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Organization as author:

Diabetes Prevention Program Research Group.

Hypertension, insulin, and proinsulin in participants with impaired glucose tolerance. Hypertension. 2002;40(5): 679-86 No author given:

21st century heart solution may have a sting in the tail. BMJ. 2002;325(7357):184

Volume with supplement:

Geraud G, Spierings EL, Keywood C. Tolerability and safety of frovatriptan with short- and long-term use for treatment of migraine and in comparison with sumatriptan. Headache. 2002;42 Suppl 2:S93-9.

Issue with supplement:

Glauser TA. Integrating clinical trial data into clinical practice. Neurology. 2002;58(12 Suppl 7):S6-12.

Article published electronically ahead of the print version: Yu WM, Hawley TS, Hawley RG, Qu CK. Immortalization of yolk sac-derived precursor cells. Blood. 2002 Nov 15; 100(10):3828-31. Epub 2002 Jul 5.

2. Books and Other Monograph Personal author(s):

Murray PR, Rosenthal KS, Kobayashi GS, Pfaller MA. Medical microbiology. 4th ed. St. Louis: Mosby; 2002.

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Tynan T. Medical improvements lower homicide rate: study sees drop in assault rate. The Washington Post. 2002 Aug 12; Sect. A:2 (col. 4).

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Dorland's illustrated medical dictionary. 29th ed. Philadelphia: W.B. Saunders; 2000. Filamin; p. 675.

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Original Article

Magnetic Resonance Imaging (MRI) Evaluation of Sellar Region Tumors with Histopathological Correlation

Yiasmeen S[1], *Karim AMMN[2], Begum M[3], Parvin SI[4], Akter F[5]

Abstract

MRI is a complex, rapidly evolving modality which has assumed an increasingly important role in the diagnosis of Sellar region tumors. It is now the preferred modality for the definitive evaluation and follow-up of the most sellar region tumors. Using different pulse sequence small lesion can be detected even without contrast. Gd-DTPA provides valuable information in MR imaging sellar region tumors, particularly in pre-operative evaluation. This study was conducted to elucidate the accuracy of MRI in pre-operative evaluation of sellar region tumors and its validity by determining sensitivity, specificity, positive and negative predictive value with histopathological correlation. This cross sectional observational study was carried out in the department of radiology and imaging in collaboration with department of Neurosurgery, Dhaka Medical college Hospital, Dhaka during the period of January 2008 to April 2009. MRI of brain was done on 42 patients referred for evaluation of sellar region tumors. The following result and observation were obtained. The age range of the patient was 20 to 80 years. The mean age (HSE) was 34.31(+2.80). Maximum patients were in age group 20-30 years and male-female ratio was 1.8:1. Most sellar region tumor located in the intrasellar with suprasellar extension. Out of 42 patients 37 (88%) patients were truly diagnosed by MRI as sellar region tumors. The sensitivity of MRI to diagnosed macro adenoma was 81.25%, specificity 80.76%, positive predictive value 72.2%, negative predictive value 87.5%, accuracy 80.95%. This study finds that MRI is a valid imaging modality in the diagnosis of pituitary adenoma and sellar region tumor.

Keywords: *MRI, sellar region tumors, pituitary adenoma.*

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INTRODUCTION

The key questions to be answered when a patient with a pituitary problem undergoes an evaluation by any imaging modality. These questions are: is there any lesion and if so, what type? How large is it? Dose it after visual pathway? Does it involve cavernous sinus? The answer to these questions is important because they affect the choice of therapy. At present high resolution high field MR imaging has become widely accepted as the most sensitive method for imaging of pituitary adenomas. Its' multi-planner imaging capability, lack of ionizing radiation, absence of beoe artifact and better soft tissue contrast has made it the investigation of choice in detecting sellar region tumors. Approximately 80% - 90% of micro adenomas are hypo intense to normal gard on TIWI, while 30%-50%are hyper intense on T2WI (Roddie and cel1997). Gd DTPA enhancement provides greater contrast between gland and relatively non enhancing tumor and increase the capaity of MRI for detection of micro adenoma.[31] Micro adenomas are usually obvious and are well shown on TIWI, which usually iso to hypo intense. On T2WI, the lesion is iso to hyper intense and adherences (enhances) uniformly with contrast media. Extension and relation to surrounding structures can be well assessed by MRI.[19]

A true positive rate of 81%-100% has been reported in MR imaging at 1.5 tesla in the detection of micro adenomas without using contrast media.[17,28]

Several other studies also suggest a higher rate of detection after gadolinium.[6,20]

Though the investigation is costly, early detection of tumor before involvement of parasellar structure especially cavernous sinus is very much beneficial for the patient, when resection is easier. Thus this study is intended to assess the efficacy of MRI in the evaluation of Sellar region tumor with histopathological correlation.

MATERIALS AND METHODS

This cross sectional observational study was carried out during January 2008 to April 2009 in the department of Radiology and Imaging, Dhaka medical Collage Hospital in collaboration with the department of Neurosurgery and Pathology of the same hospital. Total 52 patients who were clinically suspected having sellar region tumor included consecutively in this study among them 45 patients ranging from 20 - 80 years of age were selected purposively as respondents who were referred for MRI of pituitary gland with visual field defect, cranial nerve palsy, and/ or endocrinological suspicion of sellar region tumor. system. Subsequently MRI scan of brain was performed in all cases and data were collected in a predesigned structured data collection sheets (proforma). Those patients who were operated were continuously followed up after the surgery up to histopathological diagnosis was made.. Then the collected reports were correlated with findings of MRI. All this information's were collected in predesigned structured data collection sheets. After approval of research protocol from the department, ethical clearance was taken from Ethical Review Board of Dhaka medical Collage. Verbal and written informed consent from the patients was obtained. Information and records of patients were kept anonymously with maintaining confidentiality.

Imaging technique and procedure:

MR imaging was obtained with 0.3 Tesla systems TIWI MR Sagittal, Coronal, and axial scan were obtained first using short TR (500-800ms) and short TE (14-20 ms). Coronal and axial T2WI image were taken using long TR (3500-4500ms) and long TE (80ms). After bolus intravenous injection of 10ml (4.69gm) contrast media namely Magnevist (Dimeglumine gadopentate) TIWI sagittal, coronal and axial scan were taken immediately. Slice thickness was 3-5mm with a field of view 20-23cm and pictures matrix was 256x256 or 192x256.

MRI diagnostic criteria:

MRI appearance pituitary microadenoma

TIWI: Isointense to hypo intense. (Osborn 1994)

T2WI: 30% -50% micro adenoma hyper intense (Kucharczyk et al., 1986).

Post contrast: (1) Focal mass that enhance less rapidly and less intensely than normal gland. (2) Delayed scan shows enhancement of mass lesion.

MRI appearance of pituitary macro adenoma:

MRI diagnosis: (Osborn 1994, Hagga 1994)

Size- more than 10mm

Shape- figure of eight (in coronal section)

- Displacement of optic chiasma upwards may be seen
- Compression on the 3rd ventricle resulting hydrocephalus
- Lateral extension may causes encasement of Cavernous sinus
- There may be erosion of sellar floor and may involve brain stem The tumor is –

TIWI- isointense to parent gland (but may be variable if there is hemorrhage,necrosis and cyst formation; T2WI- isointense-slightly hyperintenses.[19] Post contrast-delayed strong inhomogeneous enhancement.[20] Calcification is rare & reported in 1% to 2% cases.[30]

Sellar region meningioma:

MRI diagnosis: (Osborn 1994, Hagga 1994) Smooth well defined mass supra sellar ± in location

TIWI: iso to hypo intense suprasellar mass may be associated with calcification which is hypointense in both T1 WI and T2WI; T2WI: Iso to hypo to slightly hyper intense.

Post contrast: Intense homogenous contrast enhancement is noted but not intense as adjacent

pituitary and Cavernous hemangioma Duraltail: contrast enhance duramater is pathog nomic.

Craniopharyngioma:

MRI diagnosis: (Osborn 1994, Hagga 1994)

Of all sella region mass craniopharyngioma have the most heterogeneous MR imaging spectrum signal is highly variable the most common pattern is

TIWI: hypo intense to isointense to hyper intense (depending upon its content like high protein concentration and blood degradation product in free solution or both; T2WI: hyper intense to adjacent gland

Post contrast: Strong rim enhancement but Heterogeneous.

Focal calcification low signal rim or low signal globular area in both T1 and T2.

RESULT

The main objective of the study was to establish the diagnostic usefulness of MRI in detection of sellar region tumor. This cross sectional study was done on 42 purposively selected patients whose age range from 20-80 years.

Table-1 shows the age distribution of 42 patients. The mean age (±SD) was 34.31 (±2.80) years. 47.62%, 30.95%, 9.52%, 9.52% and 2.38% patients were in age group 20-30, 31-40, 41-50, 51-60 and 71-80 years respectively. No patient was found in age group 61-70 year.

Table I: Distribution of the respondent by age: (N=42)

Age group (Years)	Frequency (N-35)	Percentage (%)	Mean age ±SE
20-30	20	47.62	
31-40	13	30.95	
41-50	4	9.52	34.31
51-60	4	9.52	±2.80
61-70	0	0	
71-80	1	2.38	
Total	42	100	

Table- II shows the clinical feature of the patients with sellar region tumor. Headache was found in 85.71% of patient followed by vomiting 35.71%, visual disturbance 35%, secondary amenorrhea 47.6%, with galactorrhoea (23.80%), polyuria and polydipsia 11.9% and 7.1% present with acromegaly.

Table II: Distribution of respondent according to clinical feature (Multiple responses)

Clinical feature	Frequency	Percentage
Headache	36	85.71
Vomiting	15	35.71
Visual disturbance	15	35.71
Secondary Amenorrhea	20	47.6
Galactorrhoea	10	23.80
Polyuria, polydipsia	5	11.90
Convulsion	5	11.90
Acromegaly	3	7.1

Table III shows location of sellar region tumor according to MRI findings.

Among 42 sample about half of the tumors were (20) in intracellar with supjrasellar Extension, 12 were Intrasellar and 7 were suprasellar.

Table III: Location of sellar region tumor according to MRI findings:

Intrasellar.	12
Suprasellar.	7
Intrasellar with supjrasellar Extension	20
Intrasellar with supjrasellar and Para sellar Extension	3
Total	42

Table IV shows that 28 tumors were truly diagnosed by MRI as pituitary adenoma, 18 of which were macro adenoma and rest 10 cases were micro adenoma within other 14 cases 6 were diagnosed as meningioma, 6 were diagnosed as craniopharyngioma and rest 2 were normal on MRI examination though they are clinically suspected and were referred for MRI].

Table IV: Distribution of respondents MRI Signal intensity

Name of the tumor	Imaging Sequence	Hypointense	Hypointense	Isointense	intensity	Total %
Macro adenoma	TIWI	3 (17%)	2 (11%)	11 (61%)	2 (11%)	100
	TIWI	0	12 (67%)	4 (22%)	0	100
Micro adenoma	TIWI	6 (60%)	0	4 (40%)	0	100
	TIWI	2 (20%)	3 (30%)	5 (50%)	0	100
Meningioma	TIWI	3 (50%)	0	3 (50%)	0	100
	TIWI	3 (50%)	0	3 (50%)	0	100
Craniopharyngioma	TIWI	3 (50%)	1 (17%)	2 (33%)	0	100
	TIWI	0	4 (67%)	0	2 (33%)	100

Table V shows the distribution of sellar region tumor according to contrast enhancement pattern; out of 40 diagnosed MRI positive sellar region tumors, all 10 micro adenoma (100%) did not show early contrast enhancement. Out of 18 macro adenomas 12 enhances homogenously and 06 enhances heterogeneously and 05 meningioma shows strong uniform homogenous enhancement and 01shows heterogenous nhancement, 04 caniopharyngioma shows ring enhancement and 02 shows heterogenous enhancement.

Table V: Distribution of sellar region tumor according to contrast enhancement pattern

Tumor	Enhancement pattern		Ring
	homogenous	heterogeneous	
Macro adenoma	12 (delayed)	6 (delayed)	
Micro adenoma	6 (delayed)	4 (delayed)	
Meningioma	5	1	
Craniopharyngioma		2	4
Normal pituitary gland	2 (early)		

Table VI shows the distribution of sellar region tumor according to MRI diagnosis; among 42 patients who underwent MRI examination, 18 patients (42.85%) diagnosed as pituitary macro adenoma and 10 (23.8%) pituitary micro adenoma; 06 (14.3%) as meningioma, others 06 (14.3%) were craniopharyngioma, where 02 (4.8%) clinically suspected patients were diagnose as normal in MRI.

Table VI: Distribution of sellar region tumor according to MRI diagnosis N=42

MRI diagnosis	Frequency	Percentage
Macro adenoma	18	42.9
Micro adenoma	10	23.8
Meningioma	6	14.10
Craniopharyngioma	6	14.3
Normal	2	4.8
Total	42	100%

Table VII shows the distribution of sellar region tumor according to histopathological diagnosis in compare with MRI diagnosed cases; out of total 42 patients 40 patients were operated and histopathological examination was done. Histopathologically 16 (40.0%), 8 (20%), 7 (17.5%) and6 (15.0%) patients were diagnosed as macro adenoma, micro adenoma, meningioma and craniopharyngioma respectively. Among the MRI diagnosed 40 cases total 37 (93.0%) cases were confirmed histopatho- logically.

Here, MRI diagnosed 18 patients who were as macro adenoma 2 of them not confirm by histopathology, likely 10 of micro adenoma 8 were diagnosed histopathologically, where all 6 meningioma and craniopharyngioma were histopathologically confirm as same tumor; but 1 case which was MRI negative but histopathologically positive as meningioma. As, 37 patients were histopathologically positive from 40 MRI positive patients of sellar region tumor of which 4 MRI positive were histopathologically negative and 1 MRI negative was histopathologically positive, then 4 cases were false positive and 1 case was false negative.

Table VII: Distribution of histopathologically confirmed cases in compare with MRI diagnosed cases

	MRI diagnosed cases		Histopathologically confirmed cases	
	Frequency	Percentage	Frequency	Percentage
Macro adenoma	18	45.0	16	40.0
Micro adenoma	10	25.0	8	20.0
Meningioma	6	15.0	7	17.5
Craniophryngioma	6	15.0	6	15.0
Total	**40**	**100%**	**37**	**93%**

Table VIII shows the distribution of sellar region tumor according to their size; among 40 MRI positives and the range of size was 6mm - 54mm. Maximum number (50%) of tumors were in size ranges 0mm-10mm 25% and 21mm-30mm 25%.

Table VIII: Size distribution of the tumor MRI:

Size	Frequency	Percentage
0-10	10	25
12-20	5	12.5
21-30	10	25
31-40	5	12.5
41-50	6	15
51-60	4	10
Total	**40**	**100**

Table IX shows the distribution of MRI findings by histopathological findings for pituitary micro adenoma among the cases 7 were diagnosed as microadenoma and confirm by histopathological evaluation as true positive. Other 3 cases were diagnosed as micro adenoma, but histopathological were negative and included as false positive. Rest 32 cases of other than microadenoma one was confirm as pituitary micro adenoma and remaining 31 were other than pituitary microadenoma by histopathology and those were included as false negative and true negative respectively.

Table IX: Distribution of respondents of MRI findings by histopathological findings for pituitary micro adenoma:

MRI	Histopathology		Total
	Positive(+)	Negative(-)	
Positive (+)	7 (TP)	3 (FP)	10
Negative (-)	1 (FN)	31 (TN)	32
Total	8	34	42

Table X shows the Sensitivity, Specificity, Accuracy, Positive and Negative Predictive Values of the MRI in the diagnosis of Pituitary micro adenoma. Sensitivity of MRI diagnosis to micro adenoma was 87.5%, specificity 91.17%; positive predictive values are 70%, negative predictive values 91.17% and accuracy 90.47%.

Table X: Sensitivity, specificity, accuracy, positive and negative predictive values and accuracy of the MRI in the diagnosis of Pituitary micro adenoma

Sensitivity	87.5%
Specificity	91.17%
Positive predictive Values	70.0%
Negative predictive Values	91.17%
Accuracy	90.47%

Table XI shows the distribution of MRI findings by histopathological findings for pituitary macro adenoma where 13 MRI diagnosed macroadenoma cases were confirmed by histopathological

findings and included as true positive. Other 5 diagnosed cases were not confirmed by histopathologically and included as false positive. Another 24 cases other than macro adenoma by MRI diagnosis, from those cases 3 were confirmed as macro adenoma and 21 were other than macro adenoma by histopathology and included as false negative and true negative respectively.

Table: XI. Distribution of the respondent's MRI findings by histological findings for pituitary macro adenoma

MRI	Histopathology		Total
	Positive (+)	Negative (-)	
Positive (+)	13 (TP)	5 (FP)	18
Negative (-)	3 (FN)	21 (TN)	24
Total	16	26	42

Table: XII shows the sensitivity, specificity, accuracy, positive and negative predictive values of the MRI in the diagnosis of pituitary macro adenoma, where sensitivity of MRI diagnosis to micro adenoma was 81.25%, specificity 80.76%, positive predictive values72.20%, negative predictive values 80.95% and accuracy was 80.95%.

Table: XII. Sensitivity, specificity, positive and negative predictive values and accuracy of the MRI in the diagnosis of pituitary macro adenoma.

Sensitivity	81.25%
Specificity	80.76%
Positive predictive Values	72.20%
Negative predictive Values	87.5%
Accuracy	80.95%

Table XIII shows the distribution of MRI findings by histopathological findings for Supra sellar meningioma where 5 from 6 MRI diagnosed meningiomas were confirmed as true positive and l case was not confirm that is false positive by histopathologically. From 36 cases other than meningioma, 2 cases were diagnosed histopathologically as meningioma, which are false negative and other 34 cases other than meningioma also confirm by histopathology and included as true negative.

Table: XIII. Distribution of the respondent's MRI findings by histological findings for Supra sellar meningioma:

MRI	Histopathology		Total
	Positive (+)	Negative(-)	
Positive(+)	5 (TP)	1(FP)	6
Negative(-)	2(FN)	34(TN)	36
Total	7	35	42

Table: XIV shows the sensitivity, specificity, accuracy, positive and negative predictive values of the MRI in the diagnosis of supra sellar region meningioma, where sensitivity of meningioma in MRI was 74.42%, specificity 97%, positive predictive values 83.33%, negative predictive values 94.44% and accuracy 92.85%.

Table: XIV. Sensitivity, specificity, positive predictive values, negative predictive values and accuracy of the MRI in the diagnosis of supra sellar region meningioma

Sensitivity	71.42%
Specificity	97.12%
Positive predictive Values	83.33%
negative predictive Values	94.44%
accuracy	92.85%

Table XV shows the distribution of MRI findings by histopathological findings for craniophary- ngioma where 5 MRI diagnosed craniophary- ngioma were confirmed by histopathologically as true positive and 1 case was not confirmed which included as false positive. From 36 cases other than craniopharyngioma 1cases was confirmed histopathologically as craniopharyngioma and 35 were other than craniopharyngioma and included as false negative and true negative respectively.

Table: XV. Distribution of the respondents of MRI findings by histological findings for craniopharyngioma:

MRI	Histopathology		Total
	Positive (+)	Negative(-)	
Positive(+)	5 (TP)	1(FP)	6
Negative(-)	1(FN)	35(TN)	36
	6	36	42

Table: XVI shows the sensitivity, specificity, accuracy, positive and negative predictive values and accuracy of MRI in the diagnosis of craniopharyngioma. Sensitivity of MRI to diagnose craniopharyngioma was 83.3%, specificity 97.22%, positive predictive values 83.3%, negative predictive values 97.2% and accuracy is 95.2%.

Table: XVI. Sensitivity, specificity, positive predictive values, negative predictive values and accuracy of MRI in the diagnosis of craniopharyngioma:

Sensitivity	83.3%
Specificity	97.22%
Positive predictive Values	83.3%
negative predictive Values	97.22%
accuracy	95.2%

DISCUSSION

Among sellar region tumor pituitary adenomas are common benign epithelial tumors that arise from adenohypophysis and constitute 10% to 15% of all intracranial tumors (olson and wells, 1997). The clinical presentation and classification depends primarily on whether they are functioning (non-secratory) from radiological perspective, it is the best to classify adenoma on the basis of their size, and those less than 10 mm in diameter being considered as micro adenoma and greater than 10 mm are macro adenoma.

