive value 84.6% and accuracy 91.3%. [Table-V]

Figure-2: *Photomicrograph of FNAC smear from squamous cell carcinoma showing group of anaplastic cells (Papanicolaou's stain X400).*

Table-IV: *Comparison of FNAC and Histopathological findings of ulcerative oral lesions*

FNAC of oral lesion	Histotype									Total
	Acute suppurative inflammation	Chronic non specific inflammation	Pleomorphic adenoma	SCCI	SCCII	SCCIII	Adenoid cystic carcinoma.	Mucoepidermoid carcinoma.	Not done	
Acute suppurative inflammation	2	0	0	0	0	0	0	0	3	5
Chronic non specific inflammation	0	6	0	2	0	0	0	0	0	8
Pleomorphic adenoma	0	0	2	0	0	0	0	0	0	2
Squmous cell carcinoma	0	0	0	33	4	1	0	0	0	38
Inadequate smear	0	1	0	2	0	0	0	0	0	3
Suspicious for malignancy	1	2	0	0	0	0	1	1	0	5
Total	3	9	2	37	4	1	1	1	3	61

SCCI- Squamous cell carcinoma grade-I, **SCCII-** Squamous cell carcinoma grade-II, **SCCIII-** Squamous cell carcinoma grade-III.

Table -V: *Statistical analytic result of fine needle aspiration cytology*

Diagnostic method	True positive (TP)	True negative (TN)	False positive (FP)	False negative (FN)	Sensitivity (%)	Specificity (%)	Positive Predictive Value (%)	Negative Predictive Value (%)	Accuracy (%)
FNAC	42	11	3	2	95.4	78.5	93.3	84.6	91.3

- True positive (TP)-Malignant and suspicious for malignancy.
- True negative (TN)- Acute suppurative inflammation, Chronic non specific inflammation, pleomorphic adenoma.
- False positive (FP)- Cytologically malignant, histologically benign.
- False negative (FN)- Cytologically benign, histologically malignant.

DISCUSSION

This study revealed that FNAC showed good result of sensitivity and specificity in the diagnosis of ulcerative oral lesions. The positive and negative predictive values for FNAC were 93.3 % and 84.6 % respectively. In the evaluation of ulcerative oral lesions there are several cytological methods in obtaining an early and prompt diagnosis. Any method for preoperative diagnosis must be reliable, accurate, easy to perform and reproducible. It is generally accepted that prior to surgical treatment a definitive diagnosis should be established. It is also found that FNAC play an important role in differentiating inflammatory from neoplastic lesion and benign from malignant neoplasm[6]. Burlo et al (2007)[8] carried out a study and found that 85.7% sensitivity and 95.9% specificity.

Study conducted by Florentin et al (2006)[9] showed that sensitivity 93%, specificity 100%, positive predictive value 100%. Maraki, Becker and Boecking (2004)[10] found that sensitivity 100%, specificity 94.3%, positive predictive value was 95.7% and Navone et al[11] also demonstrated that sensitivity 86.5%, specificity 94.3%, positive predictive value was 95.7% in their study.

Castelli et al[12] showed in their study 80.6% sensitivity and 96.9% specificity. Saha (1995)[13] observed that 85.9% sensitivity, 100% specificity, 90.2% accuracy, 100% positive predictive value and 14.04% false negative rate. In reviewing the observations of my known studies by different authors it had been seen that sensitivity of FNAC range from 80.6% to 100% and specificity range from 94.3% to 100%. The result of the present study correlate with other published studies.

The positive and negative predictive values for FNAC in this study reflect a chance of missing cancer 15.4 % and over diagnosis of cancer 6.7 %. The comparative study between FNAC and histopathology was significant ($P<0.01$).

All the findings of the present study were not always consistent with the findings of the other investigators. This study was done in a small sample, the study period was short and samples were collected only from ENT outpatient and inpatient department of Sylhet MAG Osmani Medical College Hospital. But many findings of this study were more or less similar with other investigators. On evaluation of results of known studies including this one it is noted that FNAC can accurately identify in most the cases of malignant tumors of ulcerative oral lesions.

It is concluded that this easy highly effective method would be used as a guide to surgeon about treatment plan to be undertaken.

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JALALABAD MEDICAL JOURNAL

Original article

Accuracy of Pap Smears Cytology in the Diagnosis of Cervical Lesions

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ABSTRACT

To determine the accuracy of Pap smear cytology in detection of cervical intraepithelial neoplasia and cancer, this study was conducted on 100 patients of different age group were selected from patients attending in the Obstetrics and Gynaecology outpatient department of MAG Osmani Medical College, Sylhet from January to December, 2008. Cervical smear was collected and stained with modified Papanicolaou stain. Biopsy specimen was could be taken from 70 cases, processed with Haematoxylin and Eosin stain and histopathology was done. Histopathology is the gold standard and Pap smear was compared with it. The sensitivity, specificity, positive predictive value, negative predictive value and accuracy of Paps cytology were 71.42%, 100%, 100%, 93.33% and 94.28% respectively. Pap smear cytology is a useful tool in the early diagnosis of preclinical cervical cancer.

Key words: *Pap smear, Cervical intraepithelial neoplasia, Cervical cancer.*

[Jalalabad Med J 2010; 7 (2): 56-59]

INTRODUCTION

Cervical cancer is one of the leading causes of cancer death among women worldwide. It is the second most common cancer, with an estimated 500,000 new cases per year, 79% of which occurring in the developing countries[1]. In Bangladesh cervical cancer is also the commonest malignancy and the incidence is 26%[2]. Of the 190,000 deaths from cervical cancer that occur annually worldwide, almost 80% of these deaths occur in developing countries, where cervical cancer is the leading cause of cancer mortality in women[3]. To reduce the mortality it is essential to diagnose these cases early. Incidence rates are now generally low in developed countries accounts for only 3.6% of new cancers, with a cumulative risk (0 to 64) of 0.8%[4]. Fifty-years ago in the US, cervical cancer was the leading cause of cancer death, but the death rate has declined by two-thirds and at present it is the eighth leading cause of cancer mortality. This reduced mortality is due to effectiveness of Papanicolaou cytologic screening in detecting cervical pre-cancer and accessibility of cervix to colposcopy and biopsy[5]. The aim of this study was to determine the accuracy of Pap smear cytology in detection of cervical intraepithelial neoplasia and cancer.

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MATERIALS AND METHODS

The study was carried out in the department of pathology, MAG Osmani Medical College, Sylhet, Bangladesh during the period from January 2008 to December 2008. A total of 100 patients of different age group were selected from patients attending the Gynaecology and Obstetrics out patient Department. Patients of different age group were selected for this study according to some inclusion and exclusion criteria. Inclusion criteria were, sexually active women having complaints related to cervical pathology such as per-vaginal discharge, irregular per-vaginal bleeding, post-coital bleeding, and lower abdominal pain of age 18-60 years. Exclusion criteria included menstruating women or heavy P/V bleeding during the time of examination, pregnancy, severe cervicitis, unmarried

women, patient below 18 years, patient age above 60 years and already diagnosed cases. The smears were stained by modified Papanicolaou staining method. The findings were recorded following the Revised Bethesda System, 2001. Positive test for Pap smear include: 1. Low-grade squamous intraepithelial neoplasia (LSIL), which corresponds to koilocytic change and cervical intraepithelial neoplasia grade I (mild dysplasia), 2. High grade squamous intraepithelial neoplasia (HSIL) which corresponds to cervical intraepithelial neoplasia grade II (moderate dysplasia) and cervical intraepithelial neoplasia grade III (severe dysplasia/carcinoma in situ) 3. Invasive squamous cell carcinoma. After cytological examination patients were subjected to colposcopy guided biopsy. The biopsy materials were immersed in a labeled container of 10% formalin for histopathological examination. The formalin fixed specimen was processed for Hematoxylin and Eosin stain.

All the data were evaluated by standard statistical methods and various indices such as false positive, false negative, sensitivity, specificity; accuracy and predictive value of positive and negative diagnosis were calculated by SPSS method.

RESULTS

Out of 100 cases, a total of 70 cases were subjected to biopsy who were either Paps smear positive or even negative but clinically suspicious. The age range of patients varied from 18 to 60 years with an average ±SD of 37±8.54 years. The patients were divided into five age groups showing maximum number 48 of patients belongs to the age group 31-40 years [Figure-1].

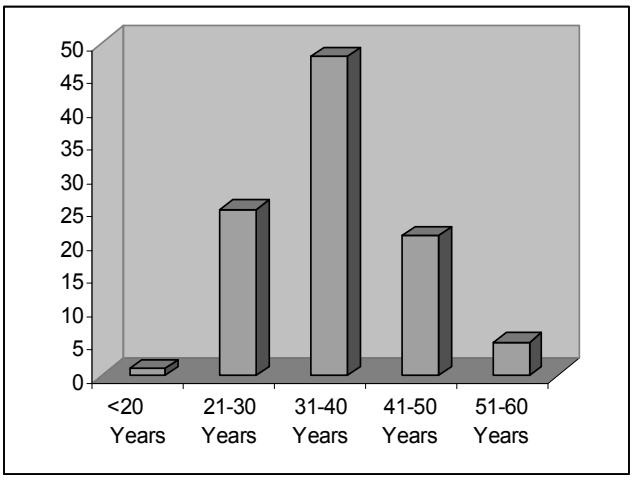

Figure-1: *Distribution of 100 patients according to age group*

Patients were divided into two groups according to their age at marriage such as those before 18 years, those after 18 years. Most of the patients (75%) were below 18 years at the time of marriage. [Figure-2]

