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Obituary

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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:

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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):

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Original Article

Effects of Short Wave Diathermy Therapy in Patients with Adhesive Capsulitis of Shoulder (ACS)

*Haque A[1], Ahsanulhoque M[2], Sadeque ABMZ[3], Rahman HH[4], Ilias M[5], Hojaifa MM[6], Baral ABB[7], Bhuiyan MK[8]

Abstract

There are varieties of management option for Adhesive capsulitis of shoulder (ACS) also known as Periarthrosis and in general population commonly known as Frozen Shoulder. Short Wave Diathermy (SWD) is one of the important therapeutic option for frozen sholder. The aim of the study is to determine effectiveness of SWD in order to improve the pain and range of motion in Adhesive Capsulitis. A total 56 subjects were selected for this non-randomized controlled trial in the Department of Physical Medicine and Rehabilitation, Chattogram Medical College Hospital with adhesive capsulitis in a period of 6 months. The subject were divided into two intervention groups; group-A with conventional treatment plan with SWD and group-B with conventional treatment only. Tool used for assessment were Visual Analogue Scale (VAS) to measure pain with Tenderness Grading (TG) and Shoulder Pain and Disability Index Score (SPADI). The analysis was done to measure the difference of effectiveness of both interventions by independent t-test with SPSS-20. Among 56 patients regarding analysis of sex in both groups male and female were matched (p>0.05) and male - female ratio was 1.66: 1. Considering socioeconomic status, poor was 21.4%, middle class was 44.6% and rich was 33.9%. Among all patients 35.7% were housewives, 16.1% were service holder, farmers were 12.5%, businessmen were 16.2% and laborers were 3.6%. In total patients, 48.2% had right shoulder involvement, 50.0% had left side involvement and one patient had both sided disease. There were 92.7% patients who had localized pain and only 7.3% had radiation. Majority of the exparienced pain in the evening was 56.4% and rest had pain at night was 43.6%. About half of the patients in both groups had constant and intermittent type of pain 47.5% and 45.5% respectively other types were sharp and dull. Significant difference between Group A and Group B was found at week 2, week 4 and week 6 follow-up (p<0.05) whereas initial follow-up was non-significant in VAS analysis (p>0.05). Significant difference between Group A and Group B was found at week 2, week 4 and week 6 follow-up (p<0.05) regarding change of tenderness grading in Group A, then Group B patients. Significant difference between Group A and Group B was found at week 2, week 4 and week 6 follow-up (p<0.05) regarding SPADI. When SWD is combined with conventional management of adhesive capsulitis it gives better reduction in pain and disability. Conventional teeatment plan with SED is more effective in the management of pain and reduce disabilities in patients with ACS.

Keywords: *Short wave diathermy, adhesive capsulitis, shoulder pain, frozen shoulder.*

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INTRODUCTION

Adhesive capsulitis is a condition characterized by painful and limited active and passive range of motion of the shoulder.[1] The American Shoulder and Elbow Surgeons Society agreed on the following definition of FS by consensus: a condition of uncertain etiology that is characterized by clinically significant restriction of active

and passive shoulder motion that occurs in the absence of a known intrinsic shoulder disorder.[2]

Adhesive capsulitis has a prevalence of 2-5% in the normal population. In diabetic patients this is increased, with a prevalence of 10% in type I and 22% in type II.It is more common between the ages of 40 and60years.[3] The incidence of this condition is higher in women than in men. Approximately 70% of patients presenting with adhesive capsulitis are women.[4]

The pathology of adhesive capsulitis remains unclear. The disease process particularly affects the anterosuperior joint capsule and the coracohumeral ligament. Evidence shows a synovial inflammation with subsequent reactive capsular fibrosis. A dense matrix of type I and type III collagen is laid down by fibroblasts and myofibroblasts in the joint capsule. Subsequently, this tissue contracts. Growth factors, cytokines, and matrix metalloproteinases are involved in the inflammatory and fibrotic cascades seen in frozen shoulder.[5]

Adhesive capsulitis is usually classified into two etiological varieties. Primary or idiopathic adhesive capsulitis is not associated with a systemic condition or history of injury[1]. Secondary adhesive capsulitis is most commonly associated with diabetes mellitus. Secondary adhesive capsulitis may also be associated with conditions such as hyperthyroidism, hypothyroidism, and hypoadrenalism, Parkinson's disease, cardiac disease, pulmonary disease, and stroke.[6]

Reeves has described 3 stages of adhesive capsulitis.[7]

1. Stage I It is mainly characterized by pain usually lasting 2-9 months.
2. Stage II *(*frozen stage); pain gradually subsides but stiffness is marked lasting 4-12 months.
3. Stage III (thawing phase); pain resolves and improvement in range of motion appears.

Diagnosis of adhesive capsulitis is mainly clinical. A diagnosis of FS is made in 75% of external rotation test positive patients and glenohumeral arthritis is the only other diagnosis (which can be excluded by radiograph) that produces a positive external rotation test.[8] Codman discussed this entity describing a slow onset of pain, felt near the insertion of the deltoid, inability to sleep on the affected side, and restriction in both active and passive elevation as well as external rotation.[9] Idiopathic adhesive capsulitis is a common medical diagnosis for patients seeking physical therapy. Modalities used to treat adhesive capsulitis were dichotomized by pain predominant and stiffness-predominant classifications, which may be more useful than existing classifications.[10] Deep heat modalities like Shortwave diathermy (SWD) are frequently used as an adjuvant treatment to exercise therapy in order to help the patient regain ROM and restore function to the affected shoulder. Studies have shown that a significant drop in tensile stress occurs with a rise in the temperature of soft tissues to between 40°C and 45°C, compared with that recorded at room temperature (25°C) and also findings suggest that deep heating (using SWD) is effective than superficial heating (using Hot packs)or stretching alone in improving shoulder pain and function in stage II adhesive capsulitis.[11] In this study an attempt has been made to see the effects of SWD in the treatment of adhesive capsulitis and their outcome. The information thus gathered may provide useful guidelines for further study about various aspects on adhesive capsulitis.

Adhesive capsulitis has an incidence of 3–5% in the general population and up to 20% in those with diabetes. This disorder is one of the most common musculoskeletal problems seen in physical medicine. Adhesive capsulitis is a poorly understood musculoskeletal condition that can be disabling.[12] Also in Bangladesh adhesive capsulitis is the commonest shoulder problem. There is no definite/ specific treatment for the condition but many options exist. Few studies showed the beneficial effects of physical agents including superficial and deep heat modalities with shoulder exercises on adhesive capsulitis.In fact SWD is a good modality of treatment in physical medicine especially to provide specific local analgesic effect for various musculoskeletal pains including adhesive capsulitis, in patients with peptic ulcer disease, bronchial asthma and renal impairment. To see the effect of SWD, if this study can show the beneficial effects on this disease in our country, then many patients will be benefitted from many physical medicine and rehabilitation centers of Bangladesh.

It's important to note that dosing the intensity of SWD is based on patient feedback and tolerance. The qualitative method of dosing intensity is widely accepted. The four dose levels are.[16]

Dose I: Just below any sensation of heat;
Dose II: Mild perception of heat;
Dose III: Moderate (comfortable) perception of heat;
Dose IV: Vigorous heating (no pain or burning). If pain threshold is reached, immediately decrease output.

Draper et al have led the way in SWD research in the United States. Their work focuses on using pulsed shortwave diathermy (PSWD) as a heating agent. It often seems counterintuitive to clinicians that PSWD can heat, but it's clear from the research that it can heat efficiently and, when used in combination with a heating and stretching regime, it can improve flexibility in subjects with tight hamstrings and plantar flexors.[17,18]

Draper et al have been able to obtain this 4° Celsius increase using pulsed short-wave diathermy (induction drum) for 15 to 20 minutes (pulse width of 400 microseconds, pulse rate of 800 pps, average output of 48 W).Thermal SWD can serve as an efficient, safe deep heating agent that can enhance the effectiveness of passive stretching, joint mobilization or soft tissue manipulation.[19]

SWD is a modality that produces deep heating via conversion of electromagnetic energy to thermal energy. Oscillation of high frequency electrical and magnetic fields produces movement of ions, rotation of polar molecules, and distortion of nonpolar molecules with resultant heat generation.[20,21] The Federal communications commission limits industrial, scientific and medical use to 13.56MHz,27.12MHz,40.68MHz.67 The 27.12MHz frequency is most commonly used. The heating pattern produced depends on the type of shortwave unit and on the water content and electrical properties of the tissue. Tissues can be grossly divided into those with high water content(muscle,skin,blood) and those with low water content (bone,fat).[22]

SWD units can be inductive or capacitive. Inductive applicators use inductive coils that apply a magnetic field to induce circular electrical fields in the tissue[21]. They achieve higher temperatures in water rich tissues with higher conductivity. These applicators typically have a cable or drum configuration.[23] Cables are semi flexible.Induction coils that can be formed to the contour of the area to be treated. Drum applicators consist of induction coils enclosed in a rigid housing or drum. For a capacitive applicator, the patient is placed between two metal condenser plates. The plates and the patients intervening tissue act as a capacitor and heat is generated by rapid oscillations in the electric field from one plate to the other. Capacitive applicators might achieve higher temperatures in water poor tissues such as subcutaneous adipose tissue.[21,23]

The aim of this study is to evaluate the effect of SWD in adhesive capsulitis.To measure and compare the improvement of pain of affected shoulder using visual analogue scale before and after treatment.

MATERIALS AND METHODS

Study design was Randomized clinical trial.

Study place was department of Physical Medicine & Rehabilitation, Chattogram Medical College Hospital, Bangladesh.

The duration of the study was 6 (Six) months from 01/07/2015 to 31/12/2015.