This cross sectional study was carried out by 0.3T MRI with 3-5mm slice thickness. The study included 42 patients, age ranging from 20 to 80 years. MRI of the sellar region was performed in all cases and 28 cases were diagnosed as pituitary adenoma among them 18 were macrodome and 10 were micro adenoma by this imaging modalities. MRI failed detect 2 micro adenoma though they had strong clinical and hormonal evidenced of pituitary adenomas and 2 macro adenomas even of their presence of mass effect .They are histologically detect as other sellar region tumor than pituitary adenoma. One of the diagnosed macro adenoma histopathologically diagnosed as meningioma so 6 MRI suspected sellar region meningioma confirm by histopathology and there is also 1 case (MRI false positive of macro adenoma) diagnosed histologically as meningioma. With this imaging technique the normal anterior pituitary gland was found to be homogenous internal signal intensity, isointense to cerebral white matter on both T1WI and T2WI (photograph la,b). TIWI sequences were found as the most sensitive in demonstrating internal signal intensity changes within the gland containing adenoma. Within 10 cases 6(60%) were TIWI hypointense and 4(40%) were TIWI isointense which strongly correlate with the findings.[18] After gadolinium the hypointense area was visible as more hypointense due to relative nonenhancement of tumor.

On T2WI, 50% of micro adenomas are isointense and 30% are hyperintense and 20% are hypointense. So, T2WI imaging methods was less sensitive as suggested[22] and 61% macro adenoma were isointense on T1WI and 22% were mixed intensity and on T2WI, 67% macro adenoma were hyperintense and 22% were isointense and 11% were isointensity 11% were mixed intensity. Contrast enhancement were noted in all cases but delayed and variable like 23 cases were homogenous, 13 were heterogeneous and 4 were ring enhancement. Contrast enhancements were noted in 95% of sellar region tumor these findings are similar to the result.[20]

In 2 cases hyper intensity was noted in both TIWI andT2WI and was diagnosed as haemorrhagic pituitary adenoma (photograph 7a, b). These patient present with acute onset of headache and blurring of vision which can be correlated with pituitary apoplexy syndrome.[27]

In three cases there was focal hypo-intensity on TIWI (photograph 8a,) which were hyper intense on T2WI and non-enhancing after contrast (photograph 5a, 8b). The signal intensity changes are characteristic of cystic degeneration within the tumor. Infundibular deviation was noted in 30 cases and also in 2 micro adenoma and 22 macro adenoma (photograph7b). Cavernous sinus invasion was noted in six cases (17%) cases. In two of them there were definit sign of cavernous sinous invasion like carotid artery encasement.[34]

Compression of optic chiasma noted in 30(71%) of sellar region (photograph 6a b). All of these patients had visual problem and in one patient there was complete loss of vision. Third nerve palsy was reported in 3(8.6%) and 15 patients (35.7%) had indentation of third ventricle (photograph 5b) and hydrocephalus noted in 4 cases (9.5%) (photograph 8b). Two of these patients had severe headache and vomiting and two had headache and convulsion. Thirteen patient of meningioma arise from tuberculum sella (Sutton etat.,1998) which may extened in to the sella and may simulate pituitary adenoma.[23] In the present series sensitivity of MRI to diagnose pituitary micro adenoma was 87.5%, specificity was 91.1%, positive predictive value was 70.0%, and negative predictive value was 91.17%, accuracy 90.47%.

In the present series the sensitivity of MRI to diagnosis macro adenoma was 81.25%, specificity was 80.76%, positive predictive value was72.20%, negative predictive value was 87.5% and accuracy was 80.95%.

In the present series the sensitivity of MRI diagnosis of sellar region meningioma was 74.42%, specificity was 97%, positive predictive value was 83.33%, negative predictive value was 94.44% and accuracy was 92.85%

In the present series the sensitivity of MRI diagnosed craniopharyngioma was 83.3%, specificity was 97.22%, positive predictive value was 83.3%, Negative predictive value 97.22% and accuracy 95.2%. Kulkarni et al. in 1988 showed 83% MR sensitivity of micro adenoma and 100% for macro adenoma.[18] demonstrated 91% and 100% sensitivity for micro adenoma and macro adenoma respectively. In this study MR sensitivity of macro adenoma was 81.25% and micro adenoma was 87.5%. The possible cause of lower sensitivity in this study was higher slice thickness (5mm) and 0.3T MRI machine.

CONCLUSIONS

The sensitivity and specificity of MRI for the diagnosis of various types of pituitary adenoma and as well as sellar region tumor were closely related with histopathological results (gold slandered) and were found in between 81% to 97%; only one exception of sensitivity of suprasellar meningioma which was 71.4%. MRI can be accepted as the most reliable imaging modality in the diagnosis of pituitary adenoma and as well as sellar region tumor. It can therefore be concluded that MRI scan is reliable modality in the evaluation of sellar region tumor. More importantly, MR scans can demonstrate the precise effect of the tumor mass on the adjacent structures, particularly those of the visual system and cavernous sinuses.

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Original Article

Isolation of Campylobacter Species in the Stool of Under Five Children With Acute Diarrhea in a Tertiary Care Hospital of Bangladesh

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Abstract

Campylobacter species is the main etiology of gastroenteritis due to bacteria. To determine prevalence of Campylobacter species in stool of children less than five years of age with acute diarrhoea, this observational study was conducted in the Department of Microbiology, Sylhet M A G Osmani Medical College, Sylhet from January to December, 2017. Stool samples were collected from 162 under-five children with acute diarrhoea admitted in the Department of Paediatrics. Isolation of Campylobacter species were done by stool culture. About two third of the children were male (65.4%) and more than one fourth of the affected children (26.65%) were in age group 6-12 months. Campylobacter species was isolated in 24 (15%) sample and among them, Campylobacter jejuni were 22 (91.7%) and Campylobacter coli were 2 (8.3%). Isolation rate of Campylobacter species did not differ significantly between age group of 6-12 months and above 12 months (p=0.211) of age; male and female children (p=0.288); among socioeconomic status (p=0.673) and between residential status (p=0.108). Isolation rate of Campylobacter species are frequent among under five children with acute diarrhea and most of the children came from low socioeconomic background and were male. However, a large multicenter study needs to be conducted to generate more evidence regarding the issue.

Keywords: *Acute diarrhoea, campylobacter species, prevalence, under five children*

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INTRODUCTION

Diarrhoea imparts some significant morbidity and mortality in the younger children worldwide, especially in developing countries. Among children under 5 years of age it is the second main cause of death and is estimated to have caused 0.5 million pediatric deaths per year.[1] This disease also has direct consequences in children include malnutrition, diminished growth and cognitive dysfunction in resource limited countries.[2]

In developing countries, like Bangladesh, among all the bacterial causes of diarrhoea, the five most common bacterial pathogens in children up to five years of age are *Campylobacter jejuni* followed by *Escherichia coli*, Aeromonas spp., Shigella and *Vibrio cholera*.[3] On the other hand, in developed country, Campylobacters are ranked fourth among top five pathogens in causing food borne infections and is estimated to cause more than 9.4 million cases of campylobacteriosis each year.[4]

The Campylobacter genus comprised of 26 species and is curved, Gram-negative, motile, and microaerophilic, nonspore producing bacillus[5]. *Campylobacter jejuni* and *Campylobacter coli* are the two most importatnt species.[6] In developed countries, about 5% - 20% of all cases of acute gastroenteritis in children younger than 5 years of age is caused by Campylobacter; whereas, in developed count ries incidence ranges from 5% - 35%.[7,8] In Pakistan and India, acute diarrhea is caused by Campylobacter spp

about 18%.[9] and 4.5% to 13%,respectively.[10] In Bangladesh, isolation rate of *Campylobacter jejuni* causing acute childhood diarrhoea is 17.4%,[3] and 12%.[11]

In general, the transmission of Campylobacter occurs to humans by eating undercooked or contaminated poultry, unpasteurised dairy products and contaminated water or coming with the contact faeces of a dog or cat. But person-to-person spread of Campylobacter is not frequent.[12] Commonly the disease occurs sporadically, but outbreaks can occur if it is transmitted by contaminated water or unpasteurised milk .[13]

The *Campylobacter jejuni* can be isolated by conventional culture method but that time consuming.[14] It is a fastidious organism, uses menaquinones as their respiratory quinones, and grows in microaerophilic environment (5%O_2, 10% CO_2 and 85% N_2).[13,15] The *Campylobacter jejuni* does not ferment, or oxidize carbohydrates.[13,15] Over the past few decades, culture-independent-based diagnostics, i.e., nucleic acid test, especially qualitative polymerase chain reaction (qPCR) performed directly from diarrhoeal stools, have provided a rapid and a highly sensitive method of diagnosis in laboratories with molecular diagnostic facilities.[16] In Bangladesh few studies have been done for detection of *Campylobacter jejuni* by PCR.[17]

Although Campylobacter enteritis is a major public health problem in both developed and developing countries, there is still paucity of data related to the prevalence and burden of Campylobacter diarrhoea across vast regions of Bangladesh. Moreover, there are no available data on Campylobacter diarrhoea from north-eastern part of Bangladesh. The present study was designed to find out the isolation rate of *Campylobacter jejuni* among the hospitalized children of less than five years of age with acute diarrhoea.

MATERIALS AND METHODS

This cross sectional observational study was conducted in the Department of Microbiology, Sylhet MAG Osmani Medical College, Sylhet during the period from 1st January, 2017 to 31st December, 2017. A total 162 under five children with acute diarrhoea (the passage of three or more loose or liquid stools per day lasts for several hours or days but not more than 14 days) admitted in the Department of Paediatrics, Sylhet MAG Osmani Medical College Hospital, Sylhet fulfilling the eligibility criteria were enrolled. Children who had received antibiotic within last two weeks were excluded from the study.

After admission of an under five children with acute diarrhoea with or without blood and mucous associated with either fever or abdominal pain or both were evaluated from history and clinical examination. Informed written consents were obtained from each parents or legal guardian. Those who fulfilled the inclusion criteria were taken as sample. In this way 162 under five years of age with acute diarrhoea were enrolled. The demographic data were taken as per questionnaire.

Collection of stool samples and culturing technique: Stool sample was collected from each patient in sterile plastic, disposable bottles with proper labeling without any preservatives before starting any antibiotic. The collected specimens were immediately transported to the Department of Microbiology, Sylhet MAG Osmani Medical College, where the samples were inoculated in the primary culturing medium for Campylobacter used was Campylobacter agar base (Lot no. 0000249244, HIMEDIA, India) with defibrinated 5% sheep blood containing Vancomycin 5 (mg/l), Trimethoprim (2.50 mg/l), Cefsulodin (2.50 mg/l) and Amphotericin B (2.50 mg/l). It was incubated at 42^{0}C (microaerophilic condition) for at least 48 hours. The culture plates were re-incubated for the next 24 hours if no growth was found after initial 48 hours. The morphology of the colony, motility test, Gram staining pattern and biochemical tests like, oxidase test, catalase test and hippurate hydrolysis test were used to find out the organism.

Statistical Analysis: After collecting all the data were registered, processed and analyzed by using SPSS (Statistical Package for Social Science) for windows version 23.0. Quantitative data were expressed as mean and standard deviation and qualitative data were expressed as frequency and percentage.

Ethical Consideration: Informed written consent was taken from each parent or legal guardian after explaining the the purpose of the study. Prior to the beginning of this study. The approval of the research protocol was obtained from the Ethical Review Committee of Sylhet MAG Osmani Medical College, Sylhet.

RESULTS

Table-1 shows the distribution of socio-demographic characteristics of the children. Among the 162 children, age of the patients ranged from 6 to 60 months with the

mean age of 16.20 ± 10.12 months. Highest number 89 (54.9%) patients were found in 6-12 months age group and lowest number 6 (3.7%) were seen in 49 to 60 months age group. Male preponderance with a ratio of male to female was 1.89:1.

Table-I Socio-demographic characteristics of the children (n=162)

Parameters		Frequency	Percentage
Age			
	6-12 Months	89	54.9
	13-24 Months	46	28.4
	25-36 months	14	8.6
	37-48 months	7	4.3
	49-60 months	6	3.7
Sex			
	Male	106	65.4
	Female	56	34.6

Table-II shows that the duration of diarrhea ranging from 1 to 12 days with the mean of 5.29 ± 2.57 days and duration 1-5 days was in 107 (66%) cases and 6-12 days in 55 (34%) cases. Among the patients 116 (71.6%) were from lower class, 29 (17.9%) were from middle class and 17 (10.5%) were from upper class of socioeconomic status. In this study 128 (79%) participants were from rural areas and 34 (21%) participants were from urban areas.

Table-II: Distribution of the patient according to duration of diarrhea and socio-economic class (n=162)

Parameters		Frequency	Percentage
Duration of diarrhea			
	1-5 days	107	66.0
	6-12 days	55	34.0
Socioeconomic status		Frequency	Percentage
	Lower class	116	71.6
	Middle class	29	17.9
	Upper class	17	10.5
Residential status			
	Rural	128	79.0
	Urban	34	21.0

Table - III shows the association of isolation of Campylobacter and various parameters of socio-demographic and economic conditions of the children. Amongst 162 children, Campylobacter species were isolated from stool of diarrheal children of under 5 years in 24 (15%) cases and remaining 138 (85%) cases revealed no growth of Campylobacter species. Campylobacter jejuni was the major isolate, 22 (91.7%) cases and a tiny portion by Campylobacter coli 2 (8.3%) cases. Isolation rate of Campylobacter species did not differ significantly between age group of 6-12 months and the age group of above 12 months (χ^2=1.565; p=0.211); male and female children (χ^2=1.140; p=0.288); among socioeconomic status (p=0.673) and between residential status (χ^2=2.590; p=0.108).

Table- III: Association of isolation of Campylobacter and various parameters of socio-demographic and economic conditions of the children(n=162).

Socio-demographic parameters		Campylobacter species		p-value
		Growth	No Growth	
Age				
	6-12 months	16	73	*p=0.211
	>12 months	8	65	
Sex				
	Male	18	88	*p=0.286
	Female	6	50	
Socioeconomic status				
	Lower class	19	97	†p=0.673
	Middle class	4	25	
	Upper class	1	16	
Residential status				
	Rural	16	112	*p=0.108
	Urban	8	26	

*Chi-squared test was done

DISCUSSION

This study revealed that Campylobacter species was isolated in 24 (15%) cases from stool of acute diarrhoea of children under 5 years. Several studies in Bangladesh revealed 13.5-17.4% Campylobacter species in diarrhoeal children.[3,11,18,19] *Campylobacter jejuni* were isolated from diarrhoeic stool samples was 15.4% in Northwest Ethiopia,[20] 12.7% in South Ethiopia,[21] 18% in Pakistan,[9] which were in accordance with the present study. But higher prevalence of Campylobacter species were detected in diarrhoeic children 21%.[21] and 47.4%,[23] in Malawi and South Africa respectively; whereas lower prevalence of 2% in Sudan,[24] 4.7% in Tanzania,[25] and 7.0% in Kolkata, India.[26] The difference in frequency of

Campylobacter jejuni in different parts of the world is probably due to varying standards of living conditions, water supply and feeding habits as the infection occurs through water and food.

In this study the age of the patients ranged from 6 to 60 months with the mean age of 16.20 ± 10.12 months. The highest number 54.9% of patients were found in 6-12 months age group and lowest 3.7% of patients were in 49-60 months age group.Huda et al.[19] found that 52.5% of diarrhoea of children were aged up to one years. Which was nearly similar to the present study. But Tafa et al.[27] reported that the mean age of the children was 37.88 ± 15.96 months (ranges, one to 59 months) and 51.1% of patients were in the age group of 48–59 months followed by the age group of 36-47 months (15.4%). Campylobacter spp. were isolated in 17.98% of patients aged between 6 and 12 months; and 10.95% of cases aged above 12 months; difference was not significant (p=0.211). This result correlated with Lengerh et al.[20] that of isolation of Campylobacter species did not differ significantly between age group of <1 years and the age group of 1-5 years (p=0.16). Several other studies supported this result.[27,28] But Huda et al.[19] reported the isolation rate of Campylobacter was 19.3% in below 1 year of age group and 5.8% was above 1 year of age group. The difference was highly significant (p<0.003).

In the present study 65.4% of patients were male and 34.6% of patients were female children with a ratio of male to female of 1.89:1. Male preponderance was reported in some, [19] while female preponderance was reported in other.[27] The isolation rate of *Campylobacter species* were 16.98% of male and 10.71% of female diarrhoeal children. The isolation of *Campylobacter species* did not differ significantly between male and female (p=0.286). This result was in agreement with several studies.[19, 20, 27, 29]

The duration of diarrhoea ranged from 1 to 12 days with the mean of 5.29 ± 2.57 days. Duration of diarrhoea was 1-5 days in 66% of cases and 6-12 days in 34% of cases. This result was consistent with the study of Lengerh et al.[20] that duration of diarrhoea was 1-5 days in 91.9% cases and 6 days or more in 8.1% cases.

In this study 71.6% of patients were from lower class, 17.9% of patients were from middle class and 10.5% of patients were from upper class of socioeconomic status. *Campylobacter species* were isolated in 5.88% of case from upper class, 13.79% of cases from middle class and 16.38% of cases from lower class of socioeconomic status. Frequency of isolation of Campylobacter species in diarrhoeal children among socioeconomic status did not differ significantly (p=0.673). This may be due to the fact that people of poor socioeconomic condition constitute the major bulk of the population in Bangladesh. The government hospital facilities were mostly availed by lower class.

In this study 79% of patients were from rural areas and 21% of patients were from urban areas. This may be due to that rural people mostly poor or middle class people and availed government hospital facilities mostly. *Campylobacter species* were isolated in 12.5% of cases of rural area and 23.53% of cases of urban area.

Frequency of isolation of Campylobacter species in diarrhoeal children between residential status did not differ significantly (p=0.108). This result was supported by the study of Lengerh et al.[20] that of isolation of Campylobacter species did not differ significantly between residential status of urban and rural areas (p=0.53).

In this study, among 24 isolated Campylobacter species 91.7% of cases were *Campylobacter jejuni* and 8.3% of cases were *Campylobacter coli*. Roy et al.[11] reported 88.89% of cases were *Campylobacter jejuni* and 11.11% of cases were *Campylobacter coli* among isolated Campylobacter spp. in Bangladesh. Mshana et al.[9] reported 80.9% of cases were *Campylobacter jejuni,* 4.5% were *Campylobacter coli* and 14.6% were other species of Campylobacter in Uganda. Feizabadi et al.[30] also showed that 85.8% were *Campylobacter jejuni* and 14.2% were *Campylobacter coli* from Iran.

Limitations of the study: (1) This study was conducted in a single centre and (2) sample size was small.

CONCLUSIONS

It may conclude that infection caused by C*ampylobacter species* is very frequent among under five children with acute diarrhoea and mostly below one year of age. Majority of the patients were male and belonged to the low socio-economic status. However further large scale study involving multicentre should be carried out to evaluate prevalence of campylobacteriosis and their antimicrobial susceptibility pattern in Bangladesh.

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Author Contributions: Dr. Suborna Dey: conceptualization, methodology, data collection and original draft preparation; Dr. Rajib Das: conceptualization, methodology and revised the manuscript; Professor Dr. Md. Moynul Haque and Dr. Premananda Das supervised the study; Dr. Shantanu Das, Dr. Farjana-Binte-Habib**,** Dr. Sultana Mehnaz Rahman Chowdhury, Dr.Mohammed Mirazur Rahman and Dr. Md. Nazmul Hasan critically review the manuscript. All the authors finally contributed to the final approval of the version to be published.

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Original Article

Clinical Profile and Outcome of Children with Congenital Heart Disease in First Year of Life

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Abstract

Diagnosis of congenital heart disease (CHD) which is a structural abnormality of the heart or intra thoracic great vessels in the earliest possible time is very important. Identifying the various modes of presentation, early referral and appropriate intervention can save lives and reduce risk of complications. The objectives of this study were to determine the clinical profile, complication and immediate outcome of children with congenital heart disease in first year of life. This cross-sectional observational study was conducted from October 2011 to March 2012 among 50 children from zero to one year of age who was diagnosed as CHD by echocardiography admitted in Department of Paediatrics of Shaheed Suhrawardy Medical College, Dhaka and Department of Paediatric Cardiology of National Institute of Cardiovascular Diseases, Dhaka, Bangladesh. Among 50 infants acyanotic CHD was detected in 70% and cyanotic in 30% infants. Major structural defects were venticular septal defect 34%, patent ductus arteriosus 30%, tetralogy of fallot's 14%, transposition of great arteries 12%, atrial septal defect 6%. Presenting features were cough 82%, dyspnea 80%, poor weight gain 70%, feeding difficulty 68% and fever 58%. Frequently observed complications were failure to thrive, pulmonary hypertension and heart failure. Among the outcome of CHD 8% cases closed spontaneously, case fatality rate was 8% and the rest were advised accordingly for surgery, intervention and medical management among which 14% had device closure within the study period. High index of suspicion, early diagnosis, close monitoring and timely intervention can reduce complication of CHD.