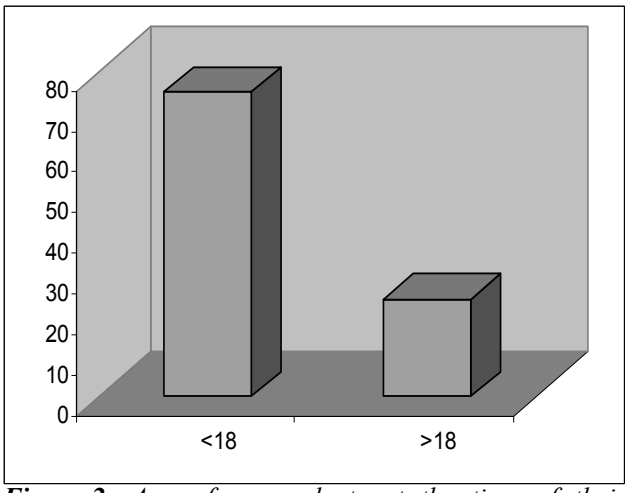

Figure-2: *Age of respondents at the time of their marriage*

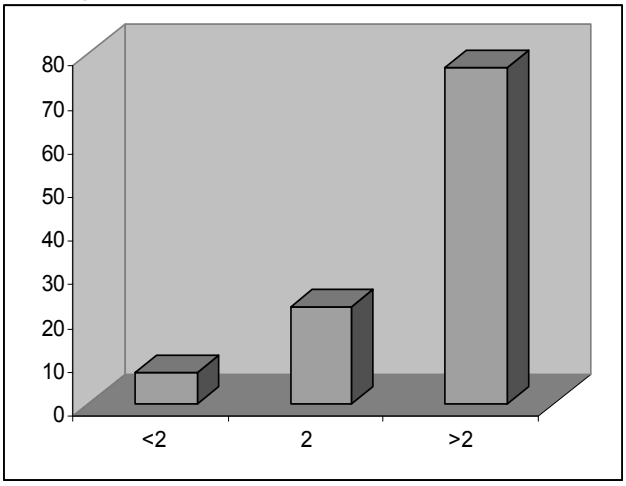

Figure-3: *Number of parity of individual*

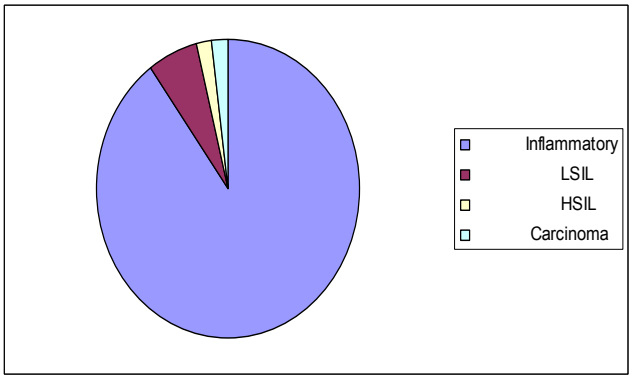

Figure-4: *Pap smears (Cytolopathological) diagnosis of 100 cases*

LSIL-Low-grade squamous intraepithelial lesion/CIN-I
HSIL-High-grade squamous intraepithelial lesion/CIN-II & III

The patient were divided into three group according to their number of parity such as those in whom the

number of parity was less than two, two and more than two groups. Maximum patients 77 (77%) were multiparous who had more than two offspring, in 22 cases the number of parity was 2 and in 7 the number of parity was less than two. [Figure-3]

Table-I: *Histopathological findings of suspected cases (n=70)*

Histopathological Findings	Frequency n (%)
Cervicitis	56 (80%)
CIN-I	10 (14.28)
CIN-II/III	2 (2.86%)
Carcinoma	2 (2.86%)
Total	70 (100%)

The results of cytopathological examination were: Of the 100 cases 2 cases were found to be of Invasive squamous cell carcinoma, 2 cases were of High grade intraepithelial lesions (HSIL), 6 cases were Low grade intraepithelial lesions (LSIL). Remaining 90 cases were diagnosed as inflammatory lesion. [Figure-4]

On histopathological examination, 56 cases were diagnosed as chronic cervicitis, mild dysplasia / CIN-I were diagnosed in 10 cases, moderate to severe dysplasia / CIN-II/III were diagnosed in 2 cases and Invasive squamous cell carcinoma were diagnosed in 2 cases.[Table-I]

In the present study there was no false positive diagnosis by Paps smear. There are 4(40%) false negative cases in the present study. The correlation of cytological examination with histological examination is shown in Table-II.

Table-II: *Correlation of Histopathological & Cytopathological findings*

Histopathological Diagnosis	Pap Smear Cytological Diagnosis			
	Inflammatory Cytology	LSIL/ CIN-I	HSIL/ CIN II-III	Carcinoma
Chronic cervicitis (56)	56 (100%)	0 (0%)	0 (0%)	0 (0%)
CIN-1 (10)	4 (40%)	6 (60%)	0 (0%)	0 (0%)
CINI-II/III (2)	0 (0%)	0 (0%)	2 (100%)	0 (0%)
Carcinoma (2)	0 (0%)	0 (0%)	0 (0%)	2 (100%)

False positive (FP) = 0 (Histologically negative but cytologically positive)
False negative (FN) = 4 (Histologically positive but cytologically negative)

On correlation with Paps smear cytology results, all of the 56 (100%) cases of chronic cervicitis, 2 (100%) CIN II/III lesions or high-grade squamous intraepithelial lesions, 2 (100%) invasive squamous cell carcinomas were correctly diagnosed by cytology. 6 (60%) of the CIN-I lesions were diagnosed as low-grade squamous intraepithelial lesions (CIN-I) and 4 (40%) were misdiagnosed as inflammatory lesions (Table II). In the present study, Pap smear cytology was diagnostically accurate in 94.28% of the cases with 71.42% (10 of 14) true positive, 28.57% (4 0f 14) false negative, 100% (56 of 56) true negative cases without any false positive.

DISCUSSION

Cervical cancer is the second most common malignancy in women worldwide, accounting for 15% of all cancers diagnosed in women[4]. The majority of cervical cancers are preceded by a pre-cancerous lesion and exit in non-invasive stage for as long as 20 years and shed abnormal cells that can be detected on cytologic examination[5]. So invasiveness of cervical cancer and mortality can be reduced if it is diagnosed at early stage. The precursor lesion from which invasive cervical cancer develops is cervical intraepithelial neoplasia (CIN). Progression from normal to invasive cervical cancer is thought to occur through increasing grades of cervical dysplasia. The probability of progression of pre-neoplastic lesions to cancer is dependent on the severity of the lesion. CIN-I represents mild to moderate dysplasia. These lesions have a high rate of spontaneous regression (~60%) and a low rate of progression to carcinoma[6]. In contrast, approximately 38% of CIN-II and CIN-III, moderate to severe dysplasia, will spontaneously regress, while 16-36% will progress to invasive cervical cancer[6]. CIN I-III, effectively detected using the Pap smear, can be treated to prevent the development of invasive cervical cancer. In more economically developed countries, Pap smear screening programs have contributed to a large decline in the incidence of invasive cervical cancer[7].

In this study age range of 100 patients was 18 to 60 years. The patients were divided into five age groups considering each decade as a single group. Out of 100 patients maximum number 48% of patients belongs to the age group 31-40 years which is similar to study done by Israt[8] and Maziah et al[9]. Distribution of patients in each group with their diseases revels that, 2

(100%) cervical cancer patients were in age group 41 to 50 years. Out of 10 CIN-I cases 2 (20%) were in the age group 21-30 years, 4 cases (40%) were in age group 31-40 years and 4 cases (40%) were in age group 41-50 years. Among 2 cases of CIN-II lesions, 1 (50%) case was found in 11-20 years age group and 1(50%) case was found in 21-30 years age group. In this study it is found that cervical cancer and most of the CIN were common in the age group 41-50 years. The age group for cervical cancer is similar to other study but age group for CIN is later than other study. Crum (2004) states that, the peak incidence of cervical cancer at age 40-45 years and about 30 years for high-grade precancer.

This study showed that cervical intraepithelial neoplasia and cervical carcinoma are more common in the group who had married at before 18 years which was similar to the findings of Sarker [10].

The present study showed that out of 100 cases maximum patients 77 (77%) was multiparous who had more than two offspring. CIN and cervical cancer are more common in multiparous women that correlate with the study done by Maziah et al[9].

In this study, Pap smear cytology findings were reviewed with histology of 70 biopsy cases and the results showed that out of 70 cases 66 (94.28%) cases were correctly diagnosed and remaining 4 (5.71%) cases were incorrectly diagnosed. Out of 14 positive cases 4(29%) were false negative. The false negative rate varies in different studies from 1.8 to 40%[11-13]. In this study there was no false positive report and the study done by Ishrat found the similar result. Among 56 (100%) negative cases all are correctly diagnosed which is similar to the findings of study done by Ishrat[8]. The sensitivity and specificity of this study is close to the study done by Branca et al[14]. They found that the sensitivity and specificity were 82.4% and100% respectively. But khanna et al found lower rate of sensitivity and specificity those were 58% and 78% respectively[15]. The accuracy of this study is 94.28% which higher than the accuracy (90%) found by Maziah et al[9].

Cervical cancer is a preventable major form of cancer. This study has demonstrated that Paps smear cytology is a useful test for preclinical diagnosis of cervical cancer. To reduce the false negative rate it can be performed along with other method like colposcoscopy.

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JALALABAD MEDICAL JOURNAL

Original article

Study on Risk Factors of Stroke & Distribution of Patients by Scandinivian Stroke Scale (SSS)

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ABSTRACT

To find out risk factors associated with stroke as well as to observe the mobility and other motor, cognitive functions in stroke patients, this prospective study was carried out on 52 hemiplegic stroke patients of both sexes admitted in Medicine and Neuromedicine units, Sylhet MAG Osmani Medical College Hospital from April 2005 to March 2006. The patients were divided into two groups on the basis of the findings of CT scan where Group I-infarction type (n-28) and group II haemorrhagic (n-24). The mean ± SD of age was 57.1± 12.4 years with male to female ratio 1.17:1. The patients were evaluated for different risk factors and initial stroke severity was assessed by full neurological examination. Level of consciousness, eye movement, power in arm and leg, orientation, aphasia, facial paresis and gait in both groups were evaluated by Scandinavian Stroke Scale (SSS). The results were compared by the unpaired Student's t, Chi Square and ANOVA tests where applicable. More patients (12) of group-I had family history of IHD which was significantly higher ($p<0.05$) than group-II. Neurological examination revealed muscle power more altered in group I patients, whereas sensory, cognitive and perceptual functions more altered in group II patients ($p<0.05$). Analysis by Scandinavian Stroke Scale revealed that severity of stroke in haemorrhagic group (mean score 20.08) was higher than infarction group (mean score 29.25) and the difference was statistically significant ($p<0.001$). Haemorrhagic stroke was more severe than infarctive type in terms of level of consciousness, eye movement, muscle power, orientation, aphasia, facial paresis and gait.