Patients of shoulder pain attending the Department of Physical Medicine & Rehabilitation outpatient department of Chattogram Medical College Hospital.

Sampling technique was Purposive sampling.

Selection criteria:

Inclusion criteria: a) Patients of adhesive capsulitis b) Age between 30 yrs to 70 yrs. c) Painful restricted movement of shoulder less than 3 months. d) Involvement of right or left or both shoulder's.

Exclusion criteria: a) Skin diseases around the affected shoulder. b) History of fracture or dislocation of shoulder joint, stroke and other neurological deficits. c) Pregnant women. d) Patients on treatment for adhesive capsulitis. e) Patients with co-morbidity e.g. uncontrolled Diabetes, Hypertension, Asthma, Heart diseases, malignancy, neck pain or radiculopathy and rheumatologic diseases.

After taking the informed consent from the patient, details history was taken and a preset data form was filled up for every patient. Past history of illness &any systemic disease was inquired cautiously.A complete physical examination including general physical examination, examination of shoulder joint and neck was done.Base line investigationswas done.

e.g. CBC,2HABF,Urine R/M/E, X-ray of cervical Spine A/P & Lateral View,CXR P/A & lateral view, X-ray of the right/left shoulder B/V was also done. All reports were properly recorded in the data sheet.

For therapeutic trial patients was divided into two groups. Group A (SWD,exercise and analgesic) and Group B (Exercise and analgesic only).

All included patients of both groups was given home shoulder mobilizing exercises – Codman/ pendulum, wall

climbing, pulley and wand exercise 5 repetitions each type 3 times daily for consecutive 6 weeks following demonstration on 1st day of enrollment in the study and subsequent follow up was done whether they were doing the exercise properly. In addition, Group A patients were treated with SWD over the affected shoulder for 20 minutes daily for consecutive 10 days except holidays.

There were three visits and these evaluations were always performed by the same examiner. In each visit patients wereassessed by the following parameters :

1. Visual Analogue Scale (VAS)
2. Tenderness index
3. Shoulder Pain and Disability Index (SPADI)

Use of Analgesics, shoulder mobilizing Exercises and SWD during treatment.

Analgesic (NSAIDS): Tab. Naproxen (250mg) twice daily after meal for pain relieve with Cap. Omeprazole (20mg) coverage for six weeks.

Randomization and blinding methods

Immediately after the examination, the patient was randomized by drawing lottery. Each patient has an equal chance of being allocated to any one of the assigned group.

Grouping :

Treatment Group -

Group A: SWD + NSAIDs + shoulder mobilizing exercises (Codman/ Pendulum, wall climbing, Pulley, Wand exercise)

Control Group -

Group B: NSAIDs + shoulder mobilizing exercises (Codman/ Pendulum, wall climbing, Pulley, Wand exercise).

Ethical clearance was taken from the ethical committee of Chattogram Medical College.

After collection of information, these data was checked, verified for consistency and edited for finalized result. After editing and coding, the coded data was directly entered into the computer by using SPSS 20 version. Data cleaning validation and analysis was performed using the SPSS and graph and chart by MS excel. The result was presented in tables in mean, standard deviation (SD) and percentages. Statistical tests for significance of difference were done using unpaired t test. A "P" value <0.05 was considered as significant.

RESULTS

Table I shows occupation of the study patients**:** among all patients 35.7% were housewives, 16.1% were service holder, farmers were 12.5%, business were 16.2% and laborer were 3.6%.

Table I: Occupation

			Group		Total
			Group A	Group B	
Occupation	House wife	Count	11	9	20
		% within Group	39.3%	32.1%	35.7%
	Service	Count	4	5	9
		% within Group	14.3%	17.9%	16.1%
	Farmer	Count	2	5	7
		% within Group	7.1%	17.9%	12.5%
	Businessmen	Count	4	5	9
		% within Group	14.3%	17.9%	16.1%
	Laborer	Count	2	0	2
		% within Group	7.1%	0.0%	3.6%
	Unemployed/Retired	Count	2	2	4
		% within Group	7.1%	7.1%	7.1%
	Other	Count	3	2	5
		% within Group	10.7%	7.1%	8.9%
	Total	Count	28	28	56
		% within Group	100.0%	100.0%	100.0%

Table II shows site of involvement of the diseases: Among all subjects 48.2% had right shoulder involvement, 50.0% had left side involvement and one patient had both sided disease.

Table II: Site of involvement of shoulder

			Group		Total
			Group A	Group B	
Site of involvement of shoulder	Right	Count	15	12	27
		% within Group	53.6%	42.9%	48.2%
	Left	Count	12	16	28
		% within Group	42.9%	57.1%	50.0%
	Both	Count	1	0	1
		% within Group	3.6%	0.0%	1.8%
	Total	Count	28	28	56
		% within Group	100.0%	100.0%	100.0%

Table III shows analysis of VAS at different follow up data in both group**:** Significant difference between Group A and Group B was found at week 2, week 4 and Week 6 follow-up (P<0.05) whereas initial follow-up was non-significant in VAS analysis (p>0.05)

Table III: VAS score at different follow up

VAS	Group	N	Mean	Std. Deviation	p value
W0 VAS	Group A	28	7.79	1.548	0.677
	Group B	28	7.96	1.644	
W2 VAS	Group A	28	5.79	1.686	0.011
	Group B	28	6.86	1.627	
W4 VAS	Group A	28	4.46	1.753	0.001
	Group B	28	6.32	1.634	
W6 VAS	Group A	28	2.14	1.880	0.001
	Group B	28	5.43	1.834	

* P value calculated by independent sample t test

Table IV shows Analysis of tenderness grading at different follow up data in both group**:** Significant difference between Group A and Group B was found at week 2, week 4 and week 6 followup (p<0.05) regarding change of tender grading in Group A then Group B patients.

Table IV: Analysis of TG at different followup

	Group	N	Mean	Std. Deviation	p value
W0 T.G	Group A	28	2.93	.663	0.443
	Group B	28	3.07	.604	
W2 T.G	Group A	28	2.07	.716	0.001
	Group B	28	2.93	.716	
W4 T.G	Group A	28	1.64	.731	0.001
	Group B	28	2.68	.723	
W6 T.G	Group A	28	.68	.723	0.001
	Group B	28	2.18	.670	

TG: Tenderness grading * p value calculated by independent sample t test

Table V shows Analysis of pain and disability index (SPADI) at different follow up data in both group: Significant difference between Group A and Group B was found at week 2, week 4 and Week 6 followup (p<0.05) regarding SPADI.

Table V: Evaluation of SPADI at different follow-up

	Group	N	Mean	Std. Deviation	p value
W0 SPADI	Group A	28	68.97	14.517	0.289
	Group B	28	73.32	15.866	
W2 SPADI	Group A	28	51.6957	12.32563	0.001
	Group B	28	66.3821	14.67031	
W4 SPADI	Group A	28	39.9621	11.48095	0.001
	Group B	28	61.3604	14.33536	
W6 SPADI	Group A	28	29.1654	12.35642	0.001
	Group B	28	56.7671	13.99734	

DISCUSSION

This present study was done in the Department of Physical Medicine and Rehabilitation ofChattogrammedical College Hospital on 56 patients of adhesive capsulitis. These patients were grouped into two. One group got SWD +NSAIDs + shoulder mobilizing exercises (Codman/ Pendulum, wall climbing, Pulley, Wand exercise) who were grouped as A. Another group was given NSAIDs + shouldermobilizing exercises (Codman/ Pendulum, wall climbing, Pulley, Wand exercise) who were grouped as B. Randomization was done by lottery method andthey were followed up for next six weeks and data were analyzed as intension to treat basis means those who were randomized included in the analysis at all weeks although some were dropped out during subsequent follow up.

Regarding analysis of gender in both groups male and female were matched (p>0.05) and male to female ratio was 1.66: 1. Majority of my participants were males (62.5%) which contradict international studies where females are predominantly sufferers from adhesive capsulitis.[5] This reverse result is most probably due to more male patients seeking medical help than females suggested by unpublished data of patients in our department.

Socioeconomic status was found different in both groups where poor was 21.4%, middle class was 44.6% and rich was 33.9%. Here sampling was purposive and only those patients were taken who visited the OPD of Chattogram medical college hospital. So this socioeconomic scenario may not represent the actual scenario of Bangladesh.

Among all patients 35.7% were housewives, 16.1% were service holders, farmers were 12.5% businessmen were 16.2% and laborers were 3.6%. Despite male participants are slightly higher, most common occupation of the patients is Housewife. It is not clear from my study why housewives are so prone to develop adhesive capsulitis. This present scenario of occupational status of the study patients may not represent the actual scenario of Bangladesh as sampling technique was purposive and taken patients attending in a tertiary care hospital.

Among all subjects 48.2% had right shoulder involvement, 50.0% had left side involvement and one patient had both sided disease. As it has no specific prediction to site both the limb can be affected. There were 92.7% patients who had localized pain and only 7.3% had radiation. Most of the pain in the evening (56.4%) and rest had pain at night (43.6%). Most of the patients in both groups had constant and intermittent type of pain (47.5% and 45.5%) other types were sharp and dull. Different study[13,14,15] support that findings regarding pain analysis.

Significant difference between Group A and Group B was found at week 2, week 4 andWeek 6 followup (P<0.05) whereas initial followup was non-significant in VAS analysis(p>0.05) .Significant difference between Group A and Group B was found at week 2, week 4 and week 6 followup(P<0.05) regarding change of tender grading in Group A then Group B patients. Significant difference between Group A and Group B was found at week 2, week 4 and Week 6 followup(P<0.05) regarding SPADI.