Keywords: *Acyanotic, CHD, cyanotic, echocardiography.*

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INTRODUCTION

Congenital heart disease (CHD) is a gross structural abnormality of the heart or intra thoracic great vessels that is actually or potentially of functional significance.[1] The incidence of CHD is 8-10/1000 live births in different parts of the world.[2] Nearly one third to half of these CHD are critical requiring intervention in the first year of life.[3] CHD is one of the most common types of anomaly that is responsible for significant morbidity and mortality in children.[1] Presence of congenital heart disease is suspected on the basis of following findings; a) presence of cardiac murmur, b) presence of cyanosis or feeding difficulty, c) cyanosis associated with feeding difficulty, d) features of congestive heart failure or failure to thrive.[1] Early recognition of CHD is important because clinical presentation and deterioration may be sudden and some treatable defects may even cause death before diagnosis.[4, 5]

CHD is divided into acyanotic and cyanotic, but there are several conditions like tetralogy of Fallot, Ebstein's anomaly, Eisenmenger Syndrome which may start as acyanotic and become cyanotic with time.[6]

Clinical profile of congenital heart disease varies according to type and severity of the defect. In neonate, the presenting features of CHD are cyanosis (with or without respiratory distress), heart failure (with or without cyanosis) an abnormal clinical sign detected on routine

examination (e.g. absent femoral pulse or a heart murmur).[7] In infancy and childhood the usual presenting features are cyanosis, digital clubbing, murmur, syncope, squatting, heart failure, arrhythmia, failure to thrive.[8] CHD is responsible for more deaths in the first year of life than any other birth defects. Some CHD heal over time, others will require treatment.[9] In some cases early diagnosis can avoid irreversible pulmonary vascular disease.[5] With currently available treatment modalities over 75% of infants born with critical CHD can survive beyond the first year of life and many can lead near normal lives thereafter. Majority of the children born in developing countries and afflicted with CHD do not get the necessary care, leading to high mortality and morbidity.[10]

Diagnosis of CHD at the earliest possible time is very important because early referral and appropriate intervention can save lives and reduce complications.

The objectives of the study was to determine the clinical profile, complications and immediate outcome of children with congenital heart disease in their first year of life who were admitted at hospital during the study period.

MATERIALS AND METHOD

This cross-sectional observational study was carried out from October 2011 to March 2012 in the Department of Paediatrics of Shaheed Suhrawardy Medical College (ShSMC), Dhaka, Bangladesh. The study enrolled 50 children of day zero to one year of age admitted in the Department of Paediatrics of ShSMC and the Department of Paediatric Cardiology of National Institute of Cardiovascular Diseases (NICVD), Sher-E-Bangla Nagar, Dhaka.

The inclusion criterion was CHD among admitted children from day zero to 1 year of age diagnosed by echocardiography and clinical evaluation.

Fifty infants with congenital heart disease were purposively selected for the study following inclusion exclusion criteria. After enrolment detailed history, presenting clinical features, age at first diagnosis, complication and immediate outcome of the cases were recorded to evaluate their clinical presentation. All the relevant data related were noted in a preformed datasheet by pre-tested semi structured questionnaire. Data were analyzed using Microsoft excel program and were presented as tables and figures.

RESULTS

Table I Shows this study was done over 50 children of CHD. Among them 62% cases were diagnosed within 6 months of age and 38% cases were between 7 to 12 months. Male patients were predominant (54%) and male female ratio was 1.17:1.

Table I: Distribution of CHD cases by age and sex (n=50).

Age group	Male n(%)	Female n(%)	Total n(%)
0-6 months	16 (51.6%)	15 (48.4%)	31 (62.00%)
7-12 months	11 (57.9%)	8 (42.1%)	19 (38.00%)
Total	27 (54%)	23 (46%)	50 (100%)

Table II Shows among 50 cases 35 (70%) were acyanotic heart lesions and 15 (30%) were cyanotic heart lesions. Among all structural defects VSD was predominant and present in 17 (34%), PDA in 15 (30%) cases, TOF in 7 (14%) and TGA in 6 (12%) cases.

Table II Distribution of cases by structural defects of CHD (n=50).

Structural Defect	Number (%)
Acyanotic	35 (70)
VSD	17 (34)
PDA	15 (30)
ASD	3 (6)
Cyanotic	15 (30)
TOF	7 (14)
TGA	6 (12)
TA with ASD	1 (2)
PS with VSD	1(2)

Table III Shows complaints of children with CHD showed cough in most cases (82%), dyspnoea in 80%, poor weight gain in 70%, feeding difficulty in 68% and fever in 58% cases.

Table III: Distribution of cases with CHD by presenting complaints on admission.

Complaints	No (%)
Cough	41 (82)
Dyspnoea	40 (80)
Poor weight gain	35 (70)
Feeding difficulty	34 (68
Fever	29 (58)
Bluish coloration of lips,fingers	15 (30)

Table IV Shows murmur was the most common (90%) presenting sign among children with CHD, followed by tachycardia (82%); cyanosis was reported in 30%, tender hepatomegaly in 28%, oedema in 12% and clubbing was found in 4% cases.

Table IV: Distribution of cases with CHD by presenting signs.

Signs	Number of child n (%)
Murmur	45 (90)
Tachycardia	41 (82)
Cyanosis	15 (30)
Hepatomegaly	14 (28)
Oedema	6 (12)
Clubbing	2 (4)

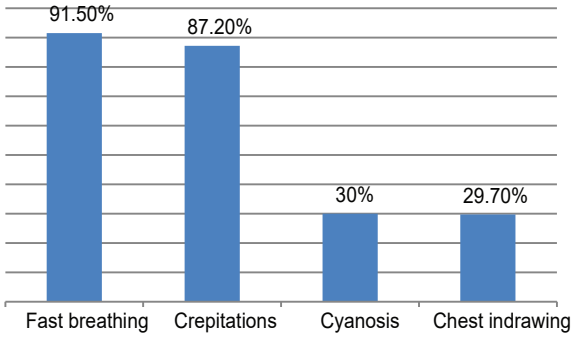

Figure 1: *Distribution of respiratory features among cases with CHD.*

Fig 1: Respiratory features were common, 47(94%) cases presented with various features of respiratory difficulties like fast breathing in 91.5%, crepitations in 87.2%, cyanosis in 30% cases, chest indrawing in 29.7% cases

Table V Shows among both age group 60% cases had history of more than two episodes of respiratory symptoms.

Table V: Distribution of cases with CHD of different age group by number of attack of respiratory problems (n=50)

Age group	Total Cases	No episode	≤2 episode	>2 episode
0- 6 months	31	3	11	17
7 - 12 months	19	0	6	13
Total n (%)	**50 (100)**	**3 (6)**	**17 (34)**	**30 (60)**

Table VI Shows among various complications with CHD, failure to thrive was detected in 76%, heart failure in 28% and pulmonary hypertension was detected by echocardiography in 34% cases.

Table VI : Distribution of cases with CHD by complication.

Complication	No (%)
Failure to thrive	38 (76)
Pulmonary hypertension	17 (34)
Heart failure	14 (28)

Table-IV shows spontaneous closure of CHD was detected in 8% cases, 14% underwent device closure and 8% cases died of which two cases were TGA, one was TOF and the other one was VSD with severe PS with renal mass.

Table-VII: Outcome of CHD in children (n=50).

	Advice for surgery &or conservative treatment	Closed Spontaneous n(%)	Device n(%)	Death n(%)
VSD (17)	14 (28)	3 (6)	0 (0)	0 (0)
PDA (15)	7 (14)	1 (2)	7 (14)	0 (0)
TOF (7)	6 (12)	0 (0)	0 (0)	1 (2)
TGA (6)	4 (8)	0 (0)	0 (0)	2 (4)
ASD (3)	3 (6)	0 (0)	0 (0)	0 (0)
TA with ASD (1)	1 (2)	0 (0)	0 (0)	0 (0)
PS with VSD (1)	0 (0)	0 (0)	0 (0)	1 (2)
Total n (%)	**35 (70)**	**4 (8)**	**7 (14)**	**4 (8)**

DISCUSSION

Diagnosis of Congenital heart disease at the earliest possible time and identifying the mode of presentation, complications and outcome is very important as early recognition referral and appropriate intervention could save the lives and reduce the risk of further complications.

In this study male patients were predominant (54%) and male female ratio was 1.17:1. Male sex preponderance in children with CHD was also found by Rahman et al.[6] Male female ratio of this study was very much consistent with another study in Bangladesh where it was reported as 1.3:1.[11]

This study found that 70% of CHD cases were acyanotic and 30% cases were cyanotic heart disease. VSD was the most common structural defects (34%) with PDA as the second common (30%), TOF was found in 14% cases, TGA in 12% cases and ASD in 6% cases. It correlates with the findings of Hussain et, al where acyanotic heart disease were found in three-forth cases among which VSD was the commonest acyanotic and TOF was the commonest cyanotic heart disease.[12] Hoque et al found VSD as the commonest CHD but Begum et al found ASD as the commonest CHD.[13,14] Structural defect of CHD varies depending upon age group; simple and potentially correctable heart defects like VSD, PDA and ASD are common at all ages.[10]

In the present study 62% of the cases presented within first 6 months of age and 38% were first diagnosed between 7 to 12 months. Many CHD may not be diagnosed during neonatal period or at the time of birth. About 30% CHD may die without a diagnosis, again in case of postnatal CHD who were discharged without a diagnosis, 35% became unwell or died by 6 weeks of age.[4,5]

The present study is almost consistent with the other study on presenting complaints of children with CHD.[11] As a presenting complaints cough was found in 82% cases, dyspnoea in 80%, poor weight gain in 70%, feeding difficulty in 68%, fever in 58% cases. Sharmin et al found dyspnoea in 60%, cough in 43.5%, poor weight gain in 41.7%, feeding problem in 26% cases.[11]

Cardiovascular examination revealed murmur in 90% and 10% of the children had no murmur but was diagnosed as CHD by clinical evaluation and echocardiogram. In contrast to the findings of this study much higher rate of absence of murmur (31.82%) in child with CHD was reported by Hoque et al and Anisworth et al (55.36%)[13,15] where the age group was limited to neonates only. Other common presenting signs among CHD cases were tachycardia in 82% children, cyanosis in 30%, tender hepatomegaly in 28% and oedema in 12%, which is also similar to sharmin et al showing cyanosis in 20%, and tachycardia in 37.4% and oedema in 10.4% cases.[11]

Out of 50 cases 47 cases presented with different respiratory features like fast breathing 91.5%, crepitation on auscultation in 87.2% and chest indrawing in 29.7% children. History of repeated respiratory tract infection was detected by Sharmin et al[11] in 34% cases and in this study in 60% cases which is higher than the previous study. Age group of children was different in two studies and rate is higher among infants below one year of age. Children with history of repeated respiratory tract infection should be sought out and screened for the possibility of CHD.

In this study complication due to CHD detected were failure to thrive in 76% cases, heart failure in 28% and various degree of pulmonary hypertension detected by echocardiography in 34% cases. Shah et al, stated that considering the age at presentation maximum number of children presented during infancy and failure to thrive was seen in 86.9% cases and heart failure in 46% cases.[16]

Six children had associated anomaly like Down syndrome, clubfoot, cleft lip/palate and hypothyroidism. All children with Down syndrome should be screened for CHD after birth. Babies with Down's syndrome were referred for early assessment and echocardiography, yet 34% remained undiagnosed by 6 weeks of age and 24% by 12 weeks.[5]

In the current study VSD were detected in 34% cases with various size. Among them large VSDs (17.65%) were referred for surgical closure, moderate and small sized VSD were reported in 47.06% cases and 17.65% cases were spontaneously closed during study period. VSDs can be closed spontaneously even up to 4 year of age.[17] Among the 15 cases of PDA 1(6.67%) case with small PDA was closed spontaneously, 7 (46.6%) cases had device closure and the rest 7 (46.6%) was on conservative management and advised for closure by one year of age. Fatema et al, found spontaneous closure in 29.16% VSD and in 33.3% PDA cases by first year of life.[18]

Among the outcome of CHD in children, spontaneous closure was detected by echocardiography in 8% cases and another 8% children died during the study period. Rest of the children was advised accordingly for surgery, intervention and medical management; among which 14% had device closure within the study period. Outcome of 70% cases could not be followed due to constrain of study period. Intervention was not possible in some of the children due to associated complications like failure to thrive, pulmonary hypertension and heart failure. Some patient left the hospital due to financial problem.

CONCLUSIONS

The modes of presentation of CHD are variable according to age, therefore high index of suspicion, early diagnosis, close monitoring and timely intervention is required for better outcome of children below one year of age. Detection and management of CHD below one year of age can prevent many complications and provide better prognosis of the disease.

ETHICAL ISSUE

This study was done with prior permission of the Directors of Shaheed Suhrawardy Medical College Hospital and National Institute of Cardiovascular Diseases. Informed written consent was taken from parents of the children. Anonymity of the participants and confidentially of information was maintained strictly.

CONFLICT OF INTEREST

We do not have any potential conflicts of interest.

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Original Article

Bone Mineral Density and Body Mass Index in Postmenopausal Women

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Abstract

Osteoporosis is a typical medical issue that overwhelmingly influences postmenopausal women. A bone density test is the only test that can diagnose osteoporosis before a broken bone occurs. The aims of this study was to find out the relationship between bone mineral density (BMD) and body mass index (BMI) in postmenopausal females. This cross sectional descriptive study was carried out in the Institute of Nuclear Medicine and Allied Sciences (INMAS), Sylhet. Study subjects comprised of 117 postmenopausal women between ages 45 to 85 years, with a mean age of 60.8 ± 9.2 years, who underwent BMD scan from January 2018 to June 2019. Duration of the study was 5 months (march 2019 to august 2019). BMD was measured by the Medilink Medix DR system. Findings of BMD of right femur showed osteopenia and osteoporosis (low BMD) in most of the women with under weight (81.0%) about one third (32.3%) of normal body weight and few (16.7%) of them over weight. Contrarily in left femur, low BMD was found in 08 (80.0%), 25 (40.3%) and 6 (16.7%) among underweight, normal, overweight patients respectively. According to BMI compare to the lumbar spine, low BMD was found in 48 (77.4%), 10 (100 %), 20 (55.6%), 03 (33.3%) among normal, underweight, overweight, and obese patients respectively. Relationship among BMD and BMI was found statistically significant in the both femurs ($p < 0.001$) and lumbar spine ($p = 0.02$). Low BMD was more severe in the 65-74 years' age group in both femurs 65.4% and 65-85 years' age group in lumbar spine 84.6% compare to other groups. The findings of this study reveal that low BMI and aging are associated with bone loss. Routine BMD checking in postmenopausal women might be important to initiate an early clinical intervention for osteoporosis.

Keywords: *Postmenopausal women, body mass index, bone mineral density test, DEXA.*

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INTRODUCTION

Natural menopause defined as amenorrhea for twelve successive months, for which no other clear pathological or physiological cause is perceived.[1] Since average life expectancy is increasing, women everywhere on the world currently have to spend almost one-third of their lives in menopause years.[2] The menopause happens in an average of 46 – 51 years in Bangladeshi female[3] with an average life expectancy of 72 years.[4] Studies have reported that Asian women have a higher tendency for osteoporosis contrast with the Caucasian partners.[5] The achievement of peak bone density in adolescent years and the rate of bone mass reduction during postmenopausal years are the important factors contributing to bone wellbeing in old females.[6] Around 35% of postmenopausal females lose bone mineral significantly during this period and are at a great risk for osteoporosis and fragility fractures later in life.[7] The decrease in ovarian estrogen production is the fundamental determinant of this imbalance, but estradiol serum levels clarify just a little proportion of inter-individual variance of BMD and bone loss. BMI is used to categorize the different level adiposity and measures body mass composition more exactly than weight alone. Obesity influences numerus sequelae of menopause including bone mineral density. Increasing body mass also affects weight bearing on the muscles that influence bone formation.[8] Many other factors seem to be involved, such as age, lean and fat mass, race, genetic factors, exercise, and smoke. The reason for this study was to find the relationship between BMI and BMD in postmenopausal women for early diagnosis of low bone density to reduce the effect of osteoporosis.

MATERIALS AND METHODS

This retrospective study was conducted in the Institute of Nuclear Medicine and Allied Sciences (INMAS), Sylhet. Study subjects comprised of 117 postmenopausal women between ages 45 to 85 years, with a mean (± SD) age of 60.8 (± 9.2) years, who were investigated BMD test from January 2018 to June 2019. The following inclusion criteria were used: age more than 45 years, natural menopause without hormone replacement therapy. Exclusion criteria were surgical menopause, taking steroid, history of bony trauma. Medilink Medix DR system was used to measure the BMD in the lumbar spine at the level of L1 to L4, right and left femur by a technician, and the interpretation was done by two nuclear medicine physicians. The output from the BMD examination includes images of the body part scanned, quantitative data from the scanned area including the bone mineral content (BMC), BMD, T-scores, and Z-scores, and a graph fitting the patient data to the reference population. The WHO criteria were used to groups the respondents based on BMD results[9]. Height was measured by measuring scale. Weight was measured by a weight machine. BMI was calculated from the weight and height by the formula weight (kg)/ [height (m)]^2. First, the variables were analyzed in descriptive means and standard deviations. For continuous variables, including mean ± standard deviation (SD), and categorical data were presented as count and percentage (%). Chi-square test was used for statistical analysis. The variables considered were age, BMI, and BMD. It was considered significant when P-value less than 0.05. We examined the relationship between BMD (T score) and BMI by bivariate Pearson's correlation for each study. Statistical analyses were done by IBM SPSS Statistics 25.

RESULTS

Table I Shows the study population consisted of 117 postmenopausal women. Age ranged from 45 to 85 years. The mean and standard deviation of age was 60.82 ± 9.22 years. The mean and standard deviation of lumbar spine T-score, right femur T-s core, and left femur T-score were-1.95 ± 1.60, -0.44 ± 1.23, and - 0.50 ± 1.3 respectively. The mean and standard deviation of BMI was 24.04 ± 4.23 kg/m^2

Table II Shows in this study, the respondents were grouped into four age groups. Around 45.3 % in the study were in the age group of 55-64 years. Approximately 53.0 %, 30.8% and 8.5% of the study subjects were normal, overweight and underweight respectively. A detailed depiction is given in .

Table I: General traits of the participants (mean ± standard deviation)

	Min	Max	Mean ± SD
BMI	15.11	38.21	24.04 ± 4.23
Age (in years)	45.00	85.00	60.82 ± 9.22
Right Femur T-score	-4.70	2.50	-0.44 ± 1.23
Left Femur T-score	-4.20	2.40	-0.50 ± 1.3
Lumber Spine T-score	-5.50	2.20	-1.95 ± 1.60

Table III Shows this study also showed that about 2.6%, 5.1% and 39.3% had osteoporosis in the right femur, left femur and lumbar spine, respectively. The postmenopausal women suffered from osteopenia in the right femur, left femur and lumbar spine of about 26.5 %, 8.2% and 29.9% respectively. According to BMI, around 100%, 100% and 66.7% obese subjects had normal BMD in right femur, left femur and lumbar spine respectively. In contrast to that, around 20%, 30% and 90% underweight subjects had osteoporosis in right femur, left femur and lumbar spine respectively. A detailed description is given in

Table II: Distribution of study subjects according to age and BMI.