[Jalalabad Med J 2010; 7 (2): 60-66]

INTRODUCTION

The term cerebrovascular disease (CVD) refers to disorders of the arterial or venous circulatory system of central nervous system. Stroke occurs when blood flow is interrupted to part of the brain by blockage (infarctive stroke) or rupture of an artery to the brain (haemorrhagic stroke). Depending on the region of the brain affected, a stroke may cause paralysis, speech impairment, loss of memory and reasoning ability, coma or death. Approximately 80% of strokes are ischaemic in origin. Focal ischaemic stroke is caused by either thrombotic or embolic occlusion of a major artery, whereas global ischaemia usually results from inadequate cerebral perfusion such as that which occurs after cardiac arrest or ventricular fibrillation. Isolated cerebral hypoxia (such as occurs in carbon monoxide poisoning or asphyxiation) is also a cause of stroke[1].

Stroke remains the third leading cause of death and the second most frequent cause of morbidity in developed countries. Stroke was a leading cause of death among Native Americans in 1990, but death rates were lower than in whites[2]. Asians specifically Chinese and Japanese have high stroke incidence rates[3]. In Japan and other Asian countries stroke is the second cause of death in patients aged 65 years or more. Stroke is also an important cause of hospital admission in

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industrialized & developing countries. Since 1990, the incidence of stroke in United States has declined by about 1.5% annually to about 0.5 to 1.0 per 1000 population. It is believed that this steady decrease is the result of improvement in general public health and is coincident with the decline of cardiovascular deaths and better control of hypertension and other risk factors like diabetes mellitus, smoking, hyperlipidaemia, atrial fibrillation, recent myocardial infarction, congestive heart failure, drugs (sympathomimetic, oral contraceptive pills, cocaine). Rates of stroke among men and women are similar, although the incidence and rate of mortality from stroke are higher in blacks than whites[1].

In two types of stroke, some risk factors are common. The association of hypertension, ischaemic heart diseases (IHD), diabetes mellitus, atrial fibrillation with ischaemic stroke was well established in western studies[4-10]. Some studies were done for risk factors of stroke and also in our country to assess stroke severity on SSS. Stroke severity was assessed by SSS to see the recovery and other aspects of stroke in other countries of the world[11-14].

MATERIALS AND METHODS

This randomized prospective study was done on hemiplegic stroke patients of both sexes admitted in Medicine and Neuromedicine units, Sylhet MAG Osmani Medical College Hospital from April 2005 to March 2006. A total number of 52 stroke patients were selected randomly by lottery method among 84 patients with age ranged from 20 to 90 years. Patients with bleeding disorders, history of previous stroke and associated with other life threatening illness were excluded from the study.

After admission, all patients were evaluated by detailed history and physical examination. In the history it was specially asked whether patients were hypertensive or diabetic or smoker or other relevant risk factors were present. They were also evaluated whether they had any family history of hypertension, diabetes mellitus, ischaemic heart disease or stroke. In general examination, special attention was paid on pulse, BP along with other parameters. Neurological and Cardiovascular system examinations were done completely. In neurological examination level of consciousness, motor, sensory, cerebellar functions, cranial nerve functions were evaluated. In CVS examination it was observed whether they had any arrhythmia, hypertension, evidence of valvular heart disease or carotid bruit. CT scan of brain, ECG, X-ray chest, fasting blood sugar and lipid profile, serum creatinine, complete blood count and urine for routine and microscopic examination were carried out in every patient.

The patients were categorized into two groups on the basis of CT scan into group I- infarctive type and group II haemorrhagic type. Then initial stroke severity was evaluated by Scandinavian Stroke Scale (SSS). The SSS is a validated and widely used neurological stroke scale in Scandinavia that evaluates level of consciousness, eye movement, power in extremities, orientation, aphasia, facial paresis and gait on a total score from 0-58 (lower scales indicate more severe stroke).

All data were collected and recorded in predesigned data collection sheet. After collection and entry of data into computer, analysis was done by unpaired student's t test, chi-square test and ANOVA test using SPSS version 12.0 software programme.

OBSERVATIONS AND RESULTS

A total of 52 patients were included in this study and the patients were categorized into two groups on the basis of CT scan. The patients with infarct were considered as group-I and with haemorrhage considered as group-II patients. Out of 52 patients, 28 (53.8%) patients had cerebral infarct and 24 (46.2%) had cerebral haemorrhage. The mean age of the patients was 57.1±12.4 years ranging from 28 to 80 years. The mean age of the group-I patients was 56.0±13.4 years and of group-II patients was 58.4±11.2 years. Analysis revealed no statistically significant mean age difference between two groups of patients ($p>0.05$). [Table-I]

It was also revealed that the proportion of male patients (60.7%) were higher in group-I patients compared to group-II patients (45.8%), but the difference was not statistically significant ($p>0.05$). [Table-II]

Analysis of personal habit and risk factors revealed that the proportion of smoking, hypertension, diabetes mellitus and ischemic heart disease were higher among the patients with cerebral infarct than the patients with cerebral haemorrhage. However, data analysis found no statistically significant difference between two groups of patients ($p>0.05$). On the analysis of family history of risk factors indicated that the proportion of hypertension, diabetes mellitus were higher among he patients with cerebral haemorrhage compared to patients with cerebral infarct. But the proportion of stroke and IHD were higher among the patients with cerebral infarct than cerebral haemorrhage. However, analysis revealed no statistically significant difference between two groups of patients ($p>0.05$), except family history of IHD ($p<0.05$), which was significantly high among the patients with cerebral infarct. [Table-III]

Table-I: *Age distribution of the patients*

Variables	***Group-I***		***Group-II***		***Total***		***p value***
	No (n=28)	**%**	**No (n=24)**	**%**	**No (n=52)**	**%**	
Age in years							
<45	4	14.3	2	8.3	6	11.5	0.503*
45-54	8	28.6	5	20.8	13	25.0	
55-64	8	28.6	9	37.5	17	32.7	
≥65	8	28.6	8	33.3	16	30.8	
Mean ± SD	56.0±13.4		58.4±11.2		57.1±12.4		

Table-II: *Distribution of patients according to sex*

Groups	***Male***		***Female***		***Total***		***P value***
	No	**%**	**No**	**%**	**No**	**%**	
Group-I	17	60.7	11	45.8	28	53.8	0.283**
Group-II	11	39.3%	13	54.2	24	46.2	

Group-I = Patients with cerebral infarct
Group-II =Patients with cerebral haemorrhage
*unpaired student's t test
**chi square test

Table-III: *Distribution of the patients by personal and family history of different risk factors*

Variables	***Study patients***				***Total***		***p value***
	Group-I		**Group-II**				
	No. (n=28)	**%**	**No. (n=24)**	**%**	**No. (n=52)**	**%**	
Personal habit and risk factors							
Tobacco consumption	23	82.1	14	58.3	37	71.2	0.059
Hypertension	19	79.2	18	64.3	37	71.2	0.238
Diabetes Mellitus	14	58.3	10	35.7	24	46.2	0.103
IHD	4	16.7	4	14.3	8	15.4	0.812
Family history of risk factors							
Stroke	11	39.3	8	33.3	19	36.5	0.657
Hypertension	15	53.6	18	75.0	33	63.5	0.110
Diabetes Mellitus	13	46.4	15	62.5	28	53.8	0.246
IHD	12	42.9	3	12.5	15	28.8	0.016

p value reached from chi square test

Analysis of the above table indicated that no statistically significant difference was found between two groups of patients in terms of tone, reflexes, activity of daily life and cranial nerves involvement ($p>0.05$). However, statistically significant difference was found between two groups of patients in terms of power grade, sensory function, cognitive and perceptional functions ($p<0.05$). This indicated that power grade were more altered in group I patients. On the other hand sensory, cognitive and perceptional functions were more altered in group II patients.