The result from 4th session assessment showed further reduction in pain both groups with patients reported mild pain with movement. Change in VAS was reported in the assessment in all the patients in group B from baseline assessment The result from independent t-test showed significant difference between the 2 intervention groups (all $p < 0.05$) at 95% confidence interval for both the dependent variables i.e. degree of pain and change in range of motion. Study suggest that the use of modalities with the mobilization and stretching exercise can increase the functional capacity of the shoulder joint as early as compared with the patient who only taking electrical modalities, similar study comparing the effectiveness of

short wave diathermy (deep heating agent) and superficial heating in combination with stretching exercise suggested that using heating modalities in conjunction with stretching lead to early increase in range of motion.[13]

CONCLUSIONS

Shoulder mobilizing exercises along with SWD use in adhesive capsulitis has better outcome in terms of pain and disability reduction in subsequent follow up.

RECOMMENDATION:

SWD can be routinely used in the pain and disability management of adhesive capsulitis.

LIMITATIONS:

a) Single center study b) Small sample size

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Original Article

Serum D-dimer Level in Patients with Acute Leukemia in a Tertiary Care Hospital

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Abstract

D-dimer is a molecule, formed by the breakdown of excessive fibrin from the activation of coagulation system. Ample evidence suggests that increased activation of coagulation system in patients with acute leukemia (AL) leads to higher D-dimer levels. Considering shortage of evidence in our perspective, the study was designed to observe the D-dimer level in acute leukemia in different morphological types and phases among the patients admitted in a tertiary care hospital. This hospital based cross-sectional study was conducted at the Department of Medicine and Department of Hematology in Dhaka Medical College Hospital, for a period of 6 months following approval of this protocol. Patients with New case (NC) of AL, at complete remission (CR) and in patient's wither lapsed (R) AL were included in the study. Purposive sampling methods were followed for sample selection. Written informed consents were taken from the all study subjects and ethical issues were ensured. Data were collected by interview using a structured questionnaire. All study population were subjected to details history taking, physical examination and relevant investigations of D-dimer level. Collected data were analyzed by the SPSS version 20.0. Among 50 patients, 58% were males and 42% were females. Mean age was 34±5.6 SD years and the height number of patients (40%) belonged to age group 21-30 years. Three fourth of the patient (76%) had diagnosed as AML and rest of them 24% had ALL. The most common subtype of Acute Myeloblastic Leukemia M3 (AML) was 47, 37% and most common subtype of ALL L2 was 50%. Most of the respondents were found as new case (80%) followed by in decreasing order complete remission case 14% and relapse case 6%. Overall, D-dimer level was 3.69 mg/dl (0.1mg/dl-40 mg/dl), and D-dimer level is slightly higher in AML group than ALL patient (4.26 vs 2.18mg/dl). Moreover, new cases have higher level of D-dimer (4.2 mg/dl) in comparison with complete remission (1.2 mg/dl) or relapse case (2.7 mg/dl). It was also found that APL patients has higher D-dimer level than other form of leukemia. D-dimer level in acute leukaemia patients 3.69 mg/dl. Higher value of AML was found in patients than ALL and increased D-dimer level is also evident in newer case particularly APL. D-dimer level rises in acute leukemia patients. However, further study is recommended with appropriate study design.

Keyword: *Serum D-dimer, acute leukemia (AL), coagulation system, acute myeloblastic leukemia (AML)*

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INTRODUCTION

With a high mortality rate acute leukemia (AL) is a malignant tumor of the blood system and frequently occurs in children, three quarters of the cases are Acute Lymphoblastic Leukemia (ALL).[1,2] While Acute Myeloblastic Leukemia (AML) is more common in adults.[3] Initially acute leukemia was classified based on morphology, French American British Classification (FAB) which classifies AL mainly in AML and ALL, their subtypes are as follows: (1) AML- M0: minimally differentiated, M1: without maturation, M2: with maturation, M3: promyelocytic, M4: myelomonocytic, M5: (a) monoblastic, (b) monocytic, M6: erythroleukemia and M7: megakaryoblastic; (2) ALL- L1: small, monomorphic, L2: large, heterogenous and L3: Burkitt-cell type. Classification of acute leukemia has evolved in recent years, from based purely on morphology [French-American-British (FAB) classification] to also include immunophenotyping, cytogenetic and molecular analysis in classification algorithm (WHO classification).

The important differences in the WHO classification compared with the FAB classification included (a) lowering of the threshold for the percentage of blast cells to 20 per cent in the blood or bone marrow, based on the fact that survival patterns for cases with 20-30 per cent blasts is similar to cases with >30 per cent blasts in the bone marrow; (b) the recognition of acute cases of leukemia with an even lower blast count if specific acute leukemia associated cytogenetic or molecular genetic abnormalities are present; (c) inclusion of AML with cytogenetic abnormalities, AML with myelodysplasia related features, and therapy related AML as distinct categories. D-dimer levels increase in AL patients at initial diagnosis. These are indicative of activated coagulation systems in AL, as reported by authors from several developed countries.[4,5] Acute Myeloid Leukemia and Acute Lymphoblastic Leukemia commonly manifest with elevated peripheral blood blast counts and in some instances, derangements of coagulation parameters.[6] Acute Promyelocytic Leukemia (APL) is well known to be associated with Disseminated Intravascular Coagulation (DIC).[7] Acute Promyelocytic Leukemia (APL) is a clinically distinct form of AML that occurs as a result of specific cytogenetic abnormality resulting in fusion of promoyelocytic leukemia (PML) and retinoic acid receptor-α gene products, which disrupts normal differentiation. Rarely, translocations involving chromosome 17 and 11 or 5 may also result in a similar clinical picture. Patients with APL are at increased risk of bleeding with or without thrombosis because of the procoagulant activity of the granules released by the APL blasts. Despite high cure rates, approaching almost 70-80 per cent in the APL, early deaths occur due to this coagulatizon abnormalities, making it a medical emergency that needs early attention. Besides supportive care and attempt to confirmation of the diagnosis by polymerase for PML-RARα fusion products, it is important to start treatment with all-trans retinoic acid (ATRA), which induces differentiation in the APL blasts. Likewise, ALL can also present with DIC, as can subsets of non-APL AMLs.[8] Formal determinations of DIC involves assessment of coagulation parameters including D-dimer levels, prothrombin time, fibrinogen concentration, and platelet counts. To assess for schistocytes, a useful morphologic feature that may be present in DIC, the morphology of red blood cells in a peripheral blood smear is frequently evaluated.[9,10] However, in a recent study of 35 patients with DIC related to neoplastic and non-neoplastic etiologies, an increase in schistocytes did not appear to be sensitive indicator of DIC found by author.[11] These parameters are reported to be independent in univariate analysis and interdependent in multivariate analysis.[8] During the treatment process of ALs, DIC occurred in one-third of non-M3 AML patients[12] and thrombotic events (TE) appeared more often in cases of APL than in other ALs, with the reported prevalence ranging from 2% to 10-15%.[13] APL may be distinguished from other AML subtypes by core markers of DIC including D-dimer.[14] DIC can also be frequently triggered or aggravated by chemotherapy induction. [12] Although no single test is sufficient to confirm or deny the diagnosis of DIC, D-dimer is still viewed as a reference of DIC diagnostic indicators.[15] As a specific product of the degradation of fibrin clots, D-dimer is regarded as a specific biomarker of fibrin formation and stabilization.[16] When hyperfibrinolysis took place, elevated D-dimer levels were detected in 91% of AML patients.[17] D-dimer was generally recognized as a good reflection of the incidence of thrombotic events and many studies showed that elevation of D-dimer values predicted adverse outcomes in AMLs.[18] APL has evolved from being a deadly to a highly curable disease, due to targeted molecular therapy with all-trans retinoic acid (ATRA). As a result, the incidence of early hemorrhagic deaths for which APL is notorious has reduced to 5-10% as reported in clinical trials.[19] These results are not replicated outside of clinical trials as is evident from recent population-based registries. High incidence of early hemorrhagic deaths remains the greatest contributor to treatment failure in this otherwise curable leukemia.

OBJECTIVES

General Objectives:

To observe D-dimer level in acute leukemia in different morphological types and phases

Specific Objectives:

To assess the demographic profile of the patients to identify APL through D-Dimer level

MATERIALS AND METHODS

This was a cross sectional observational study by selected purposive sampling method. Total 50 cases were taken for this study, 58% were males and 42% were females. Selected patients with new case of AL (NC), complete remission (CR) and in patients with relapsed (R) AL attending at the Department of medicine and hematology in Dhaka Medical College Hospital (DMCH), Dhaka, Bangladesh.

The research work was done during August 2018 to February 2019.

Inclusion Criteria

Patients labelled as new case AL (NC), at complete remission (CR) and in patients with relapsed AL (R) attending the Department of Medicine and Hematology in DMCH. Both sexes by taking informed consent, patients will be included in the study.

Study Procedure

The present study evaluated data from 50 patients that were newly diagnosed with AL or at complete remission or in relapse and were admitted into the Department of Medicine and Department of Hematology in Dhaka Medical College Hospital between August 2018 and February 2019. After initial assessment and treatment, all patients were described about the objective of the study. Informed written consent was taken from each participant. For classification of the patients, FAB classification was followed. Data were collected by interview using a structured questionnaire. All study population was subjected to details history taking, physical examination and relevant investigations. Blood samples were taken from the antecubital vein and placed in plastic tubes containing 3.8% trisodium citrate or ethylenediaminetetraacetic acid (EDTA)·K2 anticoagulant. For plasma separation, blood was centrifuged at 2,500 × g for 15 min at 4°C; blood samples were obtained prior to the initiation of any treatment for AL. Before sample collection, aseptic procedure was followed. Then the patients would be examined by the researcher and all collected data were recorded into the case record form. After completion of data collection, all data were put into the statistical software. Final analysis was done with SPSS 20 with help of a statistician.