Variables		Group	Number	Percentage
BMI	Underweight	10	8.5	
	Normal	62	53.0	
	Overweight	36	30.8	
	Obese	09	7.7	
Age (in Years)		45-54	25	21.4
	55-64	53	45.3	
	65-74	26	22.2	
	75-85	13	11.1	

Table IV Shows for additional analysis, the entire group based on the DEXA scan was grouped as low BMD and

Table III: Distribution of bone mineral density according to independent factors for lumbar spine and right femur

Independent factors		Status of bone mineral density		
		Normal N (%)	Osteopenia N (%)	Osteoporosis N (%)
Right Femur				
BMI	Underweight	2 (20.0)	6 (60.0)	2 (20.0)
	Normal	42 (67.7)	19 (30.6)	1 (1.6)
	Overweight	30 (83.3)	6 (16.7)	0
	Obese	9 (100)	0	0
Age (in Years)	45-54	24 (96.0)	1 (4.0)	0
	55-64	44 (83.0)	9 (17.0)	0
	65-74	9 (34.6)	15 (57.7)	02 (7.7)
	75-85	6 (46.2)	6 (46.2)	1 (7.7)
	Total	83 (70.9)	31 (26.5)	3 (2.6)
Left Femur				
BMI	Underweight	2 (20.0)	5 (50.0)	3 (30.0)
	Normal	37 (59.7)	23 (37.1)	2 (3.2)
	Overweight	30 (83.3)	5 (13.9)	1 (2.8)
	Obese	9 (100)	0	0
Age (in Years)	45-54	23 (92.0)	2 (8.0)	0
	55-64	41 (77.4)	11(20.8)	1(1.9)
	65-74	9 (34.6)	15 (57.7)	02 (7.7)
	75-85	5 (38.5)	5 (38.5)	3 (23.1)
	Total	78 (66.7)	33 (8.2)	6 (5.1)
Lumbar spine				
BMI	Underweight	0	1 (10.0)	9 (90.0)
	Normal	14 (22.6)	22 (35.5)	26 (41.9)
	Overweight	16 (44.4)	10 (27.8)	10 (27.8)
	Obese	6 (66.7)	2 (22.2)	1 (11.1)
Age (in Years)	45-54	10 (40.0)	10 (40.0)	5 (20.0)
	55-64	20 (37.7)	18 (34.0)	15 (28.3)
	65-74	4 (15.4)	5 (19.2)	17 (65.4)
	75-85	2 (15.4)	2 (15.4)	9 (69.2)
	Total	36 (30.8)	35 (29.9)	46 (39.3)

normal BMD. We considered osteopenia and osteoporosis as low BMD and rest as normal BMD. About 34 (29.1%), 39 (33.3%) and 81 (69.2%) subjects low BMD in right femur, left femur and lumbar spine respectively. Statistically significant association (p= <0.001) was found between different age groups and low BMD in the right femur, left femur but lack of association in lumbar spine (p =0.08). According to BMI compare to the right femur, low BMD was found in 08 (80.0%), 20 (32.3%), 06 (16.7%) among underweight, normal and overweight patients but all the obese patient had normal BMD. Contrarily in left femur, low BMD was found in 08 (80.0%), 25 (40.3%), 06 (16.7%), 0 among underweight, normal, overweight and obese patients. According to BMI compare to the lumbar spine, low BMD were found in 48 (77.4%), 10 (100 %), 20 (55.6%), 3 (33.3%) among normal, underweight, overweight, and obese patients respectively. Association between BMD and BMI was found statistically significant in the right femur ($p < 0.001$), left femur ($p < 0.001$) and lumbar spine ($p = 0.02$). Low BMD was more severe in the 65-74 years' age group in both femurs (65.4%) and 65-85 years' age group in lumbar spine (84.6%) compare to other groups. The details are depicted in

Correlation of BMI with right femur T score and lumbar spine T score were measured by Pearson's correlation

Table IV: Association between independent factors and bone mineral density

Independent factors		Status of bone mineral density		P-value
		Normal N (%)	Low BMD N (%)	
		Right Femur		
BMI	Underweight	2 (20.0)	8 (80.0)	<0.001
	Normal	42 (67.7)	20 (32.3)	
	Overweight	30 (83.3)	6 (16.7)	
	Obese	9 (100)	0 (0)	
Age (in Years)	45-54	24 (96.0)	1 (4.0)	<0.0001
	55-64	44 (83.0)	9 (17.0)	
	65-74	9 (34.6)	17(65.4)	
	75-85	6(46.2)	7(53.8)	
	Total	83 (70.9)	34 (29.1)	
		Left Femur		
BMI	Underweight	2 (20.0)	8 (80.0)	<0.001
	Normal	37 (59.7)	25 (40.3)	
	Overweight	30 (83.3)	6 (16.7)	
	Obese	9 (100)	0 (0)	
Age (in Years)	45-54	23 (92.0)	2 (8.0)	<0.0001
	55-64	41 (77.4)	12 (22.6)	
	65-74	9 (34.6)	17(65.4)	
	75-85	5(38.5)	8(61.5)	
	Total	78 (66.7)	39 (33.3)	
Lumbar spine				
BMI	Underweight	0 (0.0)	10 (100)	0.02
	Normal	14 (22.6)	48 (77.4)	
	Overweight	16 (44.4)	20 (55.6)	
	Obese	6 (66.7)	3 (33.3)	
Age (in Years)	45-54	10 (40.0)	15 (60.0)	0.08
	55-64	20 (37.7)	33(62.3)	
	65-74	4(15.4)	22(84.6)	
	75-85	2 (15.4)	11 (84.6)	
	Total	36 (30.8)	81 (69.2)	

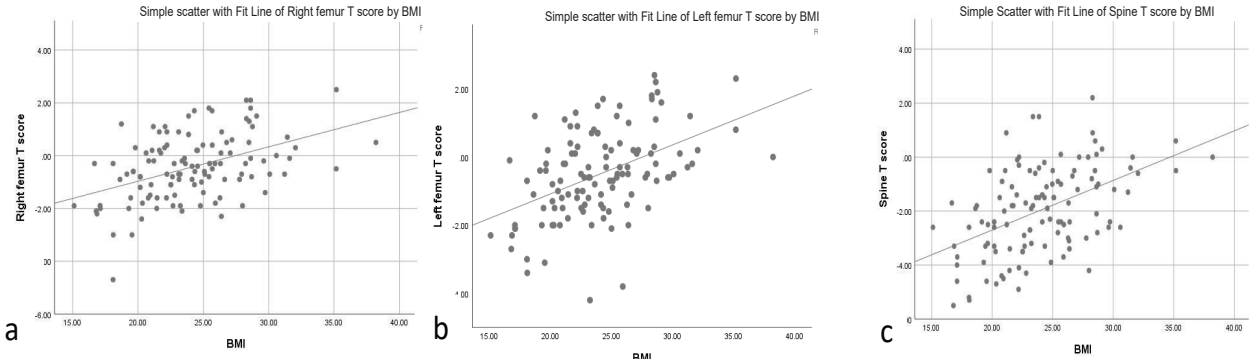

Figure 1: *Scatter diagram demonstrating a positive correlation between BMI (kg/m2) and T score of the right femur(a), left femur (b) and lumbar spine (c)*

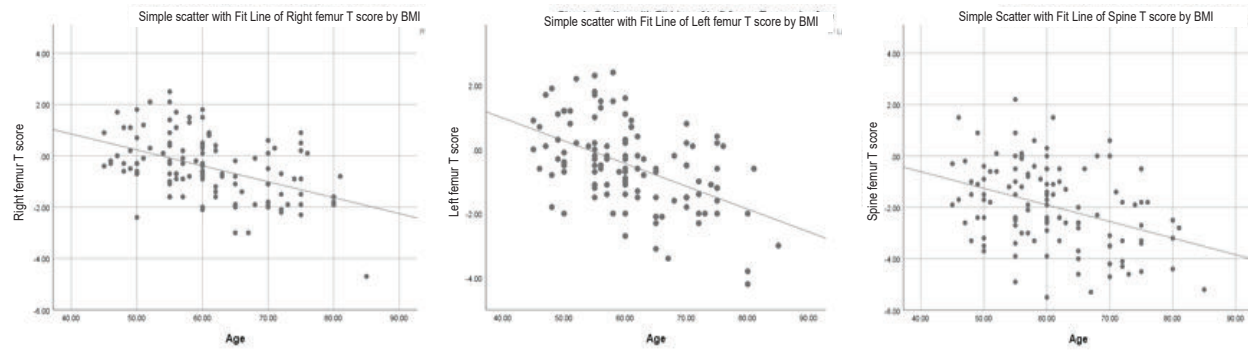

Figure 2: *Scatter diagram displaying a negative correlation between age and T score of the right femur (a) left femur (b) and lumbar spine (c)*

coefficient test. Positive significant Pearson's correlation was observed between BMI with right femur T score (r= 0.448; p=<0.001) fig-1a, left femur T score (r= 0.469; p=<0.001) fig-1b and BMI with lumbar spine T score (r=0.485, p <0.0001) Fig -1c. Pearson's correlation coefficient test showed inverse relationship between age and BMD both right femur (r =-0.464, p < 0.0001) fig 2a, left femur (r =-0.503, p < 0.0001) fig 2b and lumbar spine (r =-0.371, p < 0.0001) fig 2c.

Statistically significant difference (p <.0001) was found between right femur and left femur T score.

DISCUSSION

Osteoporosis is characterized as systemic skeletal disease described by low bone mass and micro-architectural deterioration of bone tissue, with a resulting increment in bone fragility and the risk of fracture.[10]

World Health Organization (WHO) criteria of osteoporosis (based on T-score) were used to evaluate the BMD status of the study population. Here normal BMD classified as T-score ≥-1, low bone mass (osteopenia) as T-score <-1and >-2.5 and osteoporosis as T-score ≤-2.5.

According to Classification by WHO, BMI below 18.5 kg/m^2 is considered underweight; a BMI between 18.5 and 24.99 Kg/m^2 is the ideal weight range; a BMI between 25 and 29.99 kg/ m^2 is classified as overweight; a BMI equivalent to or greater than 30kg/m^2 is obese. (Giles, 2008).[11]

In our study, among 117 study subjects regarding BMI 30.8% were overweight, 7.7% were obese, 8.5% were underweight and the rest 53.0% had normal BMI. Mean (±SD) BMI was 24.04 (±4.23) with a range of 15.11-38.21 kg/m^2 which is slightly different from Samira et al [12] which may be due to geographical variation of the study population.

In the current study statistically positive correlation of BMD with BMI was found both in the right femur T score (r= 0.448; p=<0.001), left femur T score (r= 0.469; p=<0.001) and lumbar spine T score (r=0.485, p <0.0001). The findings of this study are similar to that of the previous studies.[12-16,20] It was additionally seen that nobody had a

normal BMD value at lumbar spine in underweight group. Then again, in the overweight group 44.4%, 83.3% patients had normal BMD value at lumbar spine and both femoral neck respectively which showed statistically significant differences (P<0.001). These results are consistent with previous studies that reported increased BMD in overweight group may be due to the secretion of bone active hormones such as leptin and estrogen from adipocytes and insulin, amylin and pectin from pancreatic beta cell.[13,15]

In the present study, the inverse relationship was observed between age and BMD at right femur (r =-0.464, p < 0.0001, left femur (r =-0.503, p < 0.0001) and lumbar spine (r =-0.371, p < 0.0001). Very much comparative findings were observed in past various studies. Results showed low bone mass with advancing age in those studies [13-16]. However, there were no statistically significant difference (p =0.08) in different age groups and BMD category. The age-related decay of ovarian estrogen production and muscle strength may be responsible for low bone mass in those women.[2,15] BMD test is utilized to evaluate the strength of bone whereas BMI demonstrate the nutritional status of an individual.[15,16] BMI is a major determinant of BMD. BMI and femoral neck BMD observed was positively correlated in a cross-sectional study directed among postmenopausal women by Steinschneider et al (2003)[17]. The positive correlation between overweight and bone mass could be due to the influence of estrogen and mechanical load on skeleton [2,13,20].

Nguyen et al. [18] and Baheiraei et al.[19] additionally reported the consistent finding that lower BMD was related with lower BMI. The negative effect of low body weight on BMI is a decent marker for measurements of BMD.

CONCLUSIONS

In postmenopausal women with propelling age, risk of osteoporosis increases with the diminishing BMD. When BMI increases, BMD increases with decreasing risk of osteoporosis. A better comprehension of the relation between BMD and BMI provides an opportunity for early intervention and treatment to prevent fracture which includes life style modification in the form of exercise, supplementation of calcium and vitamin D, fall prevention along with anti-resorption therapy when needed. Maintenance of adequate body mass is important for prevention of postmenopausal bone loss.

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Original Article

Clinico-Histopathological Consistency in Dermatological Diseases

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Abstract

Skin biopsy for histopathology is the most reliable investigation for diagnosis of skin diseases. The main purpose of skin biopsy is to confirm clinical diagnosis but dermatologists usually looking for the concordance with histopathological report. The aim of the study was to observe the consistency of clinical and histopathological diagnosis of skin diseases. An observational study was conducted on 630 patients that undertaken skin biopsy and that was performed at the Department of Dermatology and Venereology, Bangabandhu Sheikh Mujib Medical University from January 2018 to January 2019. Patients who were advised for biopsy by outpatient and inpatient department and the biopsy was done accordingly was included in the study. Finally the inclusion was confirmed when the histopathological report was available. Demographic information, clinical diagnosis, type of biopsy procedure, types of specimen taken and send for histopathological procedure and the histopathological diagnosis was noted in data collection sheet. Histopathological diagnosis and its correlation with clinical diagnosis was assessed for consistency and it was the main outcome measure of the study. The mean age of patients on whom biopsy was performed was 35.14 ±16.57 years and the age range was 5-82 years. Male patients outnumbered female and the male to female ratio was 1.15: 1. Three types of biopsy were performed among them incisional biopsy was the commonest type (93.5%). In most of the cases collected specimen was skin 94.76%, others type of specimens were mucous membrane 2.6%, nail matrix 1.9% and 0.6% specimen was hair follicle. Among the cases 71.43% was diagnosed clinically. The common clinical diagnosis in which biopsy was done was psoriasis and its types 17.77%, lichen planus and its variants 14.12%, the connective tissue diseases 6.19% and infectious diseases 5.39%. In 79.52% cases histopathological diagnosis was done and 68.22% diagnosis was consistent with the clinical diagnosis. The maximum clinico-pathological concordance was found in vesiculo-bullous disease 93.33%. Then connective tissue diseases 79.48%, vasculitides 75% and lichenoid diseases 73.56%. Skin biopsy is a conclusive tool to overcome diagnostic dilemmas in dermatological diseases. The clinico-pathological concordance is assumed lower than the expectation of dermatologists but the collective efforts of dermatologists and pathologists can improve the capacity of diagnosis of biopsy samples.

Keywords: *Skin biopsy, histopathological diagnosis, clinico-histopathological consistency,*

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INTRODUCTION

In dermatology skin biopsy is a valuable surgical procedure. It plays a deciding role in dermatological practice when it needs to confirm the clinical diagnosis, exclusion of multiple differential diagnosis and when there is no responses of treatment. Though it is an invasive surgical procedure a well-equipped operation theatre required to perform that procedure. The aim of this biopsy procedure is to collect specimen for routine histo-pathology, immunohistochemistry, direct immuno-fluroscent test (DIF), PCR test and electron microscopy.[1] Skin, nail matrix, mucous membrane and hair follicle are the target specimen that are usually collected in dermatology operation theatre (OT). Various methods and types of skin biopsy are practiced according to the lesions and site of diseases. Skin biopsy and histopathology is a time consuming procedure and somewhat inconvenient to the patients because it needs at least 3 working days in histopathology department to get a report and another visit will require at least 7 days to stitch off the biopsy site.[2] The pre-biopsy evaluation includes history of any hypersensitivity to local anesthetics, any history of needle

phobia, review of any bleeding disorders, recent use of any anticoagulant and history of any bleeding tendency. Site selection for biopsy is the first step at operation theatre followed by skin sterilization and injection of local anesthesia.[3] After thoroughly wash the area with chlorhexidine or povidone iodine or alcohol swab the xylocaine 1-2% solution is injected to make the site painless. In some occasions epinephrine (1:100000) is used as an additive for reducing the bleeding at operational site and sodium bicarbonate (8.4%) can add to increase pH and reducing pain.[4,5] The precaution is needed to control adverse effects like hypersensitivity of anesthetic, pain, bleeding, infections and scarring. Various type of skin and soft tissue biopsy are practiced in dermatology incisional, excisional, punch, shave and curettage techniques are applied as per need.[6] Collected specimen by biopsy is sent for histopathology with appropriate preservative and well labelled container. Formalin is usually used as fixative for routine histopathology specimen, normal saline is used for DIF and Michael's medium is rarely used for long distance transport.[7] Boyd AS et al. had proposed 5 categories of information while sending the specimen to dermatopathologists all of that beginning with the letter 'D'. The 5 Ds included description of specimen, demographics, duration, diameter, and diagnosis. They hoped that the inclusion of this information will assist in their accurate interpretation.[8]

MATERIALS AND METHODS

The study was conducted on 630 patients who were advised for skin biopsy and was performed that accordingly at the department of Dermatology & Venereology or with referred from other department Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh. The duration of that observational study was from January 2018 to January 2019 with included all the cases to whom biopsy was performed and histopathological report were found. Age of patients, sex, clinical diagnosis, type of biopsy done, type of specimen collected and advised for histopathological process was observed and documented in a data collection sheet. In case of clinical diagnosis where only description of lesion was found was grouped as 'not diagnosed clinically'. In case of multiple differential diagnosis the first was taken as 'clinical diagnosis' for descriptive analysis but it was defined as 'consistent' with histopathological diagnosis when any one of the differential diagnosis was matched. The cases were excluded from the study if there any incomplete demographic, clinical, procedural information and lacked of histopathological report.

RESULTS:

After skin biopsy was done according to instruction 630 patients was traced with histopathological report

Table I Shows incisional biopsy was performed on maximum patients (93.5%). Fewer of them was selected for punch and excisional biopsy.

Table I: Distribution of patients according to the types of biopsy

Type of biopsy	Frequency	Percent
Punch	21	3.3
Incisional	589	93.5
Excisional	20	3.2

Table II Shows the most common specimen was taken by biopsy was skin (94.76%). Nail matrix, hair follicle and mucous membrane was the other types of specimen that was collected for histopathology.

Table II: Types of specimen was taken for histopathology:

Specimen	Number	Percent
Skin	597	94.76
Nail matrix	12	1.90
Hair follicle	4	0.60
Mucous membrane	17	2.60

Table III Shows all the specimen collected by biopsy was sent for routine histopathological processing (H & E staining) and fewer of them were sent for DIF (1.74%) and immunohistochemistry (0.31%) test along with routine test.

Table III: Distribution of patients according to types of histopathological test

Type of histopathological test	Frequency	Percent
Routine histopathology (H&E)	630	100
Direct immunofluroscent test (DIF)	11	1.74
Immunohistochemistry (IC)	2	0.31

Table IV Shows the mean age of patients was 35.14 (±16.57) years. The youngest one was 5 years old and the eldest one was 82 years. Only 14.3% patients was in pediatric age group (age below 18 years) and 85.7% was adult and elderly patients. Majority of patients (174) was in the age group 21-30 years and the next major one was 31-40 years age group (121).

Table IV: Distribution of patients by age

Age group (years)	Frequency	Percentage
0-10	20	3.17
11-20	110	17.46
21-30	**174**	**27.61**
31-40	121	19.20
41-50	87	13.80
51-60	68	10.79
61-70	35	5.55
71-80	14	2.22
81-90	1	0.15
Mean age in years	35.14	
Standard deviation	±16.57	
Age range in years (5 to 82)	77	
<18 years of age	90	14.3
≥18 years	540	85.7

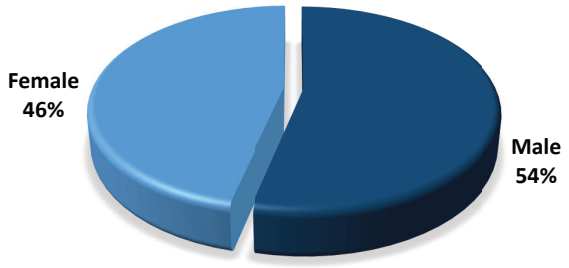

Figure I: *Distribution of patients according to sex.*

Male patients outnumbered female in that study and that was 338 (54%) and 292 (46%) respectively. The male to female ratio was 1.15: 1.

Table V Shows four hundred and fifty cases (71.42%) were diagnosed clinically and grouped as 31 categories and in 180 cases only clinical description were found in spite of diagnosis. Psoriasis was the commonest case that were undertaken biopsy. Lichen planus and variants and the connective tissue diseases were the next common diseases to whom biopsy was done.