Table-IV: *Distribution of the patients by neurological and social activity*

Variables	*Study patients*				*Total*		*p value*
	Group-I		**Group-II**				
	No. (n=28)	**%**	**No. (n=24)**	**%**	**No. (n=52)**	**%**	
Tone							
Normal	1	3.6	0	0.0	1	1.9	0.538
Increased	26	92.9	24	100.0	50	96.2	
Decreased	1	3.6	0	0.0	1	1.9	
Power Grade							
0	2	7.1	11	45.8	13	25.0	0.006
1-3	19	67.9	9	37.5	28	53.8	
4-5	7	25.0	4	16.7	11	21.2	
Reflexes							
Normal	3	10.7	1	4.2	4	7.7	0.366
Increased	24	85.7	21	87.5	45	86.5	
Decreased	1	3.6	2	8.3	3	5.8	
Activity of daily life							
Normal	2	7.1	0	0.0	2	3.8	0.493
Altered	26	92.9	24	100.0	50	96.2	
Sensory function							
Intact	21	75.0	6	25.0	27	51.9	0.001
Altered	7	25.0	18	75.0	25	48.1	
Cranial nerves							
Intact	24	85.7	20	83.3	44	84.6	1.000
Altered	4	14.3	4	16.7	8	15.4	
Cognitive & Perceptual function							
Normal	22	78.6	7	29.2	29	55.8	0.001
Altered	6	21.4	17	70.8	23	44.2	

p value reached from unpaired student's 't' test

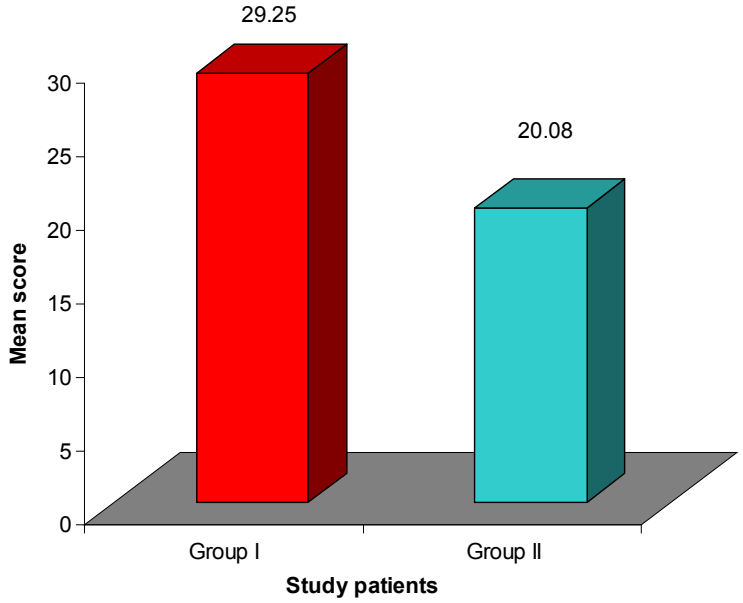

Figure-1: *Mean distribution of SSS*

Table-V: *Distribution of the patients by Scandinavian Stroke Scale*

Parameters	***Study patients***				***Mean Score***		***p value***
	Group-I (n=28)		**Group-II (n=24)**				
	No.	**%**	**No.**	**%**	**Group-I (n=28)**	**Group-II (n=24)**	
Consciousness							
Reacts to verbal command, but is not fully conscious	1	3.6	5	20.8	5.64	4.42	0.001
Somnolent can be awaked to full consciousness	3	10.7	9	37.5			
Full consciousness	24	85.7	10	41.7			
Eye movement							
Gaze palsy present	3	10.7	12	50.0	3.79	3.00	0.001
No gaze palsy	25	89.3	12	50.0			
Leg motor power							
Paralysis	2	7.1	10	41.7	3.14	1.96	0.013
Can move, but not against gravity	9	32.1	6	25.0			
Raises leg with knee flexion	15	53.6	5	20.8			
Raises straight leg with reduced strength	2	7.1	3	12.5			
Orientation							
Completely disorientated	2	7.1	7	29.2	5.29	2.75	0.000
One of these	2	7.1	8	33.3			
Two of these	0	0.0	2	8.3			
Correct for time, place and person	24	85.7	7	29.2			
Speech							
Only yes/no, less	6	21.4	8	33.3	6.86	4.88	0.111
More then yes/no, but not longer sentences	4	14.3	5	20.8			
Limited vocabulary or incoherent speech	0	0.0	2	8.3			
No aphasia	18	64.3	9	37.5			
Facial palsy							
Present	2	7.1	5	20.8	1.86	1.58	0.155
None/dubious	26	92.9	19	79.2			
Gait							
Bedridden/wheelchair	8	28.6	15	62.5	2.68	1.50	0.050
Sits without support	15	53.6	6	25.0			
Walks with help of another person	5	17.9	3	12.5			
Scandinavian stroke scale					29.25	20.08	0.001

p value reached from unpaired student's 't' test

Analysis of SSS indicated that the overall score was higher among the patients with cerebral infarct (mean score 29.25) compared to patients with cerebral haemorrhage (mean score 20.08) and the mean difference was statistically significant ($p<0.001$). Analysis of individual parameter indicated that score was better in patient with cerebral infarct than haemorrhage in terms of consciousness, eye movement, leg motor power, orientation ($p<0.05$) than patients with haemorrhage . However, no statistically significant mean difference was found between two groups in terms of speech, facial palsy and gait ($p>0.05$). But the score was higher in infarct group than haemorrhagic group patients. [Figure-1]

DISCUSSION

This study was accomplished with a view to determine risk factors of stroke and distribution of patient by Scandinavian Stroke Scale which revealed haemorrhagic stroke was more severe than infractive stroke.

In this study smoking, hypertension, diabetes mellitus, IHD were in 71.2%, 71.2%, 46.2%, 15.4% respectively. Family history of stroke, hypertension, diabetes mellitus, IHD were 36.5%, 63.5%, 53.8%, 28.8% respectively. A study conducted by Hannan A in BSMMU, Dhaka, hypertension was commonest risk factor (58.70%). Other common risk factors were increasing age (50.97%), smoking (38.7%), family history of stroke (21.29%) followed by diabetes mellitus (14.20%)[15]. Anwarullah et al found in their study hypertension in 65%, smoking in 44%, family history of stroke in 26%, diabetes mellitus in 21%, IHD in 27%, past history of stroke in 22%, rheumatic heart disease (RHD) with atrial fibrillation (AF) in 6%, lone AF in 2% and use of OCP in 2%[16]. Rozenthal et al found in their study smoking (53.6%), hypertension (43.4%), hyperlipidaemia (22%) and diabetes mellitus (21%) as main risk factors for stroke[17]. Carrieri et al found in their study that old age, high diastolic blood pressure and smoking had strong association with stroke[18].

On admission patients were evaluated in SSS (Scandinavian Stroke Scale) and it was found that tone was more increased and power was less affected in infarctive group of patients. On the other hand sensory, cognitive and perceptual functions were more affected in haemorrhagic group of patients. Analysis of SSS indicated overall scale was higher among patient with infarcts (mean scale 29.25) compared to patient with haemorrhage (mean scale 20.08) and mean difference was statistically significant ($p<0.001$).

In a study in India by Mohapatra et al in 2003 in SSS, it was found at admission 95.35% subject were non walking and 4.65% were walking with assistance. Among them 34.8% were with high initial motor impairment, 58.1% with moderate and 7.1% with mild motor impairment[19]. A study in Taiwan in 2006 done by Shu-Han Lin et al in Scandinivian Stroke Scale mean age was 59±10.1. Mean SSS score was 38±12.3 in infarctive and 36±14.5 in haemorrhagic stroke[20].

CONCLUSION

This study concludes that some risk factors like smoking, hypertension, diabetes mellitus are common for stroke. Family history of ischaemic heart disease and stroke are also found as associated factors. During assessment of functional status of acute stroke patients it is found that motor, cognitive and perceptual functions are altered in majority of stroke patients. After stroke long term expensive treatment are required & most of the stroke patients lead a crippled life. So, if we the doctors mainly physicians and neurologists come forward even in collaboration with government and media people of our developing country may help to create awareness among people regarding prevention and proper management of stroke, which is beneficial for stroke patients, their family and our developing country. Limitations of the study were short duration and small number of patient. This study needs further extensive investigation with long period in different medical college hospitals and other private institutions and in urban & rural population to draw a valid conclusion among Bangladeshi stroke patients.

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Original article

Patterns of Influenza Infection in Sylhet Division of Bangladesh

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ABSTRACT

The influenza virus infection varies globally with the genomic diversity or and clinical variations and regional detection of the patients or and viral agents are influenced by the variations of geographic, demographic condition and patient risk factors. This study is carried out to clarify about the pattern and seasonality of influenza infection during two consecutive years from July 2007 to April 2009 in Jalalabad Ragib-Rabeya Medical College Hospital, Sylhet with active collaboration of ICDDR'B and IEDCR. Three hundred eighty five (N=385) patients with acute respiratory infection were selected as case according to WHO selection criteria of avian influenza A (H5N1) virus infection. In this study throat swab and anterior nasal swab were collected as clinical specimen from the cases for detection of various types of Influenza virus by molecular or and by any other diagnostic methods (PCR & RT-PCR) in Bio-safety level-3 (BSL-3) laboratory of ICDDR'B; Mohakhali, Dhaka. Overall influenza positivity was 48 (12%), in where Flu A (n=27), Flu B (n=21) and subtypes of Flu A: H1 (n=16), H3 (n=11) & H5 (n=0). This study also suggests that peak seasonality of influenza infection is more marked in the month of July, August & September.

[Jalalabad Med J 2010; 7 (2): 67-70]

INTRODUCTION

Currently, influenza infection causes high rate of morbidity and mortality[1] due to enhance mutations in a strain of influenza or re-assortment of genetic material in a person simultaneously infected with a human and avian influenza virus can permit the virus to acquire the potential to efficiently infect a different species[2]. The influenza pandemic of 1918-1919 killed an estimated 10 million persons in India and an estimated 40 million person's worldwide[3].

Immunologically influenza viruses are differentiated into three types: A, B & C. The type A virus is highly variable. It shows continuous antigenic variation and frequently causes epidemics and periodic pandemics. It also infects animal and birds. Type B shows lesser degree antigenic variation which result in epidemics and type C antigenically stable and causes sporadic upper respiratory tract infection[4].

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National epidemics of influenza are usually caused by influenza A virus in where[5] a new strain of highly pathogenic avian influenza A (H5N1) has been circulating among birds in eastern Asia since 1996[6]. The current outbreak of H5N1 avian influenza and H1N1 swine flu affecting an unprecedented number of countries is a cause for major concern worldwide and most important for Asia. The virus has gradually expanded the host range from wild, migratory to domestic birds and animals and is becoming more pathogenic. Until December 2007, 61 countries have reported outbreaks among poultry including Bangladesh[7].