Ethical Clearance

The ethical clearance of this study was taken from research & review committee of Dhaka Medical College Hospital (DMCH).

Data Processing &Analysis

After collection of all the required data, these were checked, verified for consistency and then tabulated into the computer using the Package for Social Sciences (SPSS Inc., Chicago, IL, and version 20.0 for Windows). Statistical analysis was carried out using Statistical tests. Normality of data was checked by measures of Kolmogorov–Smirnov tests of normality. For normally distributed data, means were compared using Student's t-test for two groups. Qualitative or categorical variables were described as frequencies and proportions. All statistical tests will be two-sided and performed at a significance level of $p < 0.05$.

RESULTS

Table I shows the distributions of respondents in age group of Acute Leukemia. Among 50 patients 40% was in age group 21-30 years, followed by in decreasing order, 31-40 years 28%, 13-20 years 22%, 41-50 years (8%), 51-60 years 2% and 61-70 years 2%. Mean age was 34±5.6 SD (years).

Table I: Distribution of patients by age (n=50)

Age in year	n	%
13-20 yrs.	11	22.0
21-30 yrs.	19	38.0
31-40 yrs.	14	28.0
41-50 yrs.	4	8.0
51-60 yrs.	1	2.0
61-70 yrs.	1	2.0
Age Mean ± SD	34±5.6	

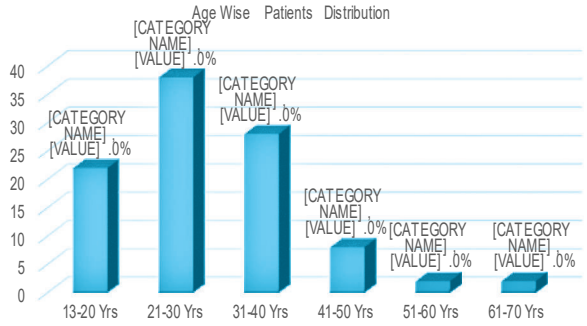

Figure 1: *Distribution of patients by age (N=50)*

Table II shows sex distribution of participants, where male 58% and 42% was female.

Table II: Distribution of respondents by gender (n=50)

Sex	n	%
Male	21	42.0
Female	29	58.0
Total	50	100.0

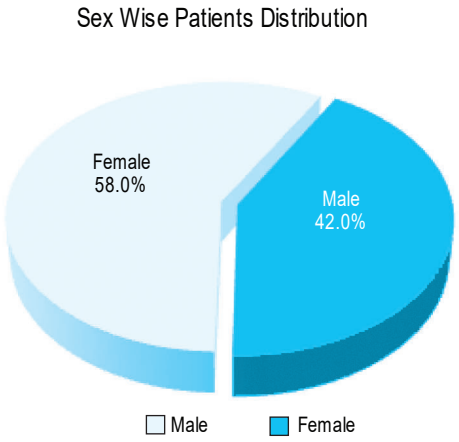

Figure 2: *Distribution of patients by Sex (N=50)*

Table III shows the respondents diagnosed as a case of Acute Myeloid Leukemia (AML) 76% and rest 24% was suffering from Acute Lymphoblastic Leukemia.

Table III: Distribution of respondents by prevalence of AML and ALL (n=50)

AML and ALL	n	%
AML	38	76.0
ALL	12	24.0

Table IV shows the total patients suffering from ALL were 12. ALL was L2 (50%) followed by in decreasing order L1 with 33.33% and L3 with 17.67%.

Table IV: Distribution of respondents by subtype of ALL (n=12)

Type of ALL	n	%
L1	4	33.3
L2	6	50.0
L3	2	16.7

Table V shows the total patients suffering from AML (38). AML M3 was 47.37% followed by in decreasing order M2 21.05%, M1 10.52%, M4 7.89%, M5 5.26%, M0 5.25%, M6 2.16% and M7 2.16%.

Table V: Distribution of respondents by subtype of AML (n=38)

Type of AML	n	%
M0	2	5.3
M1	4	10.5
M2	8	21.1
M3	17	44.7
M4	3	7.9
M5	2	5.3
M6	1	2.6
M7	1	2.6

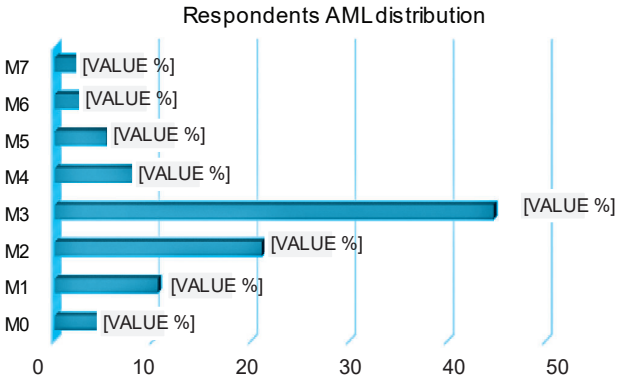

Figure 3: *Distribution of respondents by subtype of AML (n=38)*

Table IV shows the AML patients in age group, here 34% was in 21-30 years followed by 31-40 years and others. Among ALL 16% was in age group 13-20 years.

Table VI: Age wise distribution of AML and ALL diagnosed patient. (n=50)

Age group	ALL (%)	AML (%)	Total (%)
13-20 yrs.	8(16.0)	3(6.0)	11 (22.0)
21-30 yrs.	3(6.0)	17(34.0)	20(40.0)
31-40 yrs.	0(0.0)	14(28.0)	14(28.0)
41-50 yrs.	1(2.0)	2(4.0)	3(6.0)
51-60 yrs.	0(0.0)	1(2.0)	1(2.0)
61-70 yrs.	0(0.0)	1(2.0)	1(2.0)
Total	12(12.0)	38(38.0)	50(100.0)

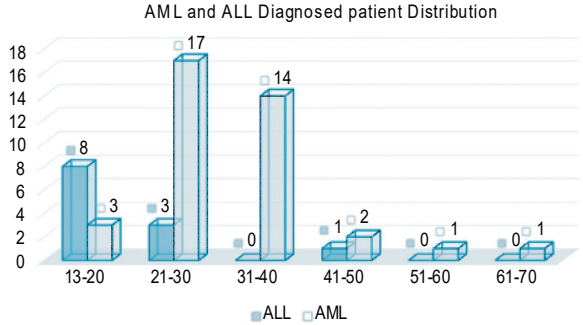

Figure 4: *Age wise distribution of AML and ALL diagnosed patient(n=50)*

Table VII shows the respondents were divided into three disease phases- New case, Relapse case and complete remission case. Respondents were found as new case 80% followed by in decreasing order complete remission case 14% and relapse case 6%.

Table VII: Distribution of AL in relation to phases of disease. (n=50)

Type of AL	M0	M1	M2	M3	M4	M5	M6	M7	ALL	Total
New Case	2(4.0)	3(6.0)	7(14.0)	16(32.0)	3(6.0)	1(2.0)	0(0.0)	0(0.0)	8(16.0)	40(80.0)
Complete Remission	0(0.0)	0(0.0)	0(0.0)	1(2.0)	0(0.0)	1(2.0)	1(2.0)	1(2.0)	3(6.0)	7(28.0)
Relapse	0(0.0)	1(2.0)	0(0.0)	1(2.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(2.0)	3(12.0)
Total	2(0.0)	4(8.0)	7(14.0)	18(36.0)	3(6.0)	2(4.0)	1(2.0)	1(2.0)	12(12.0)	50(100.0)

Table VIII shows the distrbution of complaints; fever 76% was followed by pallor 32%, bleeding disorders 22%, generalized body aches 18%, abdominal pain/distension 14%, lymph node enlargement 12%, weight loss 8% and weakness 6%. Other presenting complaints which were present in less than 5% of patients included vomiting, cough, shortness of breath, easy fatigability, headache, sore throat, flank pain, fits, amenorrhea, urinary incontinence/retention, anorexia, constipation, lacrimal gland enlargement and loss of consciousness.

Table VIII: Percentage of presenting complaints among respondents (n=50)

Presenting Complaint	n	%
Fever	38	76.0
Pallor	16	32.0
Bleeding Disorder	11	22.0
Generalized body aches	9	18.0
Abdominal Pain/distention	7	14.0
Lymph node enlargement	6	12.0
Weight loss	4	8.0
Weakness	3	6.0

Table IX shows the median value of D dimer level, it was 3.69 mg/dl ranging from .1mg/dl to 40 mg/dl. D dimer level found in ALL patient was 2.18 mg/dl ranging from .1mg/dl to 14.6 mg/dl. For AML it was 4.26 mg/dl ranging from 0.1mg/dl to 40mg/dl.

Table IX: D-dimer level in AML and ALL patients. (n=50)

Category of respondents	Count Median value of D-dimer level	Range
Total	3.69 mg/dl	0.1mg/dl-40 mg/dl
ALL	2.18 mg/dl	0.1 mg/dl-14.6mg/dl
AML	4.26 mg/dl	0.1mg/dl-40mg/dl

Table X shows the, mean value of WBC which was found around 11.4 x 10^9/l among new cases, 4.8x10^9/l among complete remission cases and 5.8x10^9/l among relapse cases. Mean Haemoglobin level was found in same chronology 75 g/l, 105 g/l and 92 g/l. Mean value of platelet was 31.1x10^9gm/l, 180x10^9gm/l and 32x10^9 gm/l respectively. Mean value of prothrombin time was 14.6 seconds, 13.7 seconds and 14.6 seconds respectively. Mean value of activated partial thromboplastin time was 36.8 seconds, 38.8 seconds and 39.8 seconds respectively. Mean value of fibrinogen value was 3.4 g/l, 3.7 g/l and 2.9 g/l.