Table V: Distribution of cases according to clinical diagnosis

Clinical diagnosis		Frequency	Percentage
1.	Psoriasis: Chronic plaque and other types	112	17.77
2.	Lichen planus and variants	89	14.12
3.	Connective tissue diseases	39	6.19
4.	Skin infections:	34	5.39
5.	Eczema/Dermatitis and variants	29	4.60
6.	Vasculitides	24	3.80
7.	Benign tumor/Lesions	18	4.44
8.	Autoimmune bullous diseases	15	2.38
9.	Cutaneous malignancy	15	2.38
10.	Neurocutaneous	11	1.74
11.	Pityriasis rubra pilaris	9	1.42
12.	Palmo-plantar keratoses	8	1.26
13.	Genodermatoses	8	1.26
14.	Error of metabolism	6	0.95
15.	Parapsoriasis	6	0.95
16.	Panniculitis	4	0.63
17.	Alopecia	4	0.63
18.	Keratosis pilaris	3	0.47
19.	Sarcoidosis	2	0.31
20.	Fixed drug eruption	2	0.31
21.	Granuloma annulare	2	0.31
22.	Arsenicosis	1	0.16
23.	Angiolipoma	1	0.16
24.	Behcets disease	1	0.16
25.	Chronic leg ulcer	1	0.16
26.	Hemangioma	1	0.16
27.	Lipodermatosclerosis	1	0.16
28.	Lichen sclerosus	1	0.16
29.	Oral erosion	1	0.16
30.	Progressive pigmentary dermatoses	1	0.16
31.	Pyogenic granuloma	1	0.16
32.	Clinically not diagnosed	180	28.57

Table VI Shows out of 630 biopsy specimen clinically and histopathologically diagnosed cases were 450(71.42%) and 501(79.52%) respectively. The chi-square statistic was 11.15 and the p-value was 0.0008 significant. With Yates correction chi-square statistic was 10.71 and the p-value was 0.001 which was significant (<0.05).

Table VI: Comparison of clinical and histopathological diagnosis

Diagnostic status	Clinically	Histopathologically	P value
Diagnosis done	450 (71.42%)	501 (79.52%)	<0.05*
Description given only	180 (28.57%)	129 (20.47%)	

*p-value obtained from chi-square test and it was significant

Table VII Shows the clinical and pathological diagnosis was most consistent in case of autoimmune bullous diseases (93.33%). Other diseases with higher clinico-pathological correlation was connective tissue diseases, vasculitides, lichen planus and variants and psoriasis and its types.

Table VII: Top ranked clinico-histopathologically consistent skin diseases

Disease group	Number of Clinically diagnosed cases	Number of Histopathologically diagnosed cases	Percent of clinico-histopathological consistency
Autoimmune bullous disease	15	14	93.33%
Connective tissue disease	39	31	79.48%
Vasculitides	24	18	75.00%
Lichenoid disease	87	64	73.56%
Psoriasis and types	112	79	70.53%

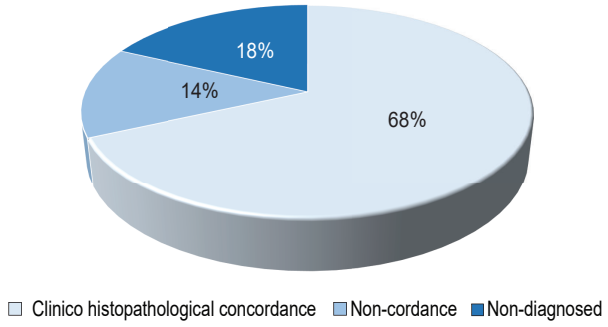

Figure II: Clinical and histopathological concordance in biopsy specimen

Four hundred and fifty cases were clinically diagnosed out of them Clinical and histopathological consistency was found in 307(68.22%) cases. Histopathologically diagnosed but non-consistent with clinical diagnosis was in 14% cases and no diagnosis was done histopathologically in 18% cases.

DISCUSSION

In dermatological practice skin biopsy is the most reliable procedure of diagnosis worldwide. To conclude in a diagnosis from multiple differential diagnoses or when there is no response with usual treatment and some occasion for research purpose skin biopsy is advised. In our study duration on an average 780 patients were attended at outpatient department of dermatology daily and only around 7 skin biopsy was performed per day the percentage was 0.08%. That figure proves the great efficiency of our dermatologists as they manage more than 99% of skin cases with clinical diagnosis. The mean age of patients to whom biopsy was performed was 35.14 ±16.57 years. Mode was 30 years and median was 32 years. Minimum age of patient was 5 and the maximum age was 82 years. Among them 14.3% was pediatric age group and the rest of them (85.7%) was adult. The majority of the patients (27.61%) was in 21-30 years age group. In a similar study regarding skin biopsy the mean age of

patients was 54.58±0.26 and the median 57 years.[9] The patients of that study were more elderly than our patients. Regarding gender issue the difference was not so wide but male outnumbered the female. There were 54% cases were male and 46% were female and male to female ratio was 1.15: 1. Corfitis et al. found that in their study on 5941 patients 48.2% were males and 51.8% Females therefore female outnumbered the male. That findings was not similar with us. Another similar study in performed in India showed that their male to female ratio was 1.16: 1 and majority (36%) of patients undertaken skin biopsy was in 16-30 years of age group.[10] Their findings were similar to us. There were three types of biopsy was done the majority of them were incisional biopsy (93.5%). Excisional biopsy was done on 3.2% cases when the diagnosis was the changing mole, Basal cell carcinoma and pyogenic granuloma. Punch biopsy was done on 3.3% cases majority was in mucous membrane involvement. In a similar retrospective study on 403 patients the investigators had conducted 73% incisional biopsy, 7.7% excisional biopsy and 19.4% punch biopsies on skin.[11] they had performed incisional biopsy as in majority of cases like our study. Single or multiple differential clinical diagnosis was found in 71.42% cases and the clinical description was found in rest of the (28.57%). Total 95 different types and sub types of diagnosis was recorded. They were classified as 32 grouped and ungrouped categories for analysis. The most common cases to whom biopsy was done was psoriasis and its sub types. A total 112 (17.77%) cases was of psoriasis category. The next common cases were lichen planus and its variants 89 (14.12%), Connective tissue diseases 39 (6.19%), infectious diseases 34 (5.39%), eczematous or dermatitis 29 (4.6%) and vasculitides 24 (3.8%). Malik et al. in a study on 2216 biopsies had shown that their common clinical diagnosis were leprosy (18%), lichenoid diseases (14.57%), psoriasis and types (6.85%) and eczema or dermatitis were 3% of all dermatoses. [10] Another study conducted in Greece with 6816 patients of biopsy they found that the common clinical diagnosis were the cutaneous malignancy (19.28%), papulosquamous diseases (12.13%), nevi (10.51%), dermatitis (8.4%) and the miscellaneous diseases was 22.49% of total dermatoses.[9] that two study had some similarity and some dissimilarity with our study. In a study of Greece malignant skin diseases are the commonest case for biopsy because of their white skin on the other hand in India leprosy is still a major burden of skin diseases but in our community psoriasis and psoriasiform skin lesions are the main concern for biopsy. Question might be raised why psoriasis was at the top of the list though it is a common and easily diagnosable disease? It could be due to treatment failure, relapse, flare and research purpose. The clinical diagnosis were found in 71.42% cases and that was confirmed by histopathological reports. In total 79.52% cases conclusive histopathological diagnosis was done and in 20.48% cases there was only description was found. That difference was significant statistically (p-value <0.05%). In 68.22% cases the histopathological diagnosis was consistent with clinical diagnosis. The clinic-pathological concordance was found 68% by Korfitis et al., 71% by Venugopal et al. and 76.8% was found by Aslan et al. in different but similarly designed studies. Their findings were nearer to our study.[9,10,11] The clinico-histopathological consistency was higher in studies conducted by Yap et al. and Gupta et al. they found the correlation were 86.8% and 85.8% respectively. [12,13,] The consistency rate was found lower than our findings in the studies of Malik et al. (61.01%) and by Balasubramanium et al. (59.80%).[14,15] The consistency rate was highest in where the pathologists had made the report with consulting the dermatologists who were responsible with the case. In current study the clinico-histopathological consistency was highest in autoimmune bullous disease (93.33%). The next higher consistency was found in Connective tissue diseases (79.48%), Vasculitides (75%), Lichen planus (73.56%) and Psoriasis (70.53%). In a similar study the clinico-pathological correlation was highest in Genodermatoses (100%). The next common consistent cases were autoimmune bullous diseases (79.01%), environmental dermatoses (73.3%) and the inflammatory dermatoses (72%). George et al. found the clinico-pathological correlation 100% in leprosy, 90.3% in morphea, 85.3% in psoriasis and 82.7% in vesiculo-bullous diseases in a study on 800 cases.[16] The rate of correlation is different in various study cause might be the wide variety of dermatological diseases and lot of factors involved in country to country.

CONCLUSIONS

Skin biopsy is an invasive procedure to diagnosis of clinically unsettled cases of dermatology. In dermatological perspective clinico-pathological consistency is needed to take decision for patient management. But the rate of concordance is lower than expectation. A coordinated and collaborative effort of dermatologists and the pathologists could improve the rate of diagnostic consistency. A large scale, multi-centric and long duration study would be more conclusive in that regards.

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Original Article

The Concentration of 25-Hydroxy Vitamin D in Chronic Liver Disease and its' Correlation with Severity

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Abstract

Chronic Liver Disease (CLD) is a common disease all over the world and the major biological factors are Hepatitis B virus (HBV) and Hepatitis C virus (HCV) in Bangladesh and Alcoholic liver disease in the western world. Life expectancy of CLD patient is increasing now a days by available modern treatment; but the long term complications are now evident. Hepatic osteodystrophy is one of the most common complication which is associated with vitamin D deficiency. Vitamin D undergoes hepatic 25-hydroxylation, but as the hepatic parenchyma is jeopardized so the metabolic activation of this vitamin is impaired. The aim of the study was to measure the concentration of 25-hydroxy vitamin D 25(OH) D in CLD patient in different etiology and to find out the relationship of level of 25(OH) D in different stages of the disease according to Child-Pugh classification. This cross sectional study was carried out in the Department of Gastroenterology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka during the period of April 2015 to March 2016. Patients attending the Gastroenterology Department with cirrhosis of liver and who fulfilled the inclusion criteria were initially enrolled for the study. Study objectives were explained and informed consent was taken from patients prior to record their clinical history, examination findings and initial investigation reports in the standard data sheet. The diagnosis of liver cirrhosis was made by combination of clinical features, blood profile and trans abdominal ultrasonography (T. USG). Endoscopy of the upper GIT was also done to see the presence of oesophageal or gastric varices which is a sign of increase portal pressure. Stages of CLD were assessed by Child-Pugh scoring system and level of 25(OH) D was measured from blood with the help of the Department of Bio-chemistry. Data was collected using a structured data sheet and analyzed by SPSS. Out of 85 patients, male-female ratio was 3:1 and mean age was 53.0 ± 10.7 year within the range of 25-70 years. Most of the patients had acites 92.9% and anorexia 90.6%; where four-fifth patients had weight loss and more than one third had Jaundice. Nearly half of the patients had abdominal pain and 42.4% had melaena. Four-fifth patients had history of blood transfusion and most of them had H/O hospitalization 94.8%, anaemia (97.6%) and Splenomegaly 92.9%. More than half (52.9%) of patients had bone pain; where jaundice 61.2% and Leukonychia 61.2% were detected in equal number of patients. Mean vitamin 25(OH) D was 16.29 ± 7.96 in 69 HBV patients and 20.14 ± 9.76 in 16 HCV patients. In this study, 28.2% patients were in child Pugh A, 36.4% in child Pugh B and 32.9% in child Pugh C stages. Mean vitamin 25(OH) D were 27.12 ± 6.11, 15.97 ± 5.40 and 9.57 ± 1.15 in Child-pugh A, Child-pugh B and Child-pugh C stages respectively. Mean vitamin 25(OH) D was observed at decreased level as the changes of stage from lower to higher. Vitamin D deficiency was highly prevalent in patients with CLD and inversely correlated with disease severity. In the case of chronic liver diseases, vitamin D seems to modulate the innate and adaptive immune system, which explains the association. This study suggest that these parameters may improve with vitamin D supplementation. Monitoring of S. 25(OH) D is reasonable in CLD patient.

Keywords: *Avitaminosis, parathyroid hormone, portal hypertension, gastric varices, child-pugh a, child-pugh b and child-pugh c.*

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INTRODUCTION

Cirrhosis may be defined as a phase of chronic liver disease or insult leads to the diffuse destruction of hepatic parenchymal cell by fibrosis and the formation of nodules,

which results in disorganization of the liver's lobular and vascular architecture. In western countries, common causes are alcohol and in developing countries, chronic hepatitis B or C virus infection.[1] Cirrhosis may be compensated or decompensated when complicated by jaundice, ascites, and hepatic encephalopathy or raised prothrombin time. It is insidious. Initially asymptomatic later present with complication.[2] The final stage of chronic inflammation in the liver is cirrhosis. Liver cirrhosis gives rise to portal hypertension and complications such as bleeding esophageal varices, ascites and encephalopathy.[3] Though the disease is progressive, indolent and having many complications, but with the development of modern treatment modalities of cirrhosis of liver life span is increased. With the effective treatment long term complications are now commonly encountered.[4] It is a common complication among individuals with long standing hepatic disease. One study was conducted in the University of Tennessee Hepatology clinic, where 118 cirrhosis patients with different aetiology were included and their 25-hydroxy vitamin D level were measured. Severity was graded as mild (20-32 ng/ml), moderate (7-19 ng/ml) or severe (<7 ng/ml), normal being > 32 ng/ml. 25(OH) D is the only vitamin D metabolite that is used to determine whether a patient is vitamin D deficient, sufficient or intoxicated. The major circulating form of vitamin D is 25(OH) D that has a half-life of approximately 2-3 weeks.[5] The result showed vitamin D deficiency is universal (92 %) among patients with cirrhosis and at least one third of them suffered from severe vitamin D deficiency. Vitamin D is a fat soluble vitamin and helps in absorption of calcium from the renal tubule and intestine. Up to 93% of patients with chronic liver disease have insufficient vitamin D levels, and almost one-third of these show severe deficiency.[6] Other studies, such as Petta et al showed 73% and Bitetto et al showed level of vitamin D deficiency was 73% and 46.4% respectively.[7] Rode et al of Australia works with 158 patient where cirrhosis (n= 65) and no cirrhosis (n= 93). They categorize the patients in Viral (60), NASH (23), Alcoholic (22), Autoimmune (12), Haemochromatosis (9), Wilson's (2) Cholestatic (5) and others (25). The study outcome also suggest that patient with cirrhosis were more likely to be deficient in 25(OH) D (75%, P= 0.028).[8] Miroliace el al. of Iran, works with CLD patient where HBV (n=26), HCV (n=28), AIH (n=19), Cryptogenic (n=17) with 40 healthy controls. The main outcome is significantly higher prevalence of vitamin D deficiency in cirrhotic versus non-cirrhotic patient.[9] There are several causes for the deficiency of vitamin D in chronic liver disease. The important potential mechanisms are reduced exogenous exposure, intestinal malabsorption, reduced endogenous production of vitamin DBP and albumin in the liver, impaired hepatic hydroxylation of vitamin D to 25(OH) D and increased catabolic removal of 25(OH) D.[10] Lange et al in 2012 also worked with 269 patient and found 74% of the cirrhotic patient with vitamin D deficiency. So, all the studies showed vitamin D deficiency with a significant P value. Osteoporosis in CLD mainly affects trabecular bone. The way in which liver failure affects osteoblasts and contributes to the development of osteoporosis is unclear. Numerous growth factors, some of which affect osteoblast function, such as IGF-1 and TGF-p are synthesized by the liver.[11] The pathogenesis of osteoporosis in CLD is complex and poorly understood. Advanced liver disease and cirrhosis are associated with an increased prevalence of osteoporosis.[12] 25(OH) D is a summation of both vitamin D intake and vitamin D that is produced from sun exposure, the biologically active form of vitamin D is 1, 25(OH) D. But this is not the ideal measure for vitamin D status due to several reasons. The circulating half-life of 1, 25(OH) D is only 4-6 hours and this is thousand fold less than 25(OH) D. Besides this, when a person become vitamin D deficient, calcium absorption from the intestine and renal tubule will be less. So, a vitamin D deficient patient may have normal or elevated levels of 1, 25(OH) D due to increase level of PTH. This makes the assay useless as a measure of vitamin D status. The only way to determine whether a person is vitamin D deficient or sufficient is to measure their circulating level of 25(OH) D. Vitamin D deficiency was defined as serum 25(OH) D levels less than 20 ng/ml (50 nmol/L) and insufficiency is defined when the level is 31-20 ng/ml, for the general population.[5, 13] The-important potential mechanism that reduce the level of vitamin D is multifactorial and van among different liver pathologies. Vitamin D3, is primarily acquired endogenously through the photochemical conversion of 7-dehydrocholestrol to previtamin D3 in the skin and transported to the liver. On the other hand, vitamin D2 reach the liver from venous circulation for hydroxylation. After hydroxylation, it is converted to 25- hydroxivitamin D (25(OH) D and secreted in the circulation again mostly bound to DBF. Further hydroxylation to 1, 25-dihydroxivitamin D in the kidney converts the vitamin into its active form.[17] The radioimmunoassay and competitive protein binding assays for 25(OH) D are useful in detecting vitamin D deficiency.

MATERIAL AND METHODS

This cross sectional study was carried out in the Department of Gastroenterology, Bangabandhu Sheikh Mujib Medical University, Dhaka during the period of April 2015 to March 2016 to assess the concentrations of 25-Hydroxy Vitamin D in chronic liver disease patient and also to find out relationship with etiology and different stage of cirrhosis. A total 85 patients with cirrhosis of liver attending the Gastroenterology Department who fulfill the inclusion criteria were initially enrolled for the study. Only adult patients with liver cirrhosis age greater or equal to 18 years were included in this study; but patients with hepatocellular carcinoma, ongoing pregnancy, severe life threatening infection, deformity or fracture in any part of body, female took hormonal contraception or in postmenopausal periods, secondary cause associated with osteoporosis or affect BMD, chronic kidney disease, diabetes mellitus, history of endocrinal disease, metastatic bone disease or other malignancies, receiving vitamin D or calcium supplements, hormone replacement therapy, corticosteroids or any drug known to affect bone density were excluded. Their clinical history, examination and initial investigation report were noted in the standard data sheet. Prior to data collection both verbal and written consent was taken from the respondents. Data were collected using a preformed data collection sheet (questionnaire). Base line information was collected from the patient after exploration of different complaints. All information regarding clinical features were recorded in a data collection sheet. S. 25-hydroxy vitamin D wow done in the Department of Bio-chemistry, Bangabandhu Sheikh Mujib Medical University Dhaka Bangladesh. The diagnosis of liver cirrhosis was made by combination of clinical features, blood profile and transabdominal ultrasound. Endoscopy of the upper GIT was done to detect the presence of oesophageal or gastric varices. Transabdominal ultrasound demonstrated a shrunken liver with increase echogenicity, with or without splenomegally and presence or absence of ascites. Stages of liver disease were assessed by Child-Pugh scoring system. Level of 25(OH) D was measured from blood from the Department of Bio-chemistry. Data was collected using a structered data sheet and analysed by using softwere SPSS.

Data processing and analysis: After collection of data, all data were checked and cleaned. After cleaning the data, statistical analysis was done by using Statistical Packages for Social Sciences (SPSS). Numerical variables were expressed as mean and standard deviation, whereas categorical variables are count with percentage. Continuous variables were compared using Student's t test; categorical variables were analyzed by Chi-square test. A p-value <0.05 were considered as statistically significant. Association of serum vitamin 25(OH) D with etiology and severity were assessed by Chi-square test. The correlation between the serum 25-hydroxy cholecalciferol and other parameters were evaluated by Pearson's correlation test. Upper gastro-intestinal endoscopy were done using a standard forward viewing endoscope. In order to prevent contamination from another patient, after each procedure endoscope and biopsy forceps were disinfected using glutaraldehyde 2% (CIDEX) solution. Instruments were immersed in solution and kept for 15 minutes. Side channels were also rinsed.

Operational Definition:

Liver failure and the Child-Pugh classification: The final stage of chronic inflammation in the liver is cirrhosis. Liver cirrhosis gives rise to portal hypertension and complications such as bleeding esophageal varices, ascites and encephalopathy. Hepato-cellular failure results in hyperbilirubinemia, hypoalbuminemia and prolonged prothrombin time. The Child-Pugh classification is a scoring system used to assess the prognosis of cirrhosis.