In Bangladesh the H5N1 virus was first detected in a poultry firm near capital Dhaka in March 2007. Since then the virus continues to spread in many poultry firms and backyard poultries in different districts. At present 20 out of 64 districts have reported outbreaks of H5N1 in poultry and authorities has so far culled 250 thousand chickens and destroyed nearly 3 million eggs[8]. Persons who had direct contact with poultry more prone to infection and apparently person to person transmissions have occurred. Results from

study of ICDDR,B & IEDCR showed that 14% of children with acute respiratory illness had influenza virus, isolated from their respiratory secretions. The incidence of influenza virus infection was 84.5 episodes/1000 children/year. 58% of isolates were influenza A (H3N2, H1N1) and 42% were influenza B (Shanghai and Hong Kong). Both strains of influenza A and Influenza B virus are circulating within Asia including Bangladesh. Recently the surveillance findings have been disseminated nationally[2].

This study was designed to determine the different patterns of influenza virus infection and also the influenza seasonality. The results of this study suggest that raised awareness and to take appropriate measure for the management of influenza infections in particular months of a year to reduce morbidity and mortality.

MATERIALS AND METHODS

This prospective study was carried out during the period of July 2007 to April 2009 in Jalalabad Ragib-Rabeya Medical College Hospital, Sylhet with active collaboration of the International Center for Diarrhoeal Disease Research' Bangladesh (ICDDR'B) and Institute of Epidemiology Disease Control & Research (IEDCR). Three hundred eighty five patients were selected randomly and included in this study.

The patients who fulfill the case definition of severe acute respiratory illness (SARI) were taken as study subject. Any patient presents with fever and cough or sore throat within 7 days were included in this study. Exclusion criteria were fever more than 7 days and those who did not give informed consent.

After selection of the participants, informed written consent was obtained from the patient and or accompanying persons with explanation of the objectives, nature, purpose and potential risk of all procedures. History (particulars of the patient, personal history & family history) was taken and clinical examinations (temperature, pulse, BP, respiratory rate, cyanosis, ronchi, crepitation etc.) with available investigation findings were recorded in data collection form. WHO guidelines for the diagnosis of avian influenza A (H5N1) virus infection was followed in this study, which covers the collecting, preserving and shipping of specimens, the use of non-sterile gloves, surgical facemasks and eye protection (modified universal precautions)[9]. According to guidelines, posterior-pharyngeal (throat) swabs and nasal swabs with nasal secretions (from the anterior turbinate area) were collected by cotton swab stick. After that both throat and anterior nasal swabs were put together into a sterile container of viral transport media (VTM) and stored in cold boxes at 2-8°C temperature. After specimen collection it was transported to the ICDDR'B laboratory as soon as possible preferably within 72 hours to maintain the required temperature.

Specimen was processed and tested in a bio-safety level 3 (BSL-3) laboratory of ICDDR'B, using Polymerize Chain Reaction (PCR) and Real time polymerize chain reaction (RT-PCR). These procedures were detecting influenza A and B as well as H1, H3 and H5. Real-time polymerase chain reaction (RT-PCR) was performed for typing and sub typing of influenza viruses using fluorescent Taqman probes.

All statistical analysis was done by using SPSS software package, 12.0 for windows. Values were presented as percentage and mean±SD.

RESULTS

Out of 385 patients, 236 were male & 149 were female with male to female ratio of 1:0.63. The age ranged from 11 months to 80 years with a mean age of (13.68±17.79). Irrespective of sex, the maximum number (n=299) of patients was found within 10 years of aged. [Table-I]

Table-I: *Age and sex status of the study subjects*

Sex n (%)		Age (years) Mean±SD
Male n(%)	236 (61.30%)	(13.68±17.79
Female n(%)	149 (38.70%)	
Total	385(100%)	

Fever was the common symptoms of most of all cases (n=373) but other prominent symptoms were cough (n=355) & running nose (n=193). Another presented symptoms were bodyache (n=24), sore throat (n=20), diarrhoea (n=19) and vomiting (n=3) etc. Among the case one was a poultry worker and four cases were health care worker. History of travel within 7 days was found in 10 cases.

Finally, this study showed that 48 (12%) patients were Flu positive out of 385 patients where Flu A was 27 and Flu B was 21. Study about subtypes of influenza A were H1 positive 16, H3 positive 11 but none one can get H5 positive. [Table-II] [Figure-1] & [Figure-2]

Table-II: *Laboratory results of influenza virus infections from July 2007 to April 2009*

Total Sample	Flu Positive	Flu Positivity %	Flu A	Flu B	Subtypes of Flu A		
					H1	H3	H5
385	48	12%	27	21	16	11	0

This study also demonstrates that peak incidence of influenza infections from July to September and infection is less prominent from November to March. [Figure-3]

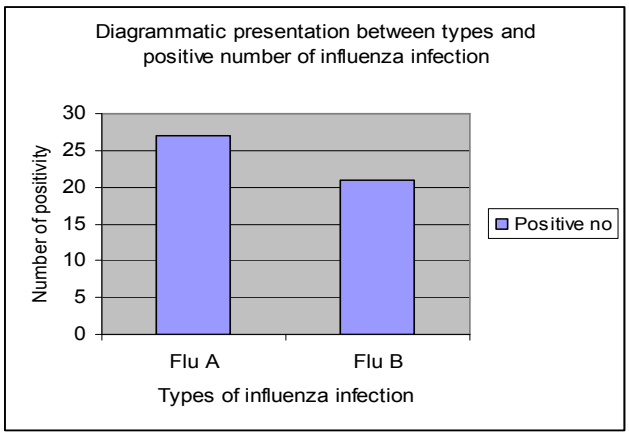

Figure-1: *Diagrammatic presentation between types and positive number of Influenza infection*

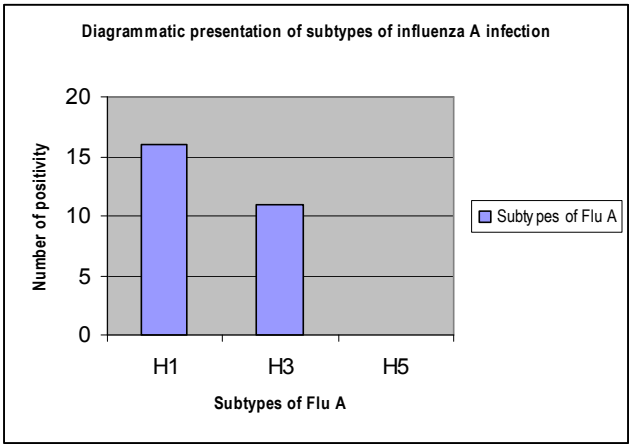

Figure-2: *Diagrammatic presentation of subtypes of influenza A infection*

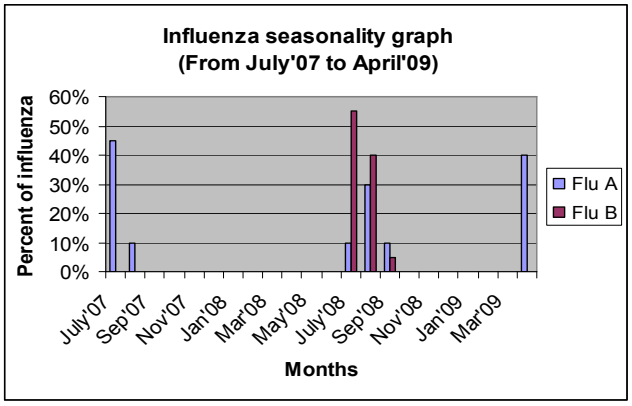

Figure-3: *Influenza seasonality graph (July'2007-April'2009)*

DISCUSSION

This study revealed that Influenza positivity was 48 (12%) and influenza A & influenza B is distinctly more marked from July to September but falling to lowest level in November to March. A study conducted by fleming & Ayres of united kingdom (1988)[1] showed that the incidence of influenza infections rising from October to February and declining to the lowest level in August and September which is not consistent with the present study. Probably, there was a geographical dissimilarity.

Another study conducted by Rao et al[10] showed that influenza positivity was 37 (5%) where 23 type A, 14 type B and two peaks: March-April in the summer & July-August in the rainy season. They were studied a total number of 763 patients who were mostly children aged 0-16 years. In the present study, flu positivity 12%, one peak of influenza July-September in the summer season which is consistent with the study of Rao et al and patient aged range from 11 months to 80 years.

Moura et al[11] studied over three thousand seven hundred eight (3,708) patients of Northeastern Brazil where influenza virus were detected in 6.3% and peak usually occurs in the rainy periods. The Brazilian study is not consistent with the present study probably due to their large sample size, multi-centre sample collection and geographical variation.

According to WHO (December 14, 2007), there were 340 influenza A (H5N1) cases were detected in world wide[12]. Bangladesh is nearer to several countries where Swine flu (H1N1) and Bird flu (H5N1) were reported as well as morbidity & mortality is increasing day by day.

This study suggests that we should take measure to prevent infection by meticulous vaccination to high risk groups particularly children and elderly persons. Now-a-days, the effectiveness of these influenza vaccines is variable due to high mutation rate of the virus. So, in association with vaccination, anti-influenza drugs such as oseltamivir & zanamivir should be available, everyone should take safety measure in poultry & be aware when it has high incidence in particular season especially July to September and prevent spread of infection from person to person by good personal health & hygiene habits. Thereby, we can prevent morbidity & mortality due to influenza infection such as swine flu, bird flu in a defined geographical area.

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JALALABAD MEDICAL JOURNAL

Review article

Foetal Loss in Diabetic Pregnancy

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ABSTRACT
The care of the diabetic mother and her offspring is rightly an interdisciplinary responsibility among the obstetrician, diabetologist and neonatologist. It is important that each has close understanding of the various problems. Fetal loss of diabetic pregnancy can be markedly reduced by good blood sugar control both in preconceptional and gestational period. The fetal outcome is presented as pre-viable fetal loss, viable fetal loss and fetal abnormalities. Pre-viable fetal loss includes those pregnancies that ended before 28th weeks and the 'viable fetal loss' is used to include perinatal, neonatal and infant loss. Fetal loss of diabetic pregnancy is higher than that of non-diabetic pregnancy.