Table X: Hematological measurements in respondents at various stages of AL.(n=50)

Hematological value	New Case	Complete Remission Case	Relapse Case
WBC, x10^9/l	11.4 (0.1-632.4)	4.8 (2.1-13.2)	5.8 (0.1-328.0)
Hb, g/l	75.0 (34.0-149.0)	105.0 (64.0-155.0)	92.0 (45.0-148.0)
PLT, x10^9/l	31.0 (5.0-235.0)	180.0 (6.0-460.0)	32.0(4.0-167.0)
PT, sec	14.6 (12.5-33.6)	13.7 (11.7-18.1)	14.6(11.9-22.8)
aPTT, sec	36.8 (26.6-75.5)	38.8 (29.1-58.8)	39.8 (25.9-59.6)
FIB, g/l	3.4 0.2-9.1	3.7 (0.6-8.5)	2.9 (0.8-8.4)

Table 11 showed the, mean value of D- dimer which was found 4.2 mg/l among new cases ranging from .54 mg/l to 7.0 mg/dl. Among complete remission cases it was found 1.2 mg/l ranging from .1mg/l to 7.2 mg/l. The value was found 2.7 mg/l among relapse cases ranging from .3 mg/l to 40 mg/l.

Table XI: D dimer level among respondents according to different disease stage. (n=50)

	New case	Complete Remission	Relapse
D dimer level	4.2 (0.54-7.0)	1.2 (0.1-7.2)	2.7 (0.3-40.0)

Table XII showed the, significant difference between D-dimer level of new cases of APL (AML, M3) and new cases of other types of AL excluding APL. It shows increased D-dimer level in APL patients.

Table XII: D-dimer level in different stage of disease. (n=50)

Characteristics	All respondents			Respondents excluding APL		
	New Case	Complete Remission	Relapse	New Case	Complete Remission	Relapse
D-dimer, mg/l	4.2* (0.54-7.0)	1.2 (0.1-7.2)	2.7 (0.3-40.0)	2.2* (0.5-10.4)	0.6 (0.1-1.6)	1.6 (0.3-17.4)

DISCUSSION

Relapsed AL remains to be associated with a dismal prognosis, despite the outstanding improvements made over the past decade regarding our knowledge of acute leukemia (AL). Acute leukemia (AL) is a clonal disease that progressively produces novel sub-clones, which exhibit altered phenotypic and cytogenetic traits. AL is divided into acute lymphoblastic leukemia (ALL) and acute myeloid leukemia (AML). AML is the most frequent type of leukemia in adults. Acute promyelocytic leukemia (APL) is a distinct subtype of AML characterized by coagulopathy and signs of disseminated intravascular coagulation.[20] Acute myeloid leukemia (AML) and acute lymphoblastic leukemia (ALL) commonly manifest with elevated peripheral blood blast counts and in some instances, derangements of coagulation parameters.[21-23] acute promyelocytic leukemia (APL) is well known to be associated with disseminated intravascular coagulation, as evidenced by abnormal coagulation parameters and low platelet counts, which can prove fatal if not rapidly treated. Likewise, ALL can also present with disseminated intravascular coagulation (DIC) as can subsets of non-APL AMLs.[24,25] While formal determination of DIC involves assessment of coagulation parameters including D-dimer levels, prothrombin time, thrombin time, fibrinogen concentration, and platelet counts, the morphology of red blood cells in a peripheral blood smear is frequently evaluated to assess for schistocytes, as a useful morphologic feature that may be present in DIC. However, to date, a large-scale statistically powered systematic evaluation of major coagulation parameters in addition to the morphologic features of red blood cells in peripheral blood specimens from patients with acute leukemia has not been performed.[26-28] This study was carried out in Medicine and Hematology department of a tertiary care hospital. Fifty patients were taken who had been diagnosed as cases of various types of acute leukemia. Patients of all disease phase were included. In this study out of 50 respondents, 40% belonged to age group 21-30 years, 28% belong to 31-40 years, 22% belong to 13-20 years, 6% belong to 41-50 years, and 2% belong to each 51-60 years and 61-70 year's group. A study by Niessen et al. on hematological malignancies found majority cases belong to 20-29 year's age group.[29] Here the age range is 13-70 which is not similar to other related studies like the study by Jill M Gore et al.[30] That study found the age range for all types of leukemia from 2-90 years old.[62] but in present study our sample was taken from 'Hematology' and 'Medicine' department of a tertiary care hospital where patients aged less than 13 years old are not usually admitted. In this study female preponderance was found with a percentage of 58% female and 42% male. This finding also differ with similar type of other studies.[28,31,32] found higher male to female ratio. Small sample size and non-probability purposive sampling method may be the reason of this dissimilarity.[31-34] 68% respondents came from urban area and 32% respondents came from rural area. 69% of them belong to middle economic class, 15% to upper class and 16% to lower class. In this study majority of the respondents were suffering for AML with a percentage of 76%. 24% respondents were diagnosed as cases of ALL. A study by Linet et al.[35] found that the frequency of AML is two times higher than that of ALL in Bangladesh. They also found that the incidence of AML is relatively common

in North America, Europe, and Oceania, while adult AML is rare in Asia and America.[35] An another study by Singh et al. [36] found Acute lymphoblastic leukemia (ALL) with a percentage of 29.7% and acute myeloid leukemia (AML) with 37.3% among all hematological malignancies.[36] Total patients suffering from ALL were 12. The most common subtype of ALL was L2 with 50% followed by in decreasing order L1 with 33.33% and L3 with 16.67%. In ALL, L2 was the most common subtype in our study. Similar L2- ALL predominance was observed by Nasim et al however Humayun et al and Gupta showed L1 as the most common subtype.[37-39] Usually ALL subtype is more prevalent in children younger than 15 years old. Study by Shah et al. found L1, L2 and L3 constituted 54.3%, 43.7 % and 2% respectively.[40] As all of our respondents were aged more than 13 years old, real scenario may come out altered here. Total patients suffering from AML were.[41] The most common subtype of AML was M3 with 47.37% followed by in decreasing order M2 with 21.05%, M1 with 10.52%, M4 with 7.89%, M5 with 5.26%, M0 with 5.25%, M6 with 2.16% and M7 with 2.16%. AML-M3 was most common AML subtype in our study which is consistent with findings of study by Nasim et al.[37] However Humayun et al found M1 as most common subtype.[38] Gupta et al and observed M2 subtype as most common in AML cases.[39] One aim of our study was to compare D-dimer level between APL (M3) patients and other AL patients. So, during sample selection, we chose non-probability purposive sampling to pick up more APL patients. Among AML patients, majority found in 21-30 years followed by in decreasing order 31-40 years and others. Among ALL majority patients found in 13-20 years. In a study by Singh et al,[36] a total 105 leukemia cases were diagnosed in children (≤15 years), in which ALL subtype was the most prevalent (n=69 cases).[36] This similar finding was observed with other studies.[37,39] While total respondents were 132, maximum cases were found as AML in adult who were 102 in number as compared to children with a number of 30 in our study. Same observation also found in studies conducted by Paul B et al.[42] Usually AML is generally a disease of older people and is uncommon before the age 45. The average of people when they are first diagnosed with AML is about.[36] ALL occurs both in children and adults with highest rates seen between the ages three and seven years.[43] This study finding [44] shows dissimilarity due to sampling method and sample size. In this study Fever (76%) was the most common presenting complaint followed by pallor (32%), bleeding disorders (22%), generalized body aches (18%), abdominal pain/distension (14%), lymph node enlargement (12%), weight loss (8%) and weakness (6%). Gore et al[45] found easy bruising, prolonged bleeding, gingival bleeding, epistaxis, or menorrhagia as frequent presenting complaint. Among 50 respondents, 80% were found as new case, 14% after complete remission and 6% as relapse case. A study by Takahashi et al. states that standard intensive chemotherapy induces complete remission in 60-80% of cases. But a significant number of patient's experience relapse of the disease.[43] In this study, we found elevated D-dimer levels in acute leukemia patients at initial diagnosis. Authors reports from several developed countries are indicative of activated coagulation systems in acute leukemia patients. Athale et al [4] reported a mean D-dimer level of 2,766 (SD 2,385.8) ng/mL in newly diagnosed case of ALL in children while Giordano et al.[5] reported a mean of 299 (SD 32) ng/ mL in children with ALL.[4,5] Comparing the incidence of elevated D-dimer level in ALL, our finding was lower than Athale's but almost similar with the result of Giordano et al [5] Another studies reported that 80% of their subjects with ALL had elevated D-dimer levels. Chojnowski et al [46] also found that 85% of AML subjects had elevated D-dimer levels. In this study, comparative blood routine and coagulation measurements were done between APL and other forms of AL. No significant changes found in median range of Hb, PLT, PT, aPTT and FIB level. WBC level was found to be raised in other forms of AL excluding APL. Statistically significant difference found in D-dimer level where D-dimer level increased in APL. Study by Shahmarvand et al, Wangqiang et al and Jawed et al. found similar findings.[43,47,48]

LIMITATION OF THE STUDY

This was a single center study. Sample size was small but large number of sample could provide more information regarding D-dimer level in acute leukaemia.

CONCLUSION

In this study, it was observed that D-dimer level raised in acute leukemia patients and higher value is noted in acute myeloid leukemia patients than acute lymphoblastic leukemia patients. Considering the treatment status, it is more prominent in new cases than complete remission cases and relapse cases. Furthermore, the level also increased in APL than other variety of leukemia. However, further larger cohort study is needed to finalize the findings.