Table : Child Pugh Score (Sherlock & Dooley, 2011)[1]

Assessment criteria	Points scored for abnormality		
	1	2	3
Encephalopathy grade	None	Mild	Marked
Ascites	None	Mild	Marked
Bilirubin (µmol/L)	<34	34-50	>50
Albumin (g/L)	>35	28-35	<28
Prothrombin Time (seconds prolonged)	< 4	4-6	>6
Or INR	< 1.7	1.7-2.4	>2.4
Individual scores should be added. Score <7 = Child's a 7-9 = Child's B >9 = Child's C			

Although it was originally used to predict mortality during surgery, it is now used to determine the prognosis, as well as the required strength of treatment and the necessity of liver transplantation. Scoring is based upon several factors: albumin, ascites, total bilirubin, prothrombin time, and encephalopathy

Survival in cirrhosis (Colledge et al. 2010)[18]

Child-Pugh grade	Survival in cirrhosis (%)			
	1 year	5 years	10 years	Hepatic deaths (%)
A	82	45	25	43
B	62	20	7	72
C	42	20	0	85

Limitations

1. Cross sectional study
2. Sample size was small
3. Study was carried out at a single point and it is not the actual reflection of total population.

RESULTS

This cross sectional study was carried out in the Department of Gastroenterology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka from April 2015 to March 2016 for a period of 1 year. A total of 85 patients with chronic liver disease were included in this study. The results were as follows:

Table-I Shows distribution of patients with CLD according to age. Maximum 36.5% patients were in age group 51-60 years followed by 23(27.1%), 16(18.8%) and 15 (17.6%) in >60, 41-50 and ≤ 40 years age group respectively. Mean age was 53.0 ± 10.7 years within the range of 25-70 years.

Table I: Distribution of patients with CLD according to age (n=85)

Age (years)	Frequency	Percentage
≤ 40	15	17.6
41-50	16	18.8
51-60	31	36.5
>60	23	27.1
Total	85	100.0
Mean ± SD	53.0 ± 10.7	
Range (Min – Max)	25 – 70	

Table-II shows distribution of patients according to gender. Male was predominant in this study. Male female ratio was 2.54:1

Table II : Distribution of patients with CLD according to gender (n=85)

Gender	Frequency	Percentage
Male	61	71.8
Female	24	28.2
Total	85	100.0

Table III show presenting complains of the CLD patients. More than 90.0% patients had ascites and anorexia. Eighty percent patients had weight loss and 71.8% patients had Jaundice. More than 40.0% patients had abdominal pain and melaena.

Table III: Presenting complain of the patients with CLD (n=85)

Presenting complains	Frequency	Percentage
Ascites	79	92.9
Jaundice	61	71.8
Abdominal pain	41	48.2
Haematemesis	33	38.8
Melaena	36	42.4
Anorexia	77	90.6
Weight loss	68	80.0
Fever	11	12.9
Pruritus	2	2.4

Table-IV shows history of past illness. Sixty (77.9%) patients had history of blood transfusion and 73 (94.8%) patients had previous hospitalization.

Table IV: History of past illness of the patients with CLD (n=85)

History of past illness	Frequency	Percentage
Blood transfusion	60	77.9
Previous hospitalization	73	94.8
Total	85	100.0

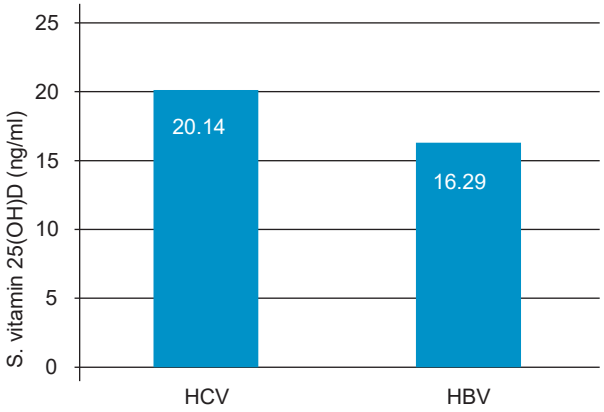

Figure-1: *Bar chart showing mean S. vitamin 25(OH)D in different aetiology stages of CLD.*

Figure 1 shows the s. vitamin 25(OH)D level in HCV and HBV. Mean vitamin 25(OH) D was 16.29±7.96 in 69 HBV and 20.14±9.76 in 16 HCV patients.

Table V shows the clinical features of the patients with CLD. Common clinical features anaemia, splenomegaly, leukonychia, jaundice, bone pain were found in 83 (97.6%), 79(92.9%), 52(61.2%), 52(61.2%) and 45(52.9%) of patients respectively. Others hepatomegaly, flapping tremor, ankle oedema, abdominal lump and lymphadenopathy were found in 32(97.6%), 23(27.1%), 8(9.4%), 5(5.9%) and 1(1.2%) of patients respectively.

Table V: Clinical features of the patients with CLD (n=85)

Clinical examination findings	Frequency	Percentage
Anaemia	83	97.6
Jaundice	52	61.2
Lymphadenopathy	1	1.2
Ankle oedema	8	9.4
Leukonychia	52	61.2
Flapping tremor	23	27.1
Bone pain	45	52.9
Splenomegaly	79	92.9
Hepatomegaly	32	37.6
Abdominal lump	5	5.9

Table VI shows level of s. vitamin 25(OH)D in different stages of CLD. Mean s. vitamin 25(OH)D was gradually decreased as the changes of stage from lower to higher. There was statistical significant difference in s. vitamin 25(OH)D among the different stages of CLD.

Table VI: S. vitamin 25(OH)D in different stages of CLD (n=85)

Stage	Mean ± SD	Range (Min – Max)	P value
Child-pugh A(n=25)	27.12 ± 5.98	19.60 – 43.50	
Child-pugh B(n=32)	15.97 ± 5.31	10.60 – 27.30	
Child-pugh C(n=28)	9.57 ± 1.15	8.20 – 13.00	
Analysis			
A vs B vs C			<0.001
A vs B			<0.001
A vs C			<0.001
B vs C			<0.001

DISCUSSION

In this study, males were predominant. Male female ratio was 2.54:1. Males were predominant and male female ratio was 2.70:1.[20] The male female ratio was in the range of 2.3:1 to 2.6:1 among the patients with cirrhosis and HCC.[21] All these results are similar to this study result. Male female ratio of patients with CLD in Malayasia was 4.4:1.[22] Maximum 36.5% patients were in age group 51-60 years followed by 23 (27.1%), 16 (18.8%) and 15 (17.6%) in >60, 41-50 and <40 years age group respectively. Mean age was 53.0 ± 10.7 years within the range of 25-70 years. Mean age of patients with CLD in Malayasia was 52 years which is almost similar to this study.[22] Regarding presenting complains, more than 90.0% patients had ascites and anorexia. Eighty percent patients had weight loss and 71.8% patients had Jaundice. Almost fifty patients had abdominal pain (48.2%) and melaena (42.4%). Haematemesis was present in 38.8% patients and fever was present in 12.9% patients. Dhole et al.[23] found jaundice in (73.0%), abdominal distension in (51.0%) and Ascites in (41.8%) Patients.[23] Ascites is more in this study compare to Dhole et al.[23] but other presenting complains are similar to Dhole et al. Regarding clinical examination findings of the CLD patients, most of the patients had anaemia (97.6%) and Splenomegaly (92.9%). More than 50.0% patients had jaundice (61.2%), Leukonychia (61.2%) and bone pain (52.9%). Hepatomegaly, flapping tremor, ankle oedema, abdominal lump and lymphadenopathy were present in 37.6%, 27.1%, 9.4%, 5.9% and 1.2% patients. Hepatomegaly was seen in 63% patients, splenomegaly was seen in 60% patients and anaemia in 56.0% patients.[23] In this study, anaemia and splenomegaly is more comparing Dhole et al. hepatomegaly was less comparing Dhole et al.[23] In this study mean s. vitamin 25(OH) D was 17.03 ± 8.41. Putz-Bankuti et al.[24] reveled mean 25(OH)D was 16.0 ± 9.2 ng/ml and Lange et al. (2011) revealed mean 25(OH)D was 17 ng/ml (range: 3-80).[24] Mean s. vitamin 25(OH) D was 16.29 ± 7.96 in 69 HBV patients and 20.14 ± 9.76 in 16 HCV patients. Mean s. vitamin 25(OH) D found in this study is almost similar to the above studies. Mean s. vitamin 25(OH) D was 7.65 ±4.19 in HBV patients which is less comparing these study.[15] Chronic hepatitis C virus (HCV) infection is one of the main causes of chronic liver disease; it is estimated to affect 130 to 150 million people worldwide, a significant number of whom also develop cirrhosis and hepatic cancer.[16] A high percentage of these patients (46% to 92%) have low vitamin D levels, and more than 25% suffer from severe deficiency.[7] It has been hypothesized that the high incidence of vitamin D deficiency in these patients may be caused by HCV's effect on direct or indirect 25-hydroxylation through cytokine induction or oxidativc stress,[28] and that the virus may suppress 25(OH)D levels due to a disruption in lipid metabolism; as shown a recent study where HCV decreases the production of 7-dehydrocholesterol, the endogenous precursor of vitamin D.[27] In this study, 28.2% patients were in child Pugh class A, 36.4% in child Pugh class B and 32.9% in child Pugh class C group. Majority of CLD patients 63.0% fall in child Pugh class A group, followed by 32.0% fall in child Pugh class B & 5.0% fall in child Pugh class C.[20] Child Pugh class B is similar in both studies but child pugh class A in higher and child pugh class C is lower in this study comparing.[20] Mean s. vitamin 25(OH) D were 27.12 ± 6.11, 15.97 ± 5.40 and 9.57 ± 1.15 in Child-pugh A, Child-pugh B and Child-pugh C stages respectively. Mean s. vitamin 25(OH) D was gradually decreased as the changes of stage from lower to higher. There were significant differences in s. vitamin 25(OH)D among Child Pugh scores with the highest levels in Child A and the lowest levels in Child C patients (Finkelmeier, 2015). The studies by Crawford et al.[26], Fisher et al.[19], Chen et al.[25] and Putz-Bankuti et al.[24] show that patients with severe cirrhosis (Child-Pugh class C) have approximately half the amount of serum 25-hydroxyvitamin D concentrations compared with patients with less severe cirrhosis (Child-Pugh class A).

CONCLUSIONS

In this study, 85 patients were enrolled and the mean S. 25(OH) D was 17.03 which was in the lower limit. The patients were also categorized according to severity with Child-Pugh classification and showed the level of vitamin D is inversely related to the severity of the disease.

RECOMMENDATION

A multicenter, population based with control and having a larger sample size study should be done. So that, it can be properly evaluated and will be more correct.

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Original Article

Comparison of the Ultrasonic Evaluation of Bi-Parietal Diameter and Femoral Length in 2nd and 3rd Trimester to Estimate the Gestational Age

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Abstract

During the gestational period, fetal biometrics are assessed through ultrasonography to observe the growth of the fetus. This study observed the corresponding of gestational age those were measured by two of the fetal diameters; gestational age were calculated from history of last menstrual period (LMP), in the last two trimesters. This descriptive type of observational study was carried out in the Department of Radiology and Imaging of Dhaka Medical College and Hospital, during the period of July, 2004 to June, 2005. Here 291 single-ton, non-complicated pregnant women of LMP were selected purposively from valid record. Bi-parietal diameter (BPD) and femoral length (FL) estimated through ultrasonography. These two parameters compared with the gestational age in second and third trimester. The study found that, before 36th week, the BPD based gestational age varied 2 to 3 days from LMP based gestational age and after that, the variation was 1 to 4 weeks. In case of FL, the ultrasonic measurement found to be 2 to 4 days backward in the second trimester and 2 to 3 days advance in the last trimester in contrast to the LMP based gestational age. In the second trimester, it has been found that, BPD has been the superior predictor of the gestational age than the FL with the correlation coefficient of 0.999 in case of BPD and 0.998 in case of FL when correlated with LMP based gestational age. Although, in third trimester, FL versus BPD predicted the gestational age with a correlation coefficient of 0.998 versus 0.978 respectively, when correlated with gestational age based on the history of LMP. This study has observed that, later in pregnancy, FL has the better predictability over BPD to determine the gestational age.

Keywords: *Gestational age, bi-parietal diameter (BPD), femoral length (FL), last menstrual period (LMP)*

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INTRODUCTION

Ultrasonic determination of the age of the fetus is one of the most common routine examination any women undergoes during the course of their pregnancy period. Accurate assessment of the gestational age and estimated delivery date are specifically important for those pregnant women who have gestational complication and who may need early intervention, as for example- early cesarean section or to identify growth restriction[1] also referred to as intrauterine growth restriction (IUGR History of LMP alone is quite undependable in these cases, as because there remain the chance of incorrect dating of the last menstruation and/or history of irregular menstruation.[2,3] Fetal age estimation as well as growth observation through diagnostic ultrasonography is widely dependent on fetal biometry.[4] Ultra-sonographic measurement of various fetal anatomic structures persistently remained the most constant method to determine the gestational age owing to its non-invasive technique and well tolerance of repetitive use.[5–7]67 twin, and 19 triplet gestations resulting from in vitro fertilization with ultrasonographic fetal biometry from 14 to 22 weeks made up the study population. A

gestational age prediction equation was derived from singletons with the use of stepwise linear regression. This equation was compared with 38 previously published equations and then applied to the twin and triplet populations.\nRESULTS: Head circumference was the best predictor of gestational age (random error [SD] 3.77 days Among the fetal biometric measurements, bi-parietal diameter and femur length remained the most popular.[1] also referred to as intrauterine growth restriction (IUGR Bi-parietal diameter (BPD) has been widely used to estimate the gestational age, as this fetal dimension is dependably measurable even by the sonographers who are comparatively less experienced.[1]also referred to as intrauterine growth restriction (IUGR This measurement estimates the gestational age at its best after 12 weeks of gestation.[8]as ultrasound is safe, easy operating and cheap. Objectives: to predict the GA with BPD and FL, to derive equations from linear regression analysis of GA with BPD and FL this could be applied to determine the fetal GA, to compare between BPD and FL. Methods: there were 100 normal pregnancies (singleton However, in the last trimester BPD showed to have less consistency due to biological variability and because of an increased likelihood of discrepancy of the shape of the cranium due to position of the fetus, therefore, requires for additional biometric measurements to evaluate the growth of fetus and to avoid miscalculating the ultra-sonographic estimation of gestational age.[9,10] Estimation of fetal age with the sonographic evaluation of femoral length has gained its wide acceptance due to its reproducibility of gestational age later in the final trimester.[9] On the other hand, femoral length (FL) has gained its popularity over several other fetal biometric observation due to exhibiting better correspondence to gestational age, and study findings gave also suggested that FL to be significantly more accurate than other fetal measurements in late pregnancy.[11] FL is best to be measured after 14 weeks of gestation.[12] Therefore, the present study is aimed to evaluate sonographic measurement of fetal bi-parietal diameter and femoral length to estimate the gestational age in second and third trimester to observe the correspondence to the gestational age calculated from the history of LMP.

MATERIALS AND METHODS

Subjects design: This descriptive type of observational study was conducted in the department of Radiology and Imaging of Dhaka Medical College and Hospital, during the period of July, 2004 to June, 2005. The study was included 291 single-ton, non-complicated pregnancy cases with 18 to 42 weeks of gestation having well defined record of last menstrual history before the pregnancy, BMI within normal range and history of regular menstruation cycle. Cases with obstetric complication with any other significant morbidity or congenital anomalies of the fetus were excluded. With prior ethical approval the study has been conducted. ritten informed consent was taken from each of the participant.

Gestational age: Gestational age was calculated by history of LMP and compared that with the sonographic evaluation of the gestational age determined by bi-parietal diameter (BPD) and femoral length (FL). Every fetus has been measured only once, and only a single measurement for each parameter was recorded. The bi-parietal diameters and femoral lengths were expressed in mm, the gestational ages were presented in weeks. The sonographic evaluation was done using gray scale real time ultrasound scanner equipped with 3.5 MHz convex transducer of GE LOGIQ^{TM} α 200 ultrasound machine, TOSHIBA, Just Vision 4000 and SIEMENS, SONOLINE G 20 ultrasound machine and Fukuda Denshi, FF SONIC, UF 4000.

Measurement of bi-parietal diameter and: The BPD was measured by the 'leading edge to leading edge technique' by Palmer.[13] The transverse section of the fetal skull was identified using scans at different angels. When the plane was found, where the fetal skull was in ovoid shape and the midline echo from the flax cerebri is interrupted by the cavum septi pellucidi and the thalami., then the gain in the ultrasound was reduced until the measurements from the outer table of the proximal skull to the inner table of the distal skull could be made. The soft tissue over the skull was excluded.

Measurement of femur length The FL was detected by the technique described by O'Brien, Queenan and Campbell.[14] After identifying the fetal lying position, the transducer was placed at the right angel to the fetal spine, and maintaining the angle the transducer is passed down the fetus and the caudal end was reached. As the fetal femur is typically flexed, the transducer was then rotated from this position through 30 to 45 degrees toward the fetal abdomen until the full length of the femur could be captured and measurement was then taken without considering the flexion rather recorded as the straight measurement.

Statistical methods: All statistical analysis was carried out using the SPSS (Statistical Package for the Social Sciences)

version 25 software (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp). Continuous data were presented as mean and standard deviation. The gestational age estimated by ultrasonic measurement of BPD and FL was correlated with the gestational age measured by the history of LMP in second and third trimesters by Pearson correlation considering the level of significance at p value less than 0.05.

RESULT

The BPD and FL of 291 pregnant cases from 18 to 42 weeks have been expressed in mm and estimated gestational age was expressed in weeks, the number of fetus with the corresponding gestational age has been depicted in Table I and II. The gestational age estimated by ultrasonic measurement of BPD and FL has been compared with the gestational age measured by the history of LMP showed in Table I and II respectively.

Table I shows the estimated gestational age calculated by the history of LMP and gestational age measured from ultrasonic measurement of BPD observed to be in close in relation up to 35th week, where the variation among these two parameters ranged between 2 to 3 days. After 35th week of gestation, the variation between gestational age measured from BPD and from LMP observed to be 1 to 4 weeks.