[Jalalabad Med J 2010; 7 (2): 71- 74]

INTRODUCTION

Up to 1950, the fetal loss from intra-uterine death, obstetric complications and neonatal death was about 40%. Today it is well known that insulin-dependent diabetes mellitus (IDDM) in pregnancies have an improved prognosis when follow-up is done by a multidisciplinary team, when there is strict control of glycemic levels and when fetal health and growth are closely monitored. Pregnancy constitutes one of the physiologic events that unmask the diabetic propensities. John Mathews Duncan made the pioneer observation that there is something quite special about pregnancy and unique consequence for foetus[1].

PATHOPHYSIOLOGY

In pregnancy, fetus derives all its nourishment from the mother. In the early stage of pregnancy serum level of oestrogen and progesterone rise and induce beta cell hyperplasia. This result in hyperinsulinemia, which favours glycogen storage in liver and muscles, increase peripheral utilization of glucose and decrease hepatic production of glucose. The net result is 10% lowering of fasting plasma glucose. If the patient continues to starve or if adequate carbohydrate is not provided in normal pregnant women, glucose is produced from breakdown of fat and protein is stopped in order to supply protein to the growing fetus. More break down of fat resulting in ketonuria. In diabetic women, fasting ketonuria is considered to be an early sign of pregnancy. Diabetic pregnant women are more prone to develop ketoacidosis as compared to non-diabetic pregnant women. In the former group18 hour's starvation will lead to ketoacidosis whereas in the later group it will take 72 hours to develop the same.

In the later half of pregnancy, placenta produces human placental lactogen (HPL), prolactin and cortisol. These act as counter regulating hormones, resulting insulin resistance. In fed state because of insulin-resistance plasma glucose cannot be brought down and hyperglycemia results. Hyperglycemia in the 1st, 2nd and 3rd trimesters of pregnancy leads to congenital malformations and macrosomia of the offsprings. This may be associated with hypotropic infant's small of dates, respiratory distress syndrome, hypoglycemia, polycythemia, hyperbilirubinemia, hypocalcaemia etc. These may lead to intra-uterine deaths. Uncontrolled diabetes mellitus and impaired glucose tolerance (IGT) also leads to maternal health hazards e.g. miscarriages, polyhydramnios, antepartum haemorrhage, toxemia of pregnancy, obstructed labour, postpartum haemorrhage etc[2].

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DISCUSSION

Diabetes is the second commonest medical disorder after hypertension complicating pregnancy with an incidence of about 1%[3]. It is known that women who subsequently develop diabetes as well as diabetic women tend to have large babies; and also that high fetal loss rate is evident before the onset of the diabetes particularly in the previous two years. In the past decades better care of diabetic mother, especially better monitoring of maternal glucose levels and of the fetal and placental functions has reduced this rate in some centers to zero for specifically diabetic problems[4].

The outcome of pregnancy complicated by established diabetes or gestational glucose intolerance was compared with the outcome of non-diabetic pregnancy between 1977 and 1990 when 169 pregnancies in women with gestational glucose intolerance were referred to the New Castle General Hospital UK. The perinatal mortality (PNM) in women with established diabetes was 8.2/1000 and the viable fetal loss was 81/1000. The PNM in the background population was 11.6/1000. Spontaneous abortion rate 15% compared with 8.7% in the background population. The spontaneous abortion rate in pregnancies 'booked' before 10 weeks of gestation was 20% in established diabetes.

In a multicenter survey in France to show the associations between outcome of diabetic pregnancy and gestational diabetes with glycaemic control, it was observed abortions 6%, perinatal death 1.8%. Perinatal mortality was slightly higher in diabetic women than those in the general population (1.8% Vs 1.2%). Fetal loss was associated with poor glycaemic control[6].

A study in Japan, Omori Y et al[7] showed that the perinatal mortality of infants decreased from 10.8% in 1971-1975 to 1.1% in 1986-1990. Gabbe SG et al[8] Enumerated a perinatal mortality rate of 46 per 1000 in diabetic women as compared to 24 per 1000 in general population.

In a study in Sweden between 1983 and 1986, 914 single births to women with diabetes mellitus before randomly selected control sample of 4000 births were identified by using the Swedish Medical Birth Registry. About 24% of diabetic women were delivered preterm as compared with 6% in the control group. The rates of late fetal death were 1.3% among infants born to women with diabetes and 0.4% in the control group. Infant mortality was 0.9% and 0.5% among infants to mothers with and without diabetes mellitus respectively. The increased rates of late fetal and infant death in the diabetes group were largely explained by higher mortality in the more prevalent preterm deliveries. Fourteen of 20 late fetal and infant deaths occurred among preterm infants in diabetic pregnancies, while in control group 17 of 33 late fetal and infant death occurred among preterm infants[9].

Jovanovich L et al[10] stated although mortality statistics of diabetic mother's infants had shown marked improvement since the advent of insulin, the outlook for these infants and their mothers was still less optimal. Mortality of the infants was found ranging from 0% to 21%. Rosenn B et al[11] in their study with women of insulin-dependent diabetes in their early pregnancies showed a spontaneous abortion rate 24%.

In a study on diabetic pregnancy in Senegal in years 1980 to 1989 by Sidibe EH et al[12] showed abortion rates 14.25% and 12% in insulin-dependent and non-insulin dependent mothers respectively.

A study in Bangladesh by Karim E et al with 34 patients of GDM and 52 patients of known case of diabetes mellitus in pregnancy (DM), showed the past obstetrical history in GDM group, miscarriage in 6 (17%) cases, previous still birth 4 (11%), previous neonatal death 1 (3%) cases were noted; whereas in DM group 8 (15%), 11 (21%), 3 (5.7%) cases respectively[13].

A study in Pakistan conducted by Zafar et al demonstrated that out of 100 diabetic pregnancy, 96% delivered babies were alive and remaining 4% died during perinatal period[3].

Though a retrospective analysis of vital records and hospital discharge data, a study carried out by Frances C et al in South Carolina in 1978. The overall diabetic perinatal mortality rate was 102 deaths per 1000 deliveries. The risk of perinatal mortality is greater for non-white (153 deaths per 1000 deliveries) and for women on insulin (182 deaths per 1000 deliveries) [14].

In a study at King's College Hospital, 90% were established diabetes and in these the perinatal loss was 33%. Peel and Oakley quoted a fetal loss of 23 % in pre-diabetic pregnancies and Gibert and Dunlop found the overall pre-diabetic fetal loss rate was twice as high as in non-diabetic pregnancy and three times as high in cases developing diabetes before the age of 45 years[15].

According to Dawn CS of India, perinatal mortality in diabetic pregnancy is 25-50% in uncared women. Under proper care this has been currently brought down to less than 5%. Perinatal death parallels with degree of diabetic control, maternal cardio-vascular and renal disease. Half of perinatal death is still birth and other half neonatal. He quoted an abortion rate of 15% in general population[16].

Simpson in his test book enumerated an abortion rate of 20%[17]. In a study in India by Kameswaran C et al[18] it was found that perinatal mortality rate, still birth rate and early neonatal death rates were 57/1000, 35.1/1000and 22.7/1000 respectively. Over the two

years period, there were 20650 births at the Maternity Hospital, Katmandu in Nepal from1985 to 1986, the perinatal mortality rates calculated for this period of two years was 48.5/1000 nevertheless it occurred with an average perinatal mortality rate worked out for India of 55/1000. A similar rate occurred in Korea 10 years before the study (53/1000)[19].

General application of health care may also improve perinatal survival and perinatal mortality is decreasing in many reported populations. The rapid reduction is well substantiated for France; where perinatal mortality is dropped from 31.2/1000 live births in 1958 to 15.7/1000 in 1976. The same data available for the population of the islands of Malta, where 95% of the deliveries occurred in maternity hospital. The prevalence of diabetes on these islands is high. The neonatal deaths decreased from 19% in 1967 to 9% of live births in 1977. Infant mortality is decreased from 27% to 14% in that decade. The still birth rate, however, remained unchanged 12% in 1967 and 10% in 1977. This is also noticeable from the data of Zimmett in Naura population which has a high prevalence of obesity and diabetes. The total perinatal mortality is dropped from 100/1000 births before 1970 to 40/1000 from 1971 onward and has since remained unchanged. The still birth rate did not change substantially oscillating between 20% to 40% from 1967 to 1976 without major trend in improvement[20].

Hussain MA of Bangladesh stated perinatal death 47/1000 total births in diabetic pregnancy, whereas it was 10/1000 total births in general population[21]. Begum S of Bangladesh in a study found that the risk of pregnancy wastage increased with increasing age and gravidity of the mothers[22].

Diabetes in pregnancy exposes the fetus to a significant hazard. If the disease is severe or uncontrolled, the rate of perinatal mortality is increased as much as nine fold over that encountered in a non-diabetic pregnancy[23].

CONCLUSION

In most cases diabetes was detected during pregnancy. The longer the duration of diabetes, the worse the prognosis. Pregnancy outcome in diabetic patient is directly related to quality of preconceptional and ante-natal care received by the expectant mothers. Adequate medical facilities should be available for proper management of diabetic mothers. Healthy pregnancy depends on well controlled blood glucose before she is pregnant and during her pregnancy period. The mother needs a good diabetes treatment plan that keeps blood glucose level within normal range.

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JALALABAD MEDICAL JOURNAL

Case Report

A Case Report on Osteogenesis Imperfecta

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ABSTRACT

Osteogenesis imperfecta is a rare hereditary disorder, characterized by increased bone fragility, resulting from abnormal type-I collagen formation. Fractures, blue sclera or dentinogenesis imperfecta are associated findings. Though it is a rare disease but can occur in our environment. So, more attention has to be given for antenatal diagnosis and postpartum clinical and radiological investigations to limit the suffering of these patients.