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Original Article

Role of Red Cell Distribution Width and Platelet Count Ratio to Predict the Severity and Outcome in Acute Pancreatitis

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Abstract

Clinical course of acute pancreatitis (AP) varies widely, its clinical features exhibit very low sensitivity for the prediction of severity of disease which is associated with high morbidity and mortality. Several single or multi parameter scoring systems have been described to evaluate the severity of AP. But sometimes, it is not clinically practicable to use these scoring systems for evaluation. This study aimed to find out the Role of Red Cell Distribution Width and Platelet Count Ratio (RPR) to predict the Severity and Outcome in AP. This prospective longitudinal study was carried out from July 2019 to July 2020, at the in-patient department of Gastrointestinal, Hepatobiliary and Pancreatic Disorders, BIRDEM General Hospital, Dhaka. Total 100 patients with AP were included for this study according to selection criteria. An informed written consent was taken from all the participants. Detail history was taken and thorough physical examination was done along with relevant laboratory investigations. Ranson's score, Modified Glasgow score, Bedside index of severity in acute pancreatitis (BISAP), red cell distribution width and platelet count ratio (RPR) were calculated. All data were recorded and analyzed by Statistical package for social sciences (SPSS) 23. In this study 44% patients were more than 60 years with a mean age of 51.34 (±15.45) year. More than two thirds patients were (67%) male. In mild acute pancreatitis mean value of Ranson's score, BISAP score and modified Glasgow score was 0.79 (±0.14), 0.90 (±0.1) and 0.80 (±0.14) and 3.29 (±1.16), 1.77 (±0.46) ,2.74 (±0.69) in moderate to severe pancreatitis respectively with statistically difference were found in both severities (p<.05). The patients with mild pancreatitis and the patients with moderate to severe pancreatitis had significant difference (p<.05) between mean RDW (14.68±1.59% versus 15.51±3.27%), mean RPR (0.043±0.06 versus .062±.002) and platelet count (340.9±841.6 cells/mm^3 Versus 236.4±825.4 cells/mm3). The ROC analysis of RPR in predicting severity of pancreatitis showed a cut-off value of ≥ 0.056 and diagnostic accuracy test showed sensitivity, specificity, PPV, NPV and accuracy as 63.6%, 82.2%, 81.4%, 64.9% and 72% respectively. Mean Ranson's score, BISAP score and Modified Glasgow score was 2.09 (±1.45), 1.34 (±0.39) and 1.83 (±1.08) in survived patients and 5.50 (±0.70), 4 and 3.50 (±0.70) in dead patients with significant difference between both groups (p<.05). Mean RDW (15.08±2.67% Vs 17.85±0.21%), mean platelet count (284.43±143×109/L Vs 236.4± 825.4×109/L) and mean RPR (0.053±0.02 Vs 0.094± 0.005) was also significant between survived and dead patients (p<.05). The ROC analysis of RPR in predicting outcome showed cut-off value of ≥ 0.06 and diagnostic accuracy test showed sensitivity, specificity, PPV, NPV and accuracy as 100%, 63.27%, 5.26%, 100% and 64% respectively. Red cell distribution width and platelet count ratio (RPR) can be used as a novel biomarker to predict the severity and mortality of acute pancreatitis in very early stage.

Keywords: *Red cell width distribution platelet count ratio, severity of acute pancreatitis, outcome of acute pancreatitis*

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INTRODUCTION

Acute Pancreatitis (AP) is defined as an acute condition presenting with abdominal pain, a threefold or greater rise in the serum levels of the pancreatic enzymes amylase or lipase, and/or characteristic findings of pancreatic

inflammation on contrast enhanced CT.[1] It is an inflammatory process in which local pancreatic injury leads to systemic inflammation through activation of cytokine cascades AP has an annual incidence of 13 to 45 per 100,000 persons and is the fifth leading cause of hospital deaths.[2] In the United Kingdom the incidence of AP is 150-420 cases per million and 330-430 cases per million in the United States. The clinical spectrum of AP patients varies widely ranging from mild local pancreas inflammation to severe multiple organ failure.[3] Several studies indicated that the mortality rate of patients with AP is currently approximately 3.8% to 7%; in severe AP, it varies from 7% to 42%. Based on the most recent updated Atlanta classification, AP can be classified into three grades: mild acute pancreatitis (MAP), moderately severe acute pancreatitis (MSAP), and severe acute pancreatitis (SAP). MAP shows no organ failure, nor local or systemic complications. The patients' symptoms usually disappear within 1 to 2 weeks' of hospitalization with low mortality; MSAP can cause transient organ failure (duration<48h) combined with local or systemic complications; SAP is manifested by persistent organ failure (duration>48h) or death with generally poor prognosis.[4]

In acute pancreatitis, early assessment of the patient which can lead to an accurate prediction of the severity is useful for several reasons. The first well established step is the need to categorize patients at risk for complications for appropriate stratification in clinical trial. Furthermore it is important to identify the patients who are at risk for developing complications in order to be able to initiate effective management before those complications developed.[5] Some scoring systems, such as Ranson's, Glasgow and APACHE, provide valuable clues to evaluate the severity and mortality of AP. In several studies, certain biological markers, such as elevated C-reactive protein, elevated creatinine, high blood glucose and hemoconcentration on admission, have been used to predict mortality.[6] Complete blood count is a laboratory test frequently used in clinical practice and comprises white blood cell, red blood cell and platelet counts, and their morphological indices, such as the red cell distribution width (RDW).[7] Red cell distribution width (RDW) is a widely used laboratory parameter for the quantification of the extent of erythrocyte anisocytosis, which is calculated by dividing SD of red blood cells (RBCs) volume by mean corpuscular volume (MCV) and multiplying by 100 to express the results as percentages, and reflects the variability of the size of the circulating erythrocytes.[8] RDW is a traditional marker which mainly be used for the classification and differential diagnosis of anemia. Recently, more and more studies have reported that RDW, as an independent maker, has been used in many pathophysiological conditions, such as cardio-vascular diseases, pulmonary diseases, type 2 diabetes mellitus, progressive inflammatory status and even cancer, and high RDW values are associated with increased mortality in both general population and patients with the above diseases.[9] As one of platelet indices, increased level of MPV serves as a biomarker of platelet activation. Platelets are shown to be as active players in antimicrobial host defense and the induction of inflammation and tissue repair. Once the production of platelet count is decreased, immature platelets are activated and become bigger, and the values of MPV increase. Huang, Zhang and Wu showed that patients with Persisting organ failure in acute pancreatitis showed a significantly higher value of MPV on admission.[10]A recent study by Reddy et al. showed that high platelet lymphocyte ratio (PLR) value is associated with very bad prognosis and poor outcome or death in acute pancreatitis[2]. Another study by Chen et al. where RDW to platelet count ratio (RPR) is used to predict hepatic fibrosis stages in patients with chronic Hepatitis B[11]. But RDW and platelet count ratio value has scarcely been investigated as, a potential biomarker of AP. Therefore, we aimed to investigate whether RPR is associated with the severity and outcome of patients with AP.

MATERIALS AND METHODS

It was a prospective observational study done in department of GastointestinalHepatobilliary and Pancreatic disorders (GHPD) in BIRDEM General Hospital from July 2019 to July 2020. Total 100 patientswith acute pancreatitis admitted in department of gastroenterology of BIRDEM General Hospital, Dhaka was considered as study population. Patients withage less than 18 years, post ERCP pancreatitis, end stage renal disease, hematological disorders such as iron deficiency anaemia, myelo-proliferative disorders, myelodysplastic syndrome and recent blood transfusion were excluded from the study. History of each patient was taken and recorded. Physical examination was done systematically. A questionnaire was filled up by the investigator which contained information about particulars of the patient including age, sex, socioeconomic condition, smoking, alcohol, drug history and other co-morbidities like diabetes mellitus, hypertension and ischemic heart disease. Presenting complains such as abdominal pain, vomiting, anorexia, jaundice was recorded. Following laboratory investigation such as serum lipase, amylase, C-reactive protein, complete blood count, serum electrolytes, serum enzymes associated with cholestasis, serum hepatic and renal function tests, bilirubin levels, fasting blood glucose, lactate

dehydrogenase, capillary gas analysis was done on admission day.Using these parameters, Ranson's score, Modified Glasgow score and BISAP score was calculated. We also calculated the red cell distribution width and platelet ratio (RPR). After measuring RPR it was compared with the usual scoring system and evaluation was done if there was any the association of RPR for prediction of the severity and outcome of acute pancreatitis. Outcome assessment was done at 5th day of follow up (in hospital mortality or survival). Statistical analysis of the study was done by computer software device as the Statistical Package for Social Science (SPSS) version 23.0. All data were interpreted with 95% Confidence Interval with accepting 5% error. In all cases, p value <.05 was considered statistically significant. The qualitative variables were expressed as frequency and percentage and the quantitative variables were expressed as mean with standard deviation. During analysis, student t testwas considered to estimate the relationship or association between the variables. Sensitivity and specificity calculation was done to test by using standard formula. ROC curve was formulated to estimate the cut off value for prediction of the severity and outcome of the acute pancreatitis cases.

RESULTS

This study was conducted in department of GHPD in BIRDEM General Hospital, Dhaka. Total number of respondents was 100.

Table 1 shows majority (44%) of the respondents were ≥ 60 years old where mean age of the respondents was 51.34±15.45 years of SD. Male was predominant (67%).

Table I: Distribution of the respondents by Sociodemographic profile (n=100)

	Frequency (n)	Percentage (%)	Mean±SD
Age group			51.34±15.45
20 to 29 years	12	12	
30 to 39 years	15	15	
40 to 49 years	18	18	
50 to 59 years	11	11	
≥60 years	44	44	
Sex			
Male	67	67	
Female	33	33	

Table II shows 45% had mild pancreatitis, 39% had moderate and 16% had severe pancreatitis.