Table I: Ultrasonic measurement of BPD to estimate gestational age and gestational age calculated from history of LMP

Estimation of Gestational Age by LMP history (in weeks)		Number of Fetuses	Bi-parietal diameter		Ultrasonic Estimation of Gestational Age by BPD	
			Mean	SD	Mean	SD
Second Trimester	18	10	40.64	1.05	18.29	0.04
	19	11	43.97	0.76	19.34	0.34
	20	11	47.86	0.62	20.43	0.27
	21	12	50.28	1.01	21.39	0.36
	22	11	54.02	1.08	22.41	0.34
	23	12	56.2	0.75	23.35	0.38
	24	13	59.23	0.08	24.37	0.33
	25	12	62.53	0.56	25.41	0.36
	26	13	65.01	0.85	26.39	0.39
Third Trimester	27	14	68.12	0.87	27.36	0.38
	28	13	70.5	0.54	28.36	0.38
	29	14	73.23	0.09	29.37	0.27
	30	12	76.68	1.07	30.42	0.43
	31	11	78.08	0.06	31.38	0.32
	32	11	80.93	0.65	32.48	0.04
	33	12	83.08	0.49	33.35	0.25
	34	12	85.3	0.78	34.39	0.33
	35	11	87.93	0.69	35.4	0.33
	36	12	89.01	0.81	35.95	0.23
	37	12	89.53	0.47	36.17	0.29
	38	10	90.05	0.48	36.43	0.24
	39	11	91.03	0.55	36.88	0.37
	40	11	92.14	0.46	37.31	0.18
	41	10	92.98	0.64	37.77	0.18
	42	10	93.92	0.4	37.95	0.13

Table II shows the gestational age measured from ultrasonic measurement of FL was 2 to 4 days behind from the estimated gestational age calculated by the history of LMP upto the 27th week of gestation. After 27th week gestational age measured from FL was 2 to 3 days advanced from gestational age measured from LMP

Table II: Ultrasonic measurement of FL to estimate gestational age and gestational age calculated from history of LMP

Gestational Age by LMP history (in weeks)		Number of Fetuses	Femoral Length		Ultrasonic Estimation of Gestational Age by FL	
			Mean	SD	Mean	SD
Second Trimester	18	10	26.22	0.52	17.45	0.32
	19	11	29.45	0.36	18.33	0.31
	20	11	32.75	0.93	19.44	0.35
	21	12	35.15	0.99	20.45	0.35
	22	11	38.78	0.64	21.67	0.31
	23	12	41.12	0.91	22.38	0.27
	24	13	43.04	0.56	23.65	0.03
	25	12	46.64	0.75	24.99	0.27
	26	13	48.9	0.94	25.66	0.32
Third Trimester	27	14	51.58	0.66	26.87	0.35
	28	13	53.97	0.96	28.29	0.04
	29	14	56.27	0.54	29.37	0.04
	30	12	59.25	0.81	30.39	0.32
	31	11	61.15	0.46	31.36	0.29
	32	11	63.02	0.56	32.36	0.03
	33	12	64.79	0.62	33.29	0.21
	34	12	67.61	0.76	34.32	0.44
	35	11	69.81	0.89	35.39	0.27
	36	12	71.86	0.56	36.37	0.42
	37	12	73.15	0.47	37.29	0.35
	38	10	75.68	0.54	38.35	0.32
	39	11	77.52	0.62	39.37	0.34
	40	11	79.49	0.52	40.29	0.33
	41	10	80.89	0.62	41.24	0.03
	42	10	82.82	0.29	42.26	0.42

Table III shows pearson's correlation coefficient the LMP based gestational age and gestational age estimated from BPD was strongly significantly correlated with the correlation coefficient of 0.999 in the second trimester and in the third trimester it was 0.978 ($p<0.001$). In case of FL, the correlation coefficient was 0.999 in the second trimester and in the third trimester it was 0.998 and the association was strongly significant in both cases ($p<0.001$)

Table III: Correlation of estimated gestational age by BPD and FL with estimated gestational age by history of LMP in second and third trimester

Trimesters	N	BPD		FL	
		R	P value	R	P value
Second Trimester	92	.999	0.000	.999	0.000
Third Trimester	199	.978	0.000	.998	0.000

DISCUSSION

Ultrasonic evaluation of the gestational age of the fetus is based on the known size of the fetus according to their age, which has been estimated from large scale studies on fetal growth, which gives rise to a standard growth chart particularly applicable for that population.[15] Due to the unpredictability of the gestational age calculated from last menstrual history of the pregnant woman, ultrasonic evaluation provides with indispensable significance to evaluate the growth of the fetus along with other developmental determinants.[3,16] The genetic inheritance of the growth velocity as well as the maternal nutritional and environmental factors play significant role in the growth spurt of the fetus.[17] Moreover, inconsistencies in gestational age assessment by the sonographic measurement of fetal biometrics also has been observed despite of the normal fetal growth.[18] Thus, continuous researches in this field can aid in to understand it better about growth evaluation. Among the various fetal biometrics BPD and FL are the widely used ones to estimate fetal growth and age. Whereas BPD is an older one to be in use and FL is comparatively newer and has proven to be more accurate.

In the present study both BPD and FL estimated the gestational age with strong precision although, FL had better precision in terms of estimating the gestational age in the last trimester. The study results showed that, in case of BPD, up to 35th week the ultrasonic estimation of the gestational age varied 2 to 3 days when compared to LMP based gestational age and after that, the variation was 1 to 4 weeks. In case of FL, the ultrasonic measurement was 2 to 4 days behind in the second trimester and 2 to 3 days advanced in third trimester. In one study, it has been recorded that up to 20th week of gestation, FL provided a range of variation to estimate the gestational age of ± 7 days, whereas after 36th week, this variation ranges up to ±16 days.[19] In case of BPD the same study reports the variation of ±8 days before 20th week and ±15 days after 24 weeks.[19] Similar to our study findings, some study results suggest that, with the progression of the pregnancy period, BPD becomes less dependable to predict the gestational age.[20–22] On the other hand, FL shows correlation with higher precision with gestational age throughout the pregnancy and FL found to be significantly more accurate than BPD in the last trimester.[11] In this study, when correlated with the LMP based gestational age, the FL predicted the same with a correlation coefficient of 0.998 and BPD predicted it with the correlation coefficient of 0.978 in third trimester. Although, in the second trimester, it has been found that, BPD was the superior predictor of the gestational age than the FL. In the second trimester, the correlation coefficient was 0.999 in case of BPD and 0.998 in case of FL when correlated with LMP based gestational age. Similar to this study findings, one research findings showed that, gestational age based on LMP found to be correlated with FL and BPD based gestational age with the correlation coefficient of 0.966 and 0.97 respectively.[12] In another study, it has been found that, the correlation between gestational age estimated from FL was stronger than gestational age estimated from BPD when compared to the LMP based gestational age.[23]

CONCLUSIONS

Gestational age estimation is a widely practiced and very important application of ultrasound in antenatal care. Ultrasonic determination of fetal age depends on the measurement of fetal growth associated biometrics. The growth of the fetus varies according to the time of gestation. In this study among BPD and FL, the latter found to be more significantly representative of gestational age in the third trimester of pregnancy.

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Case Report

Optic Chiasmatic Hypothalamic Glioma Presented as with Panhypopituitarism with Bilateral Primary Optic Atrophy

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Abstract

Optic chiasmatic hypothalamic gliomas are among common primary neoplasm of the optic nerve. It presents with decreased vision as well as features of hypopituitarism due to infiltration of the hypothalamus. In this case report, a young man presented with loss of libido, increased thirst, gradual loss of vision, bilateral optic atrophy and visual field defect. The MRI of sellar and paraseller region showed optic chiasmatic glioma with hypothalamic extension and biochemical parameter showed panhypopituitarism. We diagnosed this patient as a case of Optic chiasmatic hypothalamic gliomas (OCHGS) with panhypopituitarism with partial cranial diabetes insipidus with bilateral primary optic atrophy.The patient underwent surgery after adequate hormonal treatment but died due to post-operative complications

Keywords: *Optic chiasmatic glioma,hypothalamic glioma, panhypopituitarism, partial cranial diabetes insipidus.*

INTRODUCTION

Optic chiasmatic hypothalamic gliomas (OCHGS) are one kind of benign tumors because of their histological appearance. It is an important subset of optic pathway glioma. OCHGS are usually shown age-dependent behavior. Though, it is a benign tumor, the patients younger than five years and more than twenty years exhibit aggressive growth. It's difficult to differentiate the clinical behavior of such tumors because there are no specific pathological features. Some hypothalamic tumors can grow in the wall of the third ventricle and infiltrate the chiasm. So the distinguished point between the glioma either originates from the hypothalamus or from the chiasm that invades the hypothalamus secondarily is difficult to differentiate. Optic glioma has various kinds of presentation because of the proximity of the optic chiasm, hypothalamic-pituitary axis, and third ventricle. The pituitary gland is located at the base of the brain and very nearer to the hypothalamus. The pituitary gland has various functions within the body as it regulates the major endocrine secretion. The pituitary gland has two lobes, Anterior and posterior. The anterior pituitary is consists of hormone-producing epithelium and the posterior pituitary consists of nervous tissue. Decreased secretion of one or more than one hormone from all eight hormones known as hypopituitarism. The patient of OCGHS is frequently present with visual disturbances, active endocrinopathies, and, the features of the raised intracranial features. On fundoscopic examination optic atrophy is commonly found because of the damage of the optic nerve which carries impulses from the eye to the brain. It is the end stage of the disease process due to damage of the retinogeniculate portion of the visual pathway. Optic atrophy can be present with blurred vision and difficulties with peripheral vision and color vision. Presentation is variable between the child and adults. Sometimes children are presented with visual symptoms and adults are presented with endocrine symptoms earlier.[1-4]

CASE REPORT

A 22-year-old male came to the hospital due to the gradual dimness of vision, weight gain, decreased libido, polydypsia and polyuria for one year. The patient had no

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headache, convulsion and weakness of the limbs. The patient cannot concentrate on his study due to excessive fatigue ness. He has had a significant decrease in appetite and day to day activities for whom he consulted with a psychiatry doctor previously. The patient also has cold intolerance and constipation. He said he feels dizzy when he stands from a sitting position. On general examination shows an ill-looking, anxious man with dry and pale skin. Temperature 98F, Blood pressure- 100/60 on sitting and 85/50 on standing, the pulse is 88/min. Ophthalmologic evaluation showed visual acuity was reduced to perception of light and fundoscopy revealed bilateral primary optic atrophy. The systemic examination examination revealed no abnormality. The laboratory investigations are shown in the table-1. Perimetry could not be performed due to reduced visual acuity. Magnetic resonance imaging (MRI) of sellar and para sellar region showed optic chiasmal glioma with hypothalamic involvement. Considering all the evidence he was diagnosed as a case of hypothalamic optic chiasmatic glioma with panhypopituitarism with bilateral optic atrophy. He was treated with hormonal supplementation with thyroxine,intranasal desmopresine and prednisolone leads to improvement of his symptoms. Then a neurosurgeon was consulted and he decided to operate the patient. But, unfortunately he died after 2 days of surgery due to post- operative complication.

Table-1: Laboratory investigation profile of the patient.

Investigation	**Result**	**Reference**
Complete blood count	Hb: 9.1 gm/dl	Adult male: 15.0±2.0
	RBC: 3.01 gm/dl	Male: 5.0±0.5
Serum Electrolytes	Na^+ 158 mmol/l	137-157 mmol/L
	K^+ 3.70 mmol/L	3.50-5.10 mmol/L
Serum creatinine	1.00 mg/dl	0.3-1.4 mg/dl
Free T3	1.71 pmol/L	4.26-8.10 pmol/L
Free T4	6.56 pmol/L	10.4-19.6 pmol/L
Serum TSH	1.08 µIU/ml	0.465-4.680 µIU/ml
Serum FSH	<0.66 µIU/ml	Male: 0.95-11.95
Serum LH	<0.216 µIU/ml	Male: 1.14-8.75
Serum Prolactin	463 µIU/L	Male: 78-380
Basal cortisol	49.91 nmol/L	101.2-690.0 nmol/L
Serum ACTH	5.00 pg/ml	8.3-57.8 pg/ml
Serum Testosterone	0.025 ng/ml	Male: 2.2-10.5 ng/ml
Water deprivation test		
After water deprivation		
a)At 11.00 am		
Serum osmolality	346 m.osmol/kg	285-295 m.osmol/kg
Urine osmolarity	176 m.osmol/kg	300-900 m.osmol/kg
b)At 1.00 pm		
Serum osmolality	382 m.osmol/kg	285-295 m.osmol/kg
Urine osmolality	153 m.osmol/kg	300-900 m.osmol/kg
c)At 1.50 pm after administration of desmopressin		
Serum osmolality	354 m.osmol/kg	285-295 m.osmol/kg
Urine osmolality	459 m.osmol/kg	300-900 m.osmol/kg

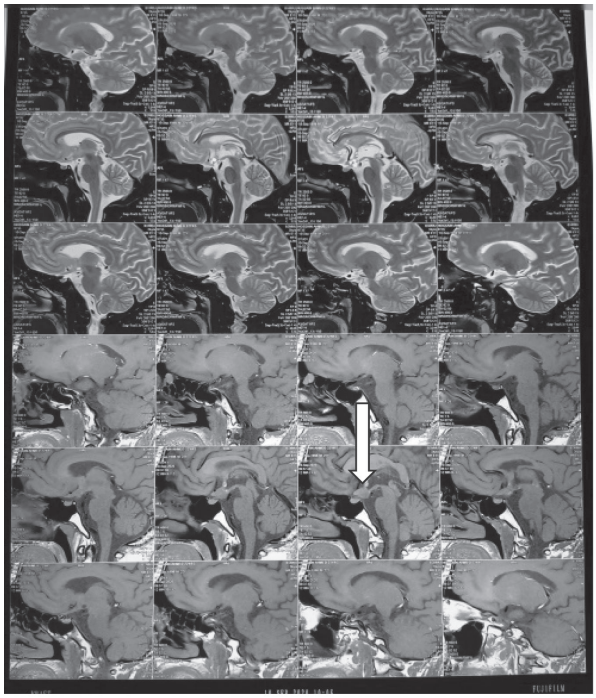

Figure 1: MRI of sellar and parasellar region T1 and T2 weighted image sagital view is showing optic chiasmal glioma with hypothalamic involvement.

DISCUSSION

Optic glioma is a tumor of childhood that can arise anywhere along the length of the optic pathway from the optic globe up to the occipital cortex including optic chiasma and hypothalamus. They constitute 2–6% of all intracranial tumors.[5] Optic chiasmatic-hypothalamic gliomas (OCHGs) is considered as an important subset of optic pathway gliomas that is often referred to as a single disease entity because the tumor that arises in the chiasm has the potential to infiltrate the hypothalamus posteriorly and hypothalamic tumors that arises from the walls of the third ventricle can grow forward and infiltrate the optic chiasm.[1,6,7] Histologically optic chiasmatic gliomas are low-grade astrocytomas and they are more invasive and aggressive than optic nerve gliomas. Although being relatively "benign" in histology, tumors can progress that can cause considerable morbidity in young children.[1,6,7]

Optic chiasmatic glioma tends to grow as a larger mass with symptoms, occur in very young children or older individuals. It may become large enough to affect the physiology of the hypothalamus and can present with endocrine abnormalities. The hypothalamic dysfunction by these lesions can present with manifestations of panhypopituitarism and also endocrine-active syndromes by secretion of hypothalamic-releasing factors from the tumors. When tumors affect the appropriate nuclei of the hypothalamus or the pituitary stalk can result in cranial diabetes insipidus due to impairment of antidiuretic hormone release. In this case study, a young boy was having OCHGs presented with panhypopituitarism and partial cranial diabetes insipidus which is consistent with the literature.

Optic chiasmatic glioma most commonly present as visual dysfunction associated with bitemporal field defects, and optic disc changes. Non-pulsatile proptosis, nystagmus, strabismus, and poor visual fixation are also common ophthalmological findings. Optic atrophy present on funduscopy. This tumor may also expand into the third ventricle and occludes the foramina of Munro that leads to the development of hydrocephalus with its feature.[8-10]but can cause additional symptoms when it is large. Local involvement within the orbit can be characterized using CT, but MRI is superior in showing the intracranial extent of the lesion. Intracranial calcification in optic pathway glioma is rare. We present a rare case of optic pathway glioma with calcification in the intracranial component. Also, we describe MR spectroscopy (MRS

Patients may have neurological symptoms such as headaches, as well as eye pain, hemiplegia, and sometimes dementia.[11]

Our patient presented with gradually decreasing vision initially involving the left eye and then the right eye and gradually visual acuity came down to perception of light only. He also had bilateral primary optic atrophy on fundoscopic examination. Although, no neurological features were present.

The evaluation of patients with optic chiasmatic gliomas involves a thorough family history, careful assessment of visual status, evaluation for signs and symptoms of raised intracranial pressure from obstruction of the third ventricle, and assessment of the patient's endocrine status, as well as evaluation of both hypopituitarism and endocrine-active syndromes. [7-10] The diagnostic evaluation consists of laboratory testing, including measurement of pituitary hormones, visual examination with measurement of acuity and visual fields, as well as imaging diagnosis. [7-10] Magnetic resonance imaging (MRI) with gadolinium enhancement use for the most accurate delineation of the lesions involved.[7-15]After appropriate investigations our patient was diagnosed as a case of hypothalamic optic

chiasmatic glioma with panhypopituitarism with bilateral optic atrophy.

Management strategies for visual pathway gliomas include observation, surgery, chemotherapy, irradiation, and a combination of these modalities. Radiation has been the standard therapy for the progressive expansion of tumors. [12] Treatment should be according to the hormonal deficiencies. Radiation therapy may have some serious adverse effects including optic nerve injury, endocrinopathy, vasculopathy, and radiation- induced second neoplasms.[12] Our patient had features of panhypopituitarism, so, he was treated with hormonal supplementations with both clinical and biochemical improvement of the symptoms. Then we discussed with neurosurgical team and endocrinology for the further course of management. The whole team decided that surgical removal of the tumor would be the best option and he was operated afterwards. But, despite all efforts he died due to post-operative complications.

CONCLUSIONS

Optic chiasmatic-hypothalamic gliomas is rare tumor of optic nerve which can also invole hypothalamus. Patient may present with endocronopathy,optic atrophy and diverse neurological manifestations . Early detection of the tumor is very important because it could be potentially vision threatening in other word could be life threatening.

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Medical News

'Crush Programme' as Part of Combined Control Programme for Culex Mosquito in Both North and South Dhaka City Corporation

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INTRODUCTION

There are 123 species of mosquitoes in Bangladesh, of which two types are dominant – Aedes and Culex.[1] The breeding season of *culex*, spreading deathly diseases, is between late November and March, while Aedes aegypti, the species responsible for causing Dengue among other diseases, breeds between March and November, especially during the rainy season.The climate change has impact on increasing the mosquito's population and risk of havin gvector-borne diseases like malaria, dengue. As a new phenomenon in this current century, people living in the tropical and subtropical climates like Bangladesh are currently at high risk of dengue epidemic. About 390 million dengue infections are estimated to occur per year, among them about 60-130 million will be clinically manifested.[2]

In recent days, both Dhaka North City Corporation (DNCC) and Dhaka South City Corporation (DSCC) have started the 'Crush Programme' to combat the mosquito menace from 8th to 16th March 2021[1]. They have already spotted 629 breeding grounds solely in DNCC and are planning to use Novaluron there, with the rest of the city area as well. For larviciding, both city corporations are using Temephos and Malaria Oil B at the stagnant water bodies for further control of mosquito inhabitants. They are also using Malathion for adulticide.[3] The concerned authority came to the decision to use this fourth-generation pesticide Novaluron (Benzoylphenyl Urea, BO urea), after considering previous efficiency of other methods based on the concept: changing the pesticides after one or two years so that mosquitoes don't get to adapt those pesticides in Dhaka.[4,5]

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BACKGROUND:

Outdoor mosquito control measures, most commonly practiced world wide are the following:

a) General Insecticides Spraying

b) Customized Insecticides Spraying

c) General Fogger Spraying

d) Mini Fogger Spraying

e) Drains and Ponds Cleaning and Treatment, among others.

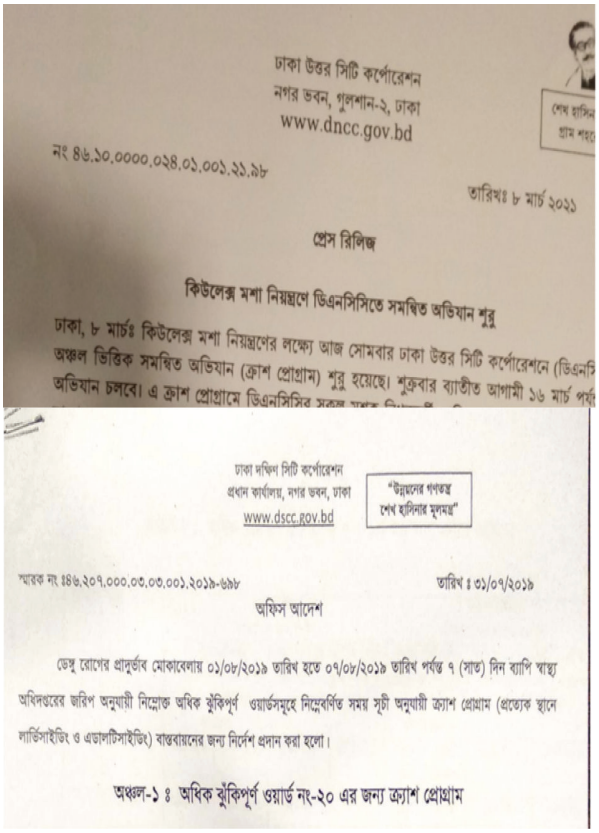
In the sixties of last century, Dhaka (previously *Decca*) City Corporation took initiatives to eradicate mosquitoes through Dichlorodiphenyltrichloroethane (DDT) spraying as part of "Global Malaria Eradication Programme" of WHO during the 1950s and 1960s. It was used until 2009 on national level in some countries to control mosquito. However, DDT is banned now, because: a) hazardous to human health, b) hazardous to environment causing air pollution, damaging crops, and ecological destruction of plants among others and c) hazardous to other species such as fish, cattle, wild animals etc.[6]

Previous research showed that Integrated Mosquito Management (IMM) could better achieved by several ecological measures: 1) seeding of drains and permanent water bodies with suitable larvivorus fish species, 2) removal of water hyacinth from urban water bodies- lakes, pond, artificial water reservoir etc. and 3) replacing them with duckweed to prevent recurrence of water hyacinth would be good control interventions in addition to the habitat manipulations, with less dependence on chemical pesticides.