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INTRODUCTION

Osteogenesis imperfecta is a heterogeneous group of genetic disorder, also known as brittle bone disease, that affect the body's ability to make strong bones resulting in low bone mass, bone fragility, blue sclera and progressive hearing loss[1]. Most of the osteogenesis imperfecta are transmitted in an autosomal dominant pattern where there is either too little type-1 collagen or poor quality of type-1 collagen synthesis caused by mutation in one of type-1 collagen genes which is the primary component of extra cellular matrix of bone and skin. A small percentage of cases are recessive pattern where mutations in other genes interfere with collagen production[2]. Most of the cases are new mutation. The incidence of osteogenesis imperfecta that is detectable in infancy is about 1/20,000. All races and genders are affected equally[3]. Type-I and IV are the mildest form which may be missed during neonatal period, type-III has been reported as 1/60,000 to 1-2/100000 live births, types V-VII are least common. It is the most common cause of osteoporosis[4].

CASE REPORT

A two days old female neonate of non-consanguineous parents was brought with the complaints of multiple deformities in both limbs and chest and softness of skull. The baby was born to a primi mother per vaginally at home. On examination, the baby was pink but having breathlessness, afebrile, weighing 2.25 kg, her head circumference was 32 cm, skull was soft, anterior fontanelle measured about 12x10 cm and measurement of posterior fontanelle was not possible. Eyes were slightly protruded, bluish sclera, and chest circumference was 26 cm. Both upper and lower limbs were short, irregular and curved medially.

On examination, there were multiple fractures present on both right and left humerus, right radius, right and left femur and right tibia. Chest was deformed in shape, respiratory rate was 90/min with abnormal chest movement, breath sound vesicular and no added sound. There were no relevant abnormal findings on cardio-vascular and gastro-intestinal systems. Central nervous system examination revealed a baby with good cry and normal neonatal reflexes.

A clinical diagnosis of osteogenesis imperfect was made. Radiological examination confirmed the diagnosis of osteogenesis imperfecta. X-ray shows multiple fractures involving the long bones of the upper and lower limbs with excessive callus formation. The rib-cage appeared irregular with multiple fractures at different stages of healing. The long bones ends were flared and all of them appeared short and

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irregular in outline. The distal bones were bowed. The spinal column was normal. The patient was managed by supportive treatment and was referred to BSMMU for further treatment.

Figure-1: *A neonates with osteogenesis imperfecta*

Figure-2: *Radiographic picture shows multiple fractures*

DISCUSSION

Osteogenesis imperfecta is a complex disorder of collagen production. Because the collagen is defective, all systems of the body are affected. The infant may present with fractures, bone deformities, thin skin and loose joints[5]. Early identification of these infants is extremely important to minimize the extent of fractures, reduce the patient's pain and provide support and accurate information to the parents to make decision about their child care[6].

Clinical picture, radiological evidence and positive family history form the basis of diagnosis and classification. Sillence classification is the commonest one used in prognostication, type-I is usually detected in childhood due to its mild phenotype, type-II is perinatally lethal, type-III is progressively deforming, and type-IV is of variable severity[7].

Study conducted by Byers et al[8] showed that typical manifestation were multiple bone fractures and deformities which was consistent with this case. Approximately 60% are still born, usually from respiratory failure. Infants with osteogenesis imperfecta have bones that appear bent may lead to multiple intra-uterine fractures as well. They have soft and thin skull bone, rib cage and under developed lungs, blue sclera and thin, fragile skin. Roentgenogram appearance of the long bones, especially of the femora shows diffuse osteopenia[9].

Skin biopsy and collagen studies can be used to confirm the diagnosis. 85% to 90% of cases, the test reveal abnormalities in type-I collagen. A careful history and clinical assessment are the single most important diagnostic tool[10].

Congenital hypophospatasia and battered baby syndromes are common differential diagnosis in the early neonatal period[11]. Management is mostly supportive and follow up includes a good orthopedic management and rehabilitation. Regular hearing assessment is vital for early detection of hearing deficit. Respiratory infections and neurological complications like basilar invagination and brainstem compression are frequent.

No curative therapy exists and using bisphosphonates in order to reduce osteoclast mediated bone resorption has targeted increased bone turnover in osteogenesis imperfecta. Cyclical intravenous pamidronate and calcitriol administration reduces bone pain and fractures incidence, with increased bone density and level of ambulation, with minimal side effects[12]. Growth hormone therapy has also been tried with variable results depending on type of osteogenesis imperfecta. Gene therapy may be the answer in future[13].

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JALALABAD MEDICAL JOURNAL

Case Report

Juvenile Nasopharyngeal Angiofibroma: Case Report

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ABSTRACT
Juvenile angiofibroma is benign but aggressive. Advances in imaging techniques have now facilitated more accurate staging of this disease. Tumours limited to the nasal cavity, nasopharynx and extension to sphenoid sinus can be resected by transpalatal approach as shown in this case report.

Key words: *Juvenile, Nasopharyngeal Angiofibroma.*

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INTRODUCTION

Juvenile angiofibroma is an uncommon, locally invasive, histologically benign & extremely vascular tumour that arises in the tissue within the sphenopalatine foramen. It accounts for less than 0.5% of all head neck tumour. It develops exclusively in adolescent male.

Its aggressive nature is apparent as it spreads along natural tissue planes and foramina. It can extend into nasal cavity, nasopharynx, paranasal sinuses, pterygopalatine fossa, orbit and infratemporal fossa. Intracranial extension can occur through the floor of middle cranial fossa, via foramen rotundum into cavernous sinus, or through the sphenoid sinus into cavernous sinus. It is a well defined lobulated tumour covered by nasopharyngeal mucosa. It consists of proliferating irregular vascular channels within a fibrous stroma. Blood vessel lacks smooth muscle & elastic fibre[1]. Androgen receptors, angiogenic growth factor (VEGF)[3], proliferative marker Ki67[4], IGFII gene (located in short arm of chromosome 11)[5], adenomatous polyposis coli (APC) gene (located on chromosome 5q)[6] play a role in pathogenesis..

Recurrent severe epistaxes with progressive nasal obstruction are the classical symptoms at the time of presentation. Tumour growth & extension presents with swelling of cheek, trismus, deafness (due to Eustachian tube obstruction), anosmia & plummy voice. Invasion of orbit & sphenoid causes proptosis, diplopia, visual loss, facial pain & headache[1].

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CASE REPORT

Master Hitesh , aged 11 years, from Deri , Sunamgang was admitted in the department of Otolaryngology & Head-Neck Surgery, Jalalabad Ragib-Rabeya Medical College Hospital, Sylhet, Bangladesh on 14th Feburary 2010 with the complaints of unilateral nasal

obstruction (right) for 4 months, occasional epistaxis for 3 months & headache. Anterior & posterior rhinoscopy revealed a reddish lobuated mass at the posterior end of right nasal cavity. Nasoendoscopy with Hopkins rod telesope also detected the mass at the posterior end of right nasal cavity & nasopharynx.

CT scan of nose and para nasal sinuses were performed in axial and coronal cut. Axial cut demonstrate the mass at the posterior end of right nasal cavity in close proximity to the sphenopalatine territory with extension to nasopharynx. Coronal cut showed extension to sphenoid sinus. No extension to cranial cavity, orbit, maxillary sinus, ethmoid sinus, pterogopalatine fossa & infratemporal fossa was noted .According to Fisch staging system it is a Type 2 condition.

Figure-1: *CT scan in axial cut demonstrates mass in the right posterior nasal space, in close proximity to the sphenopalatine territory with extension to nasopharynx*

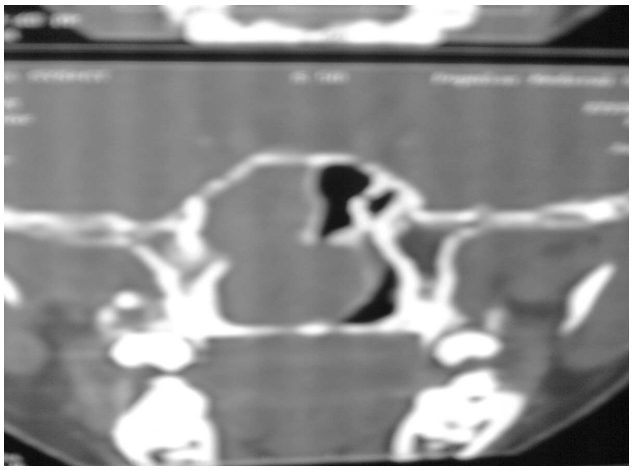

Figure-2: *CT scan in coronal cut showed extension to sphenoid sinus.*

On 24th February 2010, surgical excision of nasopharyngeal angiofibroma was done by transpalatal approach. A firm reddish lobulated mass was palpated. The tumour was then carefully dissected from its attachments. Blood loss was minimum & only one bag was transfused peroperatively. Postoperative period was uneventful. Final histopathology revealed thin walled vessel in a dense fibrous tissue stroma, diagnostic of angiofibroma.

Patient was free from epistaxes, nasal obstruction, nasal discharge, wound dehiscence & recurrence at follow up.

DISCUSSION

The treatment of juvenile angiofibroma will depend on accurate staging of the disease & appropriate choice of treatment modality. Treatment modality includes preoperative embolization, preoperative chemotherapy, surgical resection and radiotherapy. A number of patients died as a direct result of blood loss. Attempts were made preoperatively to reduce blood supply and to shrink them chemically[7].

Now diagnosis & staging is based on CT & MRI appearance[1]. Lloyd et al[8] in his review of 20 years of imaging, illustrated that CT is not only diagnostic but also prognostic. Here in this case we did CT scan to stage this disease following Fisch method. Various staging systems have been developed but that of Fisch staging is the most robust & practical[9].

Preoperative selective embolization is not done in this case as it is not required here. It is usually undertaken before endoscopic resection & open resection of more extensive tumour. Preoperative chemotherapy with non-steroidal androgen receptor blocker flutamide or with estrogen was not tried as it was not an advanced case with intracranial extension[1].

Surgical approaches are mainly two types: open & endoscopic approach. Open method include transpalatal, lateral rhinotomy & combined trans-nasal & trans-antral via Weber fergusion or mid facial deglobing approach. Open approach can be used for tumour of all stages. Endoscopic approaches are suitable for Fisch type 1, type 2 or some type 3 tumours[1].