Table II: Distribution of the respondents by Severity of Acute pancreatitis (n=100)

Severity of pancreatitis	Frequency (n)	Percentage (%)
Mild	45	45
Moderate pancreatitis	39	55
Severe pancreatitis	16	16
Total	100	100

Table III shows mean value of Ranson's score, Modified Glasgow score in mild and moderate to severe acute pancreatitis patients (P<0.01). Significant difference has been found among the score in different types of severities. Beside mean RDW and Platelet countin mild pancreatitis and moderate to severe pancreatitis are also shown. Significant difference has been found with RDW, platelet and RPR in different types of severity (P<0.01).

Table III: Association between mild pancreatitis and moderate-severe pancreatitis in Ranson's score, BISAP score, Modified Glasgow score, RDW (%), Platelet count, and RPR count (n=100)

Score	Mild Pancreatitis	Moderate-severe Pancreatitis	p value
Ranson's score	0.79±0.14	3.29±1.16	*<0.01
BISAP score	0.90±0.1	1.77±0.46	*<0.01
Modified Glasgow score	0.80±0.14	2.74±0.69	*<0.01
RDW (%)	14.68±1.59	15.51±3.27	*<0.01
Platelet (109/L)	340.9±841.6	236.4±825.4	*0.006
RPR	0.043±0.06	0.062±0.02	*<0.01

*p value was determined by Independent sample t test.

The ROC analysis of RPR for the prediction of severity of acute pancreatitis showed an AUC of 0.747 (95% CI 0.650-0.843) which is statistically significant (p<0.01). A cut-off value of ≥ 0.056 showed 63.6% sensitivity and 82.2% specificity.

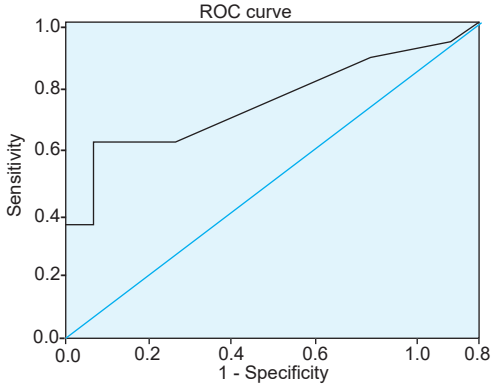

Figure I: *ROC curve analysis of RPR for the prediction of acute pancreatitis*

Cut off value	AUC	Std. Error	p value	95% Confidence interval	sensitivity	specificity	PPV	NPV	Accuracy
≥0.066	0.756	0.05	<0.01	0.659-0.853	50.91	93.33	90.32	60.87	70
≥0.056	0.747	0.05	<0.01	0.650-0.843	63.6	82.2	81.4	64.9	72
≥0.046	0.659	0.06	0.01	0.546-0.772	78.18	51.11	66.15	75.71	66

A cut-off value of RPR ≥ 0.056 to predict severity of acute pancreatitis showed sensitivity, specificity, PPV, NPV and accuracy as 63.6%, 82.2%, 81.4%, 64.9% and 72% accordingly.

Table IV shows 51% patients had no complications, 47% experienced complications. Mortality was 2%.

Table IV: Distribution of the respondents by Outcome (n=100)

Outcome		Frequency (n)	Percentage (%)
Survived	Pancreatitis without complication	51	51
	Pancreatitis with complication	47	47
Death		2	2
	Total	100	100

Table V shows mean RDW, mean platelet was 284.43±143 (109/L) and mean RPR was 0.053±0.02 in survivor death patients. Significant difference had been found between both groups. Beside mean Ranson'sscore, mean BISAP score and mean Modified Glasgow score was 1.83±1.08 in survivor patients in dead patients shows significant difference.

Table V: Association of RDW, Platelet count, RPR count, Ranson's score, BISAP score and Modified Glasgow score with mortality of patients (n=100)

Parameters	Survival	Death	p value
RDW (%)	15.08±2.67	17.85±0.21	*<0.01
Platelet (109/L)	284.43±143.70	236.4±825.4	*0.001
RPR	0.053±0.02	0.094±0.005	*<0.01
Ranson's score	2.06±1.45	5.50±0.70	*<0.01
BISAP score	1.34±0.39	4	*<0.01
Modified Glasgow score	1.83±1.08	3.50±0.70	*<0.01

*p value was determined by Independent sample t test.

The ROC analysis of RPR for the prediction of mortality in hospital due to acute pancreatitis showed an AUC of 0.969 (95% CI 0.918-1.0) which is statistically significant (p<0.01). A cut-off value of ≥ 0.06 showed 100% specificity and 63.27% sensitivity.

A cut-off value of RPR ≥ 0.06 for prediction of mortality in hospital due to acute pancreatitis showed sensitivity, specificity, PPV, NPV and accuracy as 100%, 63.27%, 5.26%, 100% and 64% accordingly.

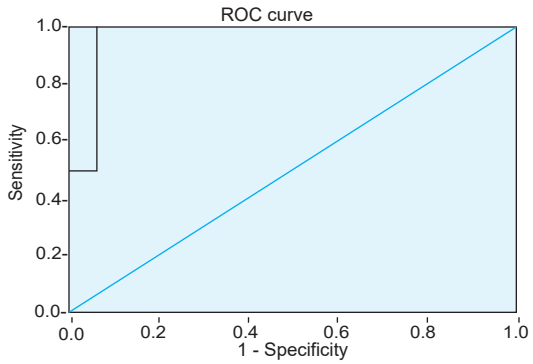

Figure 2: *ROC curve analysis of RPR for the prediction of mortality in hospital*

Cut off value	AUC	Std. Error	p value	95% Confidence interval	sensitivity	specificity	PPV	NPV	Accuracy
≥0.07	0.540	0.07	0.54	0.404-0.676	76.53	100	77	8.0	100
≥0.06	0.969	0.06	<0.01	0.918-1.0	63.27	100	64	5.26	100
≥0.05	0.517	0.06	0.778	0.401-0.632	40.82	100	42	3.33	100

DISCUSSION

Acute pancreatitis is one of the most common diseases of the gastrointestinal tract. Several prognostic scoring systems and biological markers have been used to predict severity and mortality in AP. However, most of them are complex. The ratio of RDW to TPC known as RPR can be evaluated as a prognostic index to know the degree of severity of SIRS and hence the outcome in acute pancreatitis.

In this study 44% respondents were equal or more than 60 years. Mean age of the respondents was 51.34±15.45. Pancreatitis often develops in people with older age because of cell and tissue changes and organs also change with increasing age. Aging organs slowly lose function. In western countries pancreatitis associated with gallstones and other causes peaks in the seventh decade beside in New York and Atlanta the peak age incidence of pancreatitis is 44 and 38 years respectively and in our country the incidence of acute pancreatitis may be differ due to lower life expectancy of Bangladeshi people.[12] In a previous study by Zhou et al., it was observed that among 406 patients' mean age was 57 years ranging from 44 to 71 years.[13]

Among the respondents of our study, 67% were male and 33% were female. Smoking, alcohol consumptionis some risk factors of pancreatitis which is more common in male in Bangladeshi perspective. This can be the reason of higher number of male patients.Ahmed et al. observed out of 50 patients 32 patients were male and 18 were female where male to female ratio was 1.78:1.[12] Barad et al. did a similar type of study and observed out of 60 patients 31 were male and 29 patients were female[14]. Cetinkaya et al. observed among all the 102 patients 59 were female and 43 were male patients.[7]

In the current study 45% patients had mild pancreatitis, 39% had moderate and 16% had severe pancreatitis. In a previous study by Gravito et al. observed 146 (46.8%) patients had mild AP, 75 (24.0%) had moderately severe AP and 91 (29.2%) patients had severe AP[15]. Barad et al. observed that among 60 patients 31 patients were having mild form of acute pancreatitis whereas 29 patients were having moderately severe or severe form of the disease[14].

In our mean Ranson's score was 0.79±0.14, BISAP was 0.90±0.1 and Modified Glasgow score was 0.80±0.14 in mild pancreatitis patients beside mean Ranson's score was 3.29±1.16, BISAP was 1.77±0.46 and Modified Glasgow score was 2.74±0.69 in moderate to severe pancreatitis patients. There was significant difference found among the groups.In a previous study by Barad et al. observed mean Ranson's score was 0.774, BISAP score was 0.194 and modified Glasgow score was 0.839 in mild pancreatitis patients whereas mean Ranson's score was 4, BISAP score was 1.897 and modified Glasgow score was 3.276 in moderate to severe pancreatitis patients. Significant difference had been found between both group of patients[14]. Another study by Zhou et al. observed in mild pancreatitis patients mean Ranson's score was 1 and BISAP score was 1 where as in moderately severe patients mean Ranson's score was 2 and BISAP score was 2 and in severe pancreatitis patients mean Ranson's score was 4 and BISAP score was 3 that was significantly higher according to severity of patients[13].

In this study mean RDW was 14.68±1.59, Platelet count was 340.9±841.6 and RPR was 0.043±0.06 those who had mild pancreatitis beside mean RDW was 15.51±3.27, platelet count was 236.4±825.4 and RPR was 0.062±0.02 among those who had moderate to severe pancreatitis. Significant difference had been found with RDW, platelet and RPR between severities of AP. A cut-off value of RPR ≥ 0.056 showed sensitivity, specificity, PPV, NPV and accuracy as 63.6%, 82.2%, 81.4%, 64.9% and 72% accordingly in predicting severity of acute pancreatitis.Barad et al. observed mean RPR value in mild acute pancreatitis group was 0.038 as compared to 0.068 in the severe acute pancreatitis group. In ROC curve analysis it was found that at a cut of value of 0.045 RPR has a sensitivity of around 90% and specificity of around

73% in predicting the severity of the disease[14]. About 51% patients had no complications, 47% had complications and 2% died according to data of our study.Zhou et al. mentioned total mortality rate was 3.45%[13]. Another study by Baradet, al. observed a total of 49 patients were cured of the disease and discharged and 11 patients died of the disease[14].