In Dhaka city a 6-week programme of cleaning drains, seeding them with guppy and use of Malariol B could give good mosquito control for several months, which was adapted by DCC during nineties for mosquito control measure.[7]

Later, WHO has clarified vector control strategies in 2017's report, where suggestion is made emphasizing environment a public health concern of using any insecticide indoor or outdoor for using as larvicide or adulticide including source reduction methods[8]. This was highly welcomed by DNCC and DSCC at once.

DNCC has undertaken an initiative called "400-gauge by 400-gauge", where there are supervisors to monitor the activities of workers engaged in mosquito control in every 400 square-gauge area of a ward. Presently, there are 15 workers in every ward who work with DNCC in this regard[1]. Along, DSCC is planning to adapt Bacillus thuringiensis subspecies israelensis (BTI), a bacteria that will kill larvae once mixed with water. According to DNCC sources, the special mosquito eradication campaign which started on February 20, 2021 ending on 7th March.



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তারিখঃ ৮ মার্চ ২০২১

প্রেস রিলিজ

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স্মারক নং ৪৬.২০৭.০০০.০৩.০৩.০০১.২০১৯-৬৯৮

তারিখ : ৩১/০৭/২০১৯

অফিস আদেশ

ডেঙ্গু রোগের প্রাদুর্ভাব মোকাবেলায় ০১/০৮/২০১৯ তারিখ হতে ০৭/০৮/২০১৯ তারিখ পর্যন্ত ৭ (সাত) দিন ব্যাপি স্বাস্থ্য
অধিদপ্তরের জরিপ অনুযায়ী নিম্নোক্ত অধিক ঝুঁকিপূর্ণ ওয়ার্ডসমূহে নিম্নেবর্ণিত সময় সূচী অনুযায়ী ক্র্যাশ প্রোগ্রাম (প্রত্যেক স্থানে
লার্ভিসাইডিং ও এডাল্টিসাইডিং) বাস্তবায়নের জন্য নির্দেশ প্রদান করা হলো।

অঞ্চল-১ ঃ অধিক ঝুঁকিপূর্ণ ওয়ার্ড নং-২০ এর জন্য ক্র্যাশ প্রোগ্রাম

Picture 1: Screenshots of the government acknowledgement on launching 'Crush programme'. (*Source- DCC website.,http://www.dncc.gov.bd/, http://www.dscc.gov.bd/)*

An Integrated Vector Management (IVM) system is undergoing, entailing four elements - environmental control, biological control, larvicide and adulticide, which is mandatory to control the mosquito problem in cosmopolitan city. Within this purpose, larviciding will be carried out each day from 6am to 12pm and adulticiding will take place from 4pm to 6pm in this campaign programme. In essence, mosquito repellent is sprayed in the capital with the fogging machine weighing around 25 kg, carried by the extermination vehicle with workers of city corporation. In addition, as a known fact, stagnant water is the breeding ground for the mosquitoes, water treatment is ongoing too. During this special operation, around 45,000 roads, sewers, water reservoirs, installations etc. were inspected. Of these, 210 were found with mosquito larvae and 30,129 mosquito breeding grounds were destroyed applying pesticides, besides taking judicial actions.[1] Both Dhaka North and South health department, waste management department, and health engineering department will collaborate to ensure the successful completion of the 'crush campaign' targeting to eradicate *culex* mosquitoes mainly and in a continuation of the combing operation to kill the *aedes aegypti* mosquitoes as well. For biological control measure of the mosquitoes, DCC released fish in Dhanmondi and Khilgaon lakes so that they eat up the larvae.

Figure 2: Poster picture of the Dhaka City Corporation. (*Source-DNCC (http://www.dncc.gov.bd/)*

Bangladesh has experienced horrifying dengue epidemic in 2019, where 101,354 people were hospitalized.[9] Therefore, Dhaka City Corporation both North and South has undertaken an integrated mosquito eradication program that is used world wide following WHO guideline for eradication program.[10] For example:

a) The insecticide in the fog is not harmful for human if used at the low concentrations.

b) It has presumably no odour.

c) Fogging operations are conducted in the early morning or late afternoon which is also undergoing in Dhaka.

d) Citizens are advised not to be concerned about the fog or the repellent. They are requested to leave their doors and windows open when the fogging machine is in their area with repellent spraying action, so that the fog can kill mosquitoes inside the house.

e) Residents are also advised that they need to continue to prevent dengue mosquitoes breeding spots inside or around their home.[11] For instance, in the stagnant water in the hidden pits, behind the window, backyards, old unused tires etc.

Public health concern; health and environmental hazards along current crush programme:

The Plant Protection Wing of the Department of Agricultural Extension and Institute of Epidemiology Disease Control and Research (IEDCR) has certified and approved the use of Novaluron as pesticide to use in Dhaka after testing. The recommendation for proper monitoring and field testing is done by public health expert in Bangladesh regarding the Novaluron. Like any tools, all pesticides and insecticides have limitations. The potential for adverse ecological and human health impacts as a result of excessive and indiscriminate insecticide use have been documented about Novaluron.[12] The prescribed amount use is non-alarming and so far, the harm is avoidable. In this regard, WHO and FAO reports have not found any sizable health and environmental hazards of the pesticide.[13, 14] On the other hand, the effectivity of the Novaluron as larvicide for *culex* mosquitoes has been documented for vector control, which is rather promising in recent research.[15] In addition, in current mosquito eradication program in Bangladesh, Temephos and Malaria Oil B are also used besides Malathion for adulticide.

Probable health hazards of the pesticide could include, respiratory symptoms, such as irritation, cough, runny nose, reddening of eyes etc. Children of early age could get affected negatively if get in touch of high concentration of mosquito repellents, which contains heavy to light particles. However, as part of precaution measure, asthma patients are asked to stay indoors during the 'Crush programme'.[16]

As environmental hazards, certain types of fishes happened to die due to the Novaluron mixed in water in higher concentration.[12] The Malathion is a known air pollutant in above usual level. It could produce harmful effect if used excessive amount. Concentrated amount of Temephos (aka 'Abate') could work as water pollutant and kill the flora and disrupt the homeostasis of the underwater ecosystem. Although, Temephos was found as resistant for the *aedes aegypti*in Brazilian study,[17] it is used in Dhaka as efficient in mosquito eradication program.

CONCLUSIONS

The effectiveness of the pesticide and insecticide implemented in the 'Crush programme' to eradicate mosquitoes in Dhaka, is promising in current setting. The adequate actions taken by both wings of Dhaka City Corporation heralded to alter the mosquito breeding and growth, thus improving the public health in general. Nonetheless, it could in effect control the vector borne diseases, such as Dengue, Malaria, Filaria, Chikungunya and many other potential life threatening illnesses among Dhaka dwellers and prevent the devastating after effect by reducing the burden of these diseases.

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Obituary News September-2020

BMA would like to express deep condolence on deaths of the following notable physicians in recent past:

Sl.No.	Name & Address	Date of Death
1	Dr. Main Uddin Ahmed Assistant Professor of Medicine Sylhet MAG Osmani Medical College	15/4/2020
2	Professor Dr. Col (Ex) Moniruzzaman Hematology & Laboratory Medicine Specialist Anwer Khan Modern Medical College Hospital, Dhaka	03/5/2020
3	Professor Dr. Anisur Rahman Forensic Medicine Specialist Northern International Medical College, Dhaka.	11/05/2020
4	Freedom Fighter Major (Ex) Dr. Abul Mukarim Md. Mohasin Uddin Radiologist, Ex. Student of Mymensingh Medical College (11th Bach)	12/05/2020
5	Dr. Md. Azizur Rahman Raju Ex. Student of Mymensingh Medical College (13th Bach)	18/05/2020
6	Dr. MA Matin Member BMA Moulvibazar Branch Assistant Director Helth, DGHS, Dhaka	22/05/2020
7	Dr. Kazi Dilruba Ex. Student, Sylhet MAG Osmani Medical College	22/05/2020
8	Dr. SM Jafar Hossain Medical Officer, Chattogram Maa-O-Shishu Hospital	25/05/2020
9	Dr. Amina Khan Senior Consultant, Gynaecology (Retd.) Life Member, BMA	26/05/2020
10	Dr. Abdur Rahman Anesthesia and ICU Specialist	26/05/2020
11	Dr. Md. Mosarraf Hossain Ex-Head, Department of Orthopaedic Sher E Bangla Medical College, Barihal	27/05/2020
12	Dr. A F M Saidul Islam Retd. Captain, Army Medical Core Ex-Student, Sher E Bangla Medical college (1st Bach)	28/05/2020
13	Dr. Wahiduzzaman Akand Bablu Ex. Student, Sylhet MAG Osmani Medical College (14th Bach)	31/05/2020
14	Dr. Manzoor Rashid Chowdhury Retd. Consultant of Urology Dhaka Medical College Hospital, Dhaka Ex. Student, Sylhet MAG Osmani Medical College(14th Bach)	02/06/2020

Sl.No.	Name & Address	Date of Death
15	Dr. A.S.M. Ehsanul Karim Associat Professor and Head, Department of Medicine Marine City Medical College Hospital, Chattogram	03/06/2020
16	Dr. Md. Mohiuddin Professor, Department of Microbiology Ibrahim Medical College, Dhaka Ex. Student of Chattogram Medical College(17th Bach)	03/06/2020
17	Dr. K.M. Wahidul Haquee Ex. Student, Sylhet MAG Osmani Medical College (10 Bach)	03/06/2020
18	Professor Dr. Habibur Rahman Forensic Medicine Specialist	04/06/2020
19	Dr. Muhidul Hasan EMO, Chattogram Medical College & Hospital	04/06/2020
20	Professor Dr. N. I. Khan Ex. Professor and Head Department of Medicine Dhaka Medical College	04/06/2020
21	Professor Dr. A.S.M. Golam Kibria Ex. Chairman, Department of Urology Bangabandhu Sheikh Mujib Medical University Ex. Student of Sylhet MAG Osmani Medical College (6th Bach)	04/06/2020
22	Dr. Ehsanul Kabir Chowdhury Retd. Upazila Health & Family Planning Officer Ex. Student of Rangpur Medical College(4th Bach)	04/06/2020
23	Dr. Abul Kashem Khan Retd. Senior Medical Officer, EPZ, Saver Ex. Student of Sylhet MAG Osmani Medical College (9th Bach)	06/06/2020
24	Dr. Mirza Nazim Uddin Senior Consultant and Director, Medical Services Square Hospital, Dhaka Life Member, BMA	07/06/2020
25	Dr. Rajia Sultana Ex. Student of Mymensing Medical College (16th Bach)	08/06/2020
26	Dr. Sakhawat Hossain Consultant (Anesthesia), Labaid Hospital, Dhaka Ex. Student of Community Based Medical College, Mymensingh (5th Bach)	08/06/2020
27	Dr. Anwar Hossain Chairman, Rahat Anwar Hospital, Barisal Ex. Student of Sher E Bangla Medical College, Barihal (14th Bach)	09/06/2020

Sl.No.	Name & Address	Date of Death
28	Professor Dr. Jalilur Rahman ICU Incharge and Senior Consultant Impulse Hospital, Dhaka	09/06/2020
29	Dr. Tanzila Rahman Head of Quality, Department of Maternity, Marystops Bangladesh Ex. Student of Z H Sikder Women's Medical College & Hospital, Barihal (4th Bach)	10/06/2020
30	Professor Dr. Gazi jahirul Hasan Professor of Pediatric Surgery, BSMMU Ex. Student of Mymenging Medical College (17th Bach)	12/06/2020
31	Dr. Mahmud Monwar Assistant Professor, Department of Cardiology National Heart Institute Hospital	12/06/2020
32	Dr. A K M Fazlul Haque Associate Professor, Department of Opthalmology Z H Sikder Women's Medical College & Hospital, Dhaka	12/06/2020
33	Dr. Arif Hasan Ex. Student of Dhaka Medical College (K-49 Bach)	12/06/2020
34	Dr. Md. Sazzad Hossain Head, Department of ICU BRB Hospital, Dhaka, Retd. Associate Professor, Anesthesia Ex. Student of Chattogram Medical College (20th Bach)	13/06/2020
35	Dr. Sadekur Rahman Life Member, BMA Ex. Student of Chattogram Medical College (17th Bach)	14/06/2020
36	Dr.Tawfikun Nesha Retd. Additional Chief Medical Officer, BCIC Ex. Student of Mymensingh Medical College (7th Bach)	15/06/2020
37	Dr. ANM Abdul Hai Ex. Civil Surgeon, Cox's Bazaar Ex. Student of Sylhet MAG Osmani Medical College (7th Bach)	15/06/2020
38	Professor Dr. A K M Mujibur Rahman Ex. Director, Shahid Suhrawardy Medical College Hospital Ex. Student, Sir Salimullah Medical College (4th Bach)	16/06/2020
39	Dr. Md. Ashrafuzzaman Retd. Associate Professor, Burn Unit, Dhaka Medical College Ex. Student of Rangpur Medical College (8th Bach)	17/06/2020
40	Dr. Md. Shah Abdul Ahad Ex. Director, M Abdur Rahim Medical College Hospital, Dinajpur	17/06/2020

Sl.No.	Name & Address	Date of Death
41	Dr. Md. Nurul Haque Ex. Student, Chattogram Medical College (38th Bach)	17/06/2020
42	Dr. Md. Rafiqul Hayder Liton Ragistrar, Department of Endocrinology Saver Enam Medical College & Hospital Ex. Student of Sylhet MAG Osmani Medical College (23th Bach)	17/06/2020
43	Dr. Md. Emdadullah Khan Senior Consultant Dermatology Ex. Student Barisal General Hospital & Sher E Bangla Medical College (12th Bach)	19/06/2020
44	Dr. Md. Shafiq Ahmed Ex. Student, Sir Salimullah Medical College (1st Bach)	20/06/2020
45	Dr. Mujibur Rahman Ripon Associate Professor, Deptment of Pediatric Central Medical College, Cumilla	20/06/2020
46	Dr. Bazlur Rahman General Surgeon, Impulse Hospital, Dhaka	20/06/2020
47	Dr. Sunil Kumar Sarker Retd. Associate Professor, Cardiac Surgery, NICVD, Dhaka	21/06/2020
48	Dr. Lalit Kumar Dutt ENT Specialist Ex. Student, Chattogram Medical College (2th Bach)	21/06/2020
49	Freedom Fighter Dr. Md. Ali Ajgar Retd. Physician Narayanganj General Hospital	23/06/2020
50	Dr. Upendra Nath Pal Ex. Upazila Health and Family Planning Officer Fakirhat Upjazila, Bagerhat,	23/06/2020
51	Dr. Md. Yunus Ali Khan Elderly Physician & Eye Specialist, Shajadpur, Sirajgang Ex. Student of Rajshahi Medical College (4th Bach)	24/06/2020
52	Dr. Md. Samirul Islam Babu Associate Professor, Orthopedic Surgery, Chattogram Medical College Life Member, BMA Ex. Student of Sher E Bangla Medical college (19th Bach)	24/06/2020
53	Dr. S M Saiful Isalm Director & Diabetes Specialist, Al Manar Hospital, Dhaka. Ex. Student of Dhaka Medical college (K-17 Bach)	24/06/2020
54	Dr. Firoza Banu Minu Ex. Student, Rajshahi Medical College (14th Bach)	25/06/2020

Sl.No.	Name & Address	Date of Death
55	Dr. Mohammad Hossain Retd. Medical Officer, Chattogram City Corporation Life Member, BMA Ex. Student of Chattogram Medical College (17th Bach)	26/06/2020
56	Dr. Md. Asaduzzaman Medical Officer, ENT Oncology National Institute of Cancer Research & Hospital (NICRH) Ex. Student of Sylhet MAG Osmani Medical College (30th Bach)	27/06/2020
57	Professor Dr. Gopal Shankar Day Ex. Head, Department of Psychiatry Ex. Student of Sylhet MAG Osmani Medical College (11th Bach)	27/06/2020
58	Professor. Dr. Golam Sarwar Ex. Head, Department of Pediatric International Medical College, Gazipur Ex. Student of Chattogram Medical College(15th Bach)	01/07/2020
59	Dr.Md. Ruhul Amin Eye Specialist and Surgeon Director, Al Raji Hospital Dhaka	01/07/2020
60	Professor Dr. M A Ohab Medicin Specialist & Ex. Head of Department Holy Family Red Crescent Medical College, Dhaka	01/07/2020
61	Professor Dr. Muntakim Chwudhary Ex. Head, Department of Physiology Sir Salimullah Medical College Life Member, BMA Ex. Student of Dhaka Medical college (K-26 Bach)	04/07/2020
62	Professor Dr. A K M Nurul Anwar Ex. Director General, Directorate General of Health Services Life Member, BMA	05/07/2020
63	Dr. Md Sazzad Hossain Civil Surgeon, Feni Ex. Student of Sylhet MAG Osmani Medical College (25th Bach)	07/07/2020
64	Dr. Sultana Latifa Jaman Irin Registrar, Gynecology and Obstetrics Chattogram Maa O Shishu Medical College Hospital Ex. Student of Cumilla Medical College(14rd Bach)	14/07/2020
65	Dr. S M Noor Uddin Al Baki Rumi Assistant Professor of Surgery, Kushtia Medical College Ex. Student of Chattogram Medical College(3rd Bach)	17/07/2020

Sl.No.	Name & Address	Date of Death
66	Dr. Abdul Hamid Retd. Senior Medical Officer, Bangladesh Post Office Ex. Student of Rajshahi Medical College (3rd Bach)	17/07/2020
67	Dr. Koel Karim (Kuhu) Indoor Medical Officer (Medicine) Dhaka National Medical College and Hospital Ex. Student of Mymensingh Medical College (22th Bach)	07/07/2020
68	Professor. Abul Hossain Khan Chowdhary Heart Specialist, Ex. Director, NICVD, Dhaka Life Member, BMA Ex. Student of Dhaka Medical College (K-29 Bach)	18/07/2020
69	Professor Dr. T I M Abdullah Al Faruk Principal, Popular Medical College, Life Member BMA Ex. President & Secretary Society of Surgeons of Bangladesh Ex. Student of Sher-e-Bangla Medical College, Barishal (1st Bach)	28/07/2020
70	Dr. Md. Nazrul Islam Chowdhury Taslim Associate Professor, Orthopaedic Surgery Chattogram Medical College, Life Member, BMA Ex. Student of Sylhet MAG Osmani Medical College (21th Bach)	03/08/2020
71	Dr. F B M Abdul Latif Director, Homeopathic and Alternative Medicine Directorate General of Health Education Life Member BMA	06/08/2020
72	Dr. Md Golam Mustafa Precident, BMA Rajbari Branch Ex. Student of Chattogram Medical College (6th Bach)	08/08/2020
73	Dr. Rezwanul Bari Shamim Assistant Professor Ortho Surgery Shahid Monsur Ali Medical College, Sirajganj Life Member, BMA Ex. Student of Rajshahi Medical College (30th Bach)	09/08/2020
74	Professor Dr. Md. Mostaq Hossain Ansari Retd. Professor, Department of Community Medicine Rajshai Medical College, Life Member, BMA Ex. Student of Rajshahi Medical College (17th Bach)	10/08/2020
75	Professor Dr. Md. Asadul Haque Khan Ex. Head, Department of ENT Sir Salimullah Medical College Ex. Student of Rajshahi Medical College (5th Bach)	11/08/2020

Sl.No.	Name & Address	Date of Death
76	Dr. Aftab Uddin Ahmed Retd. Upazila Health and Family Planning Officer Life Member, BMA Ex. Student of Rajshahi Medical College (1 4th Bach)	16/08/2020
77	Dr. Md Abdur Rahman Ex. Director, Directorate of Health Life Member, BMA Ex. Student of Rajshahi Medical College (14th Bach)	16/08/2020
78	Dr. Syed Akhter Hossain Principal, MATS, Moulobibazar Retd. Deputy Director, Directorate of Family Planning Life Member, BMA Ex. Student of Sylhet MAG Osmani Medical College (7th Bach)	20/08/2020
79	Dr. A B M Siddiqul Islam Retd. Assistant Director IPH Life Member, BMA Ex. Student of Mymensingh Medical College (10th Bach)	20/08/2020
80	Dr. Abdullah Al Mahmud Elderly Physician Life Member, BMA & EC Member, BMA Moulobi bazar Ex. Student of Sylhet MAG Osmani Medical College	28/08/2020
81	Freedom Fighter Dr.Md. Abdul Matin Patwari Ex. Civil Surgeon, Cumilla Life Member BMA Ex. Student of Mymensingh Medical College (11th Bach)	28/08/2020

May Allah bless the departed souls.
Our heartiest commiseration to the deceased's family, our prayers are with them during this difficult moment of their life.

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