Extensive tumour with intracranial extension are treated by combined otolaryngological & neurosurgical team. Here adequate exposure is achieved with a subtemporal preauricular infratemporal fossa approach usually combined with a middle fossa craniotomy[1].

In this case the tumour is removed by transpalatal approach. This tumour can also removed by endoscopic approach. But transpalatal approach does not require preoperative selective embolization, removal of anterior end of middle turbinate & medial wall maxilla. Endoscopic approach require all these steps. Tanspalatal approach does not produce facial scarring or anasesthesia like other open approaches. Very extensive & recurrent tumour are treated by radiotherapy with a dose of 30-55G y.

CONCLUSION

The diagnosis should be made on the basis of imaging & not biopsy. Both CT & MRI are required for staging. Complete surgical resection is the treatment of choice. Transpalatal resection is a suitable approach for small Juvenile angiofibroma involving nose, nasopharynx & sphenoid sinus.

REFERENCES

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Miscellaneous

News

Orientation of 16th batch of JRRMC

The orientation of 16th batch of JRRMC was held on 12.01.2010 at college premise participated by freshers, teachers, doctors, guardians, journalists and guests. The program was presided over by the Principal, JRRMC, Maj Gen (Retd) Prof Md Nazmul Islam. The Vice-Chancellor of Shahjalal University of Science and Technology, Prof Dr Md Saleh Uddin was present as the chief guest. As special guests, founder of the college Danabir Ragib Ali; Prof MA Ahabab, Principal of Sylhet MAG Osmani Medical College; Brigadier General Kazi ATM Ibrahim, Director of Sylhet MAG Osmani Medical College Hospital; Mr. Abdul Hye Tipu, Son of Danabir Ragib Ali; Prof ATMA Jalil, Vice-principal JRRMC; Prof Md Abed Hossain were presented in the session.

Inauguration of Vaccination program of Pandemic Influenza H1N1

The vaccination program of Pandemic Influenza H1N1 was inaugurated by the Principal, JRRMC, Maj Gen (Retd) Prof Md Nazmul Islam on 18.05.2010 in JRRMCH. The Vice-principal of JRRMC, Prof ATMA Jalil; Director, Prof Md Abed Hossain; teachers, doctors, students, officers & staffs were presented in the session.

Seminars

The following seminars held in JRRMCH during the January 2010 to June 2010

1. A seminar on **"Conversion Disorder"** held on 07-01-2010 organized by Department of Psychiatry, JRRMCH.
2. A seminar on **"Acute Renal Failure in Obstetrics"** held on 14-01-2010 organized by Department of Obstetrics & Gynecology, JRRMCH.
3. A seminar on **"Blepharospasm & Role of Duxorubicin & Botox"** held on 04-02-2010 organized by Department of Ophthalmology, JRRMCH.
4. A seminar on **"Rheumatic Fever"** held on 11-02-2010 organized by Department of Cardiology, JRRMCH.
5. A seminar on **"Gastric Lymphoma"** held on 25-02-2010 organized by Department of Surgery, JRRMCH.
6. A seminar on **"Childhood Obesity"** held on 11-03-2010 organized by Department of Paediatrics, JRRMCH.
7. A seminar on **"Nasopharyngeal Angiofibroma in a Boy of 11 years"** held on 25-03-2010 organized by Department of Otolarygology & Head Neck Surgery, JRRMCH.
8. A seminar on **"Osteoporosis"** held on 15-04-2010 organized by Department of Orthopaedics, JRRMCH.
9. A seminar on **"Vitiligo"** held on 29- 04-2010 organized by Department of Dermatology & Veneralogy, JRRMCH.
10. A seminar on **"Neck Dissection"** held on 13-05-2010 organized by Department of Otolaryngology & Head Neck Surgery, JRRMCH.
11. A seminar on **"Mitral Stenosis"** held on 03-06-2010 organized by Department of Cardiology, JRRMCH.
12. A seminar on **"Intussusceptions Saga"** held on 10-06-2010 organized by Department of Paediatrics Surgery, JRRMCH.
13. A seminar on **"Diagnosis of Diseases of the Urinary Tract & Basics of Interventional Radiology"** held on 24-06-2010 organized by Department of Radiology & Imaging, JRRMCH.

Instructions for Author(s)

Manuscripts on clinical, review, experimental and historical topics pertinent to medical sciences are accepted for the publication in this journal. The papers are accepted for the publication with an understanding that they are solely submitted for this journal. The statements, comments or opinions expressed in the papers are exclusively of author(s), not of editor(s) or publisher. The manuscripts are to be prepared as described in following instructions. 3 (three) hard copies are to be submitted. Letters about potentially acceptable manuscripts will be sent after review process is complete. No manuscripts will be returned if not accepted for publication. In addition an electronic/digital version of the manuscript composed in MS word 98/2000 should be submitted in a diskette.

Preparation of manuscripts

Manuscripts should be typewritten, double-spaced throughout (including references and tables) on one side of good quality A4 sized paper, with margins of at least 25 mm. Each component of the manuscript should begin on a new page in the sequence of title or cover page, abstract with key words, text, acknowledgement, references, tables and legends for illustrations.

Title page will contain

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Abstract and key words

An informative abstract not more than 250 word should briefly describe the objectives, materials and methods, results and conclusion. Number of key words should not more than ten and none that are in the title.

Text should contain Introduction, Materials and Methods, Results and Discussion in sequence.

Introduction

It should briefly disclose the purpose of study. It will help the readers with the problem finding. It should be clear in nature and purpose.

Materials and Methods

Clearly it should include materials, experimental procedures, methods etc. Mention the nomenclature, source of material, equipment with manufacturer's details in parentheses. Describe new methods in sufficient detail indicating their limitation. Established methods should be cited with authentic references. Ethical standards should be followed in reporting experiments done in human subjects. Precisely identify the dosage and route of administration, when drugs or chemicals are used. Measurements and data should be stated in SI unit, or if SI unit does not exist, use an internationally accepted unit. Abbreviations and acronyms should be used for widely used terms and names, which occurs consistently and frequently in the manuscript.

Results

It should be presented in logical sequence in text, tables or illustrations. Duplications of data in the tables or illustrations should be avoided. Emphasize or summarize only important observations.

Discussion

Emphasize the new and important aspects of the study and conclusion derived from them. Detail data written in introduction and other portions of text should not be repeated. The implication of results and their limitations including suggestion for future research should be included in the discussion.

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Number the references consecutively in order mentioned in the text. Full list of reference should include all authors. Avoid using abstracts as references. References to paper accepted but not yet published should be designated as 'in press' or 'forthcoming'. Authors should obtain written permission to cite such papers as well as verification that they have been accepted for publication. Information from manuscripts submitted but not accepted should be cited as 'unpublished observations' with written permission from the source. Use the styles of example below, which are based on the formats used by US National Library of Medicine (NLM) in the Index Medicus. The title of journals should be abbreviated according to the style used in Index Medicus.

Article in journal

a) List all six authors when six or less

Vega KJ, Pina I, Krevsky B. Heart transplantation in associated with an increased risk for pancreatobiliary disease. Ann Intern Med 1996; 124 (11): 980-3.

As an option, if a journal carries continuous pagination throughout a volume (as many journals do) the month and issue number may be omitted.

b) More than six authors
Parkin DM, Clayton D, Black RJ, Masuyer E, Friedl HP, Ivanov E, et al. Childhood leukaemia in Europe after chernobyl: 5 year follow-up. Br J Cancer 1996; 73:1006-12.
c) No author given
Cancer in South Africa (editorial). S Afr Med J 1948; 84:15
d) Organization as author
The cardiac society of Australia and New Zealand. Clinical exercise stress testing. Safely and performance guidelines. Med J Aust 1990; 146: 267-9.

Books and monographs
a) Personal author(s)
Laurence DR, Bennett PN, Brown MJ. Clinical Pharmacology. 8th ed. New York: Churchill Livingstone; 1997.
b) Editor(s),compiler(s) as author
Norman IJ, Redfern SJ, editors. Mental health care for elderly people. 5th ed. New York: Churchill Livingstone; 1999.
c) Organization as author and publisher
World Health Organization. Ethical criteria for medical drug promotion. Geneva: World Health Organization; 1988.
d) Chapter in a book
Phillips SJ, Whisnant JP. Hypertension and stroke. In: Laragh JH, Brenner BM, editors. Hypertension: pathophysiology, diagnosis and management. 2nd ed. New York: Raven Press; 1995. p 465-9.
e) Dissertation or thesis
Kaplan SJ. Post hospital home health care: the elderly access and utilization (dissertation). St. Louis (MO): Washington Uni; 1995.

Other published material
a) Newspaper article
Lee G. Hospitalization tied to ozone pollution: study estimates 50,000 admissions annually. The Washington post 1996; June 21; sect. A: 3 (col. 5).
b) Dictionary and similar references
Student's medical dictionary. 26th edi. Baltimore: Williams and Wilkins; 1995. Apraxia; p.119-20.

Unpublished material
a. In press
Leshner AI. Molecular mechanisms of cocaine addiction. N Eng J Med (in press) 1997.

Electronic material
a) Journal articles in electronic format
Morse SS. Factors in the emergence of infectious diseases. Emerg Infect Dis [serial online] 1995 Jan-Mar [cited 1996 June 5]; 1(1): [24 screens]. Available from: URL: http://www.cdc.gov/ncidod/EID/eid.htm
b) Monograph in electronic format
CDI, clinical dermatology illustrated [monograph on CD-ROM]. Reeves JRT, Maibach H. CMEA Multimedia group, producers. 2nd ed. Version 2.0. San Diego: CAEA; 1995.
C) Computer files
Haemodynamics III: The ups and downs of haemodynamics [computer program]. Version 2.2. Orlando (FL): Computerized Educational Systems; 1993.

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Acknowledgement should appear at the end of the manuscripts before references.

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