In our study mean Ranson's score was 2.09±1.45, BISAP score was 1.34±0.39 and Modified Glasgow score was 1.83±1.08 in survivor patients beside mean Ranson's score was 5.50±0.70, BISAP score was 4 and Modified Glasgow score was 3.50±0.70 in death patients. Significant difference had been found between both groups.In a previous study by Barad et al. observed mean Ranson's score was 1.653, BISAP score was 0.551 and modified Glasgow score was 1.653 in survivor patients whereas mean Ranson's score was 5.364, BISAP score was 3.091 and modified Glasgow score was 3.636 in death patients. Significant difference had been found between both groups[14]. Another study by Zhou et al observed in survival patients mean Ranson's score was 2 and BISAP score was 1 where as in death patients mean Ranson'sscore was 4 and BISAP score was 3 that was significantly higher from survival patients[13].

In this study mean RDW was 15.08±2.67, platelet count was 284.43±143.70 and RPR was 0.053±0.02 in survivor beside mean RDW was 17.85±0.21, platelet was 236.4±825.4 and RPR was 0.094±0.005 in death patients. There was significant difference between both outcome groups with RDW, platelet count and RPR.A cut-off value of RPR ≥ 0.06 showed sensitivity, specificity, PPV, NPV and accuracy as 100%, 63.27%, 5.26%, 100% and 64% accordingly in predicting mortality.Barad et al. found the mean RPR value was 0.044 in the survivor group and 0.089 in the death group and observed that at a cut-off value of 0.071 RPR has a sensitivity of 82% and specificity of 96% in predicting mortality in patients with acute pancreatitis[14]. Cetinkaya et al. observed with a cutoff value of 0.000067, RPR had a PPV 26.67%, NPV 96.39%, sensitivity 80% specificity, 70.08% in prediction of mortality[7].

CONCLUSIONS

RPR on admission can be used to stratify the severity in acute pancreatitis patients. Patients with a high RPR value should be transferred to an intensive care unit and frequent monitoring of the condition is required in these patients.

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Original Article

Vitamin D Status in Hypothyroid Patients

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Abstract

Vitamin D deficiency is a global health problem. It is estimated that about 25-50% of patients commonly encounter vitamin D deficiency in clinical practice. Recent studies show hypothyroid patients suffer from significantly low vitamin D level. As vitamin D and thyroid hormone act through steroid receptors, one can affect the other's action. Considering the scientific evidence, the study was aimed to assess the vitamin D level among the subjects with hypothyroidism. This hospital-based case-control study was conducted among 70 subjects including 35 cases and 35 controls at the Departments of Medicine and Endocrinology in Dhaka Medical College Hospital in 6 months duration following approval of this protocol. Data were collected by face to face interview, using a structured questionnaire and case record review. Hospital records including laboratory reports were also reviewed. Thirty-five cases and thirty-five control samples were screened for vitamin D levels. Data analysis was done using Statistical Package for Social Sciences (SPSS) version 23. Among the participants, 55 were female with a male-female ratio of 1: 3.67. The mean age was 44.6 ± 11.69 year. The highest number of patients were in between 41 to 55 year (41%). The majority of cases were from rural areas (67.0%). There was no significant differences in socio-demographic profiles between the cases and control groups (P >0.05). Hypovitaminosis D was found in 67% of cases. Among them 39.0% had mild insufficiency (20-29 ng/ml), 21.0% had moderate deficiency (10-19 ng/ml) and 7.0% had severe deficiency (< 10 ng/ml). The mean vitamin D level was 23.79 ± 8.1 ng/ml. Serum 25(OH)D level was markedly reduced in hypothyroid cases in comparison to the euthyroid control group [22.14 ± 8.02 and 26.22 ± 7.53 respectively); P < 0.005]. Data showed hypothyroid patient is likely to develop Hypovitaminosis D 3.37 times higher compared to a euthyroid patient (OR=3.37; 95% CI:1.644-9.7440; P=0.02). Moreover, this lower level is not associated with the difference in age, sex and occupation (P< 0.005). Hypovitaminosis D is associated with hypothyroidism with no variation in respect to age, sex and occupation. The hypovitaminosis D is significantly associated with hypothyroi- dism in the study population.

Keywords : *Hypovitaminosis D , hypothyroidism, euthyroid, serum TSH , serum 25(OH)D, vitamin D status*

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INTRODUCTION

Vitamin D is called "the Sunshine Vitamin." Exposure to sunlight has been a significant source of Vitamin D in humans.[1] This fat-soluble steroid prohormone is mainly produced photochemically in the skin from 7-dehydro-cholesterol. [2] The ultraviolet light with a wavelength of 290–320 nm action makes Cholecalciferol (as denoted by Vitamin D) by acting on 7- dehydrocholesterol found in the skin of humans. After being made in the skin or ingested, vitamin D is transported to the liver from the kidney, where it is hydroxylated into 25-hydroxy vitamin, the primary circulating form of vitamin D.[3] Over the last few years, vitamin D has gained much attention.[4] Though initially thought to be uncommon, recent epidemiological data suggest that it is widespread. It was assumed that over a billion people worldwide are vitamin D deficient or insufficient.[5] Due to sufficient exposure to sunlight, Vitamin D deficiency is less common in tropical countries- this was the previous assumption.

Nevertheless, surprisingly, 80% of the population in South Asia suffers from vitamin D deficiency (<20 ng/mL), and almost 40% of them are severely deficient (<10 ng/mL).[6] In India, the prevalence rate is around 50-90%.[7]Goswami et al. evidenced that more than 90% of the healthy population has below-normal serum levels of 25-hydroxy Vitamin D (25(OH)D) with almost undetectable values during winter in India.[8] In Nepal, among adults, the prevalence is 73.7%.[3] In Bangladesh, most of the studies have focused on the children, and Ahmed AMS et al. showed 42·3 % insufficient, 31·2 % deficient and 3·4 % severely vitamin D deficiency in his study group.[9] On the other hand, the prevalence of vitamin D deficiency among women in the reproductive age group in Bangladesh is 81%.[10]

Vitamin D has been well-known for its role in bone metabolism and is an essential element for calcium and phosphate metabolism and skeletal health.[12] Deficiency in child cause rickets, whereas adult deficiency increases the propensity for osteoporosis.[12] In recent time, effects on extraskeletal tissue has also been observed.[13] Low Vitamin D level has been identified as a risk factor for diabetes mellitus, cancers, multiple sclerosis, atherosclerosis, infectious diseases, and other autoimmune diseases, including autoimmune thyroid diseases.[9,14,15] Several studies suggest that low levels of vitamin D have also been associated with autoimmune thyroid diseases like Hashimoto's thyroiditis and Graves' disease.[11,15-17] Moreover, impaired vitamin D signaling has been reported to encourage thyroid tumorigenesis.[16,17]

Vitamin D exerts its action through binding to vitamin D receptors (VDR) and activating VDR-responsive genes.[14] Initially thought to be vitamin D just affecting calcium homeostasis, researchers have shown that this steroid hormone works in more than 36 cell types with VDR, such as the thyroid gland; its role in regulating cell proliferation and differentiation has also been shown.[14,18] As both vitamin D and thyroid hormones act through steroid receptors; therefore, one may affect the action of another.[5] So, a lower level of vitamin D is likely to aggravate the systemic abnormalities associated with hypothyroidism.[18] The study was aimed to assess the vitamin D level among the subjects with hypothyroidism.

MATERIALS AND METHODS

This case-control study was conducted in the Departments of Medicine and Endocrinology in Dhaka Medical College Hospital. A total of 70 subjects were selected for the study; 35 were considered cases, and the rest 35 as control. Cases were diagnosed patients of hypothyroidism and control were healthy adult of similar age and sex. Hypothyroidism was defined as failure of the thyroid gland to produce sufficient thyroid hormone to meet the metabolic demands of the body. Symptoms of hypothyroidism include weight gain, cold intolerance, fatigue, dry skin, dry hair, menorrhagia, constipation, hoarseness, muscle aches and pain, depression, impotence, infertility.Signs of hypothyroidism include weight gain, hoarse voice, malar flush, periorbital edema, anemia, bradycardia, hypertension, delayed relaxation of deep tendon reflex, dermal myxedemaHypothyroidism is diagnosed if serum thyroid stimulating hormone (TSH) is >5.7 μU/mL (reference interval: 0.7-5.7 μU/mL) and free T4 (fT4) is <0.7 ng/dL (reference interval: 0.7-1.9 ng/dL).

Levels of vitamin D were categorized as:

- more than 30ng/ml is considered to be normal
- 20-29ng/ml (<50nmol/L) is insufficient
- less than 20ng/ml (<25nmol/L) is deficient
- less than 10ng/ml (12.5nmol/L) signifies severe deficiency.

Newly diagnosed patients with hypothyroidism and older than 13 years of age, both sexes, were included in the study as 'cases'. On the other hand, diagnosed patients with hypothyroidism on treatment or diagnosed with CKD, intestinal disease including Crohn's disease, cystic fibrosis and celiac disease, cholestatic liver disease, and strictly vegans were excluded from the study. Moreover, critically ill patients and pregnant women were also excluded. Informed written consent was taken from every patient. Ethical clearance was obtained from the ethical review committee of the Dhaka Medical College & Hospital. About 5ml of fasting sample was collected from each patient and control for testing of Serum T3, T4, TSH, and Vitamin D levels. Testing was done by ELISA using standard protocols. Besides this, socio-demographic parameters and duration of the illness were also recorded during the interview. Following the interview, collected data were recorded into the case-record form. Collected data were cleaned and cross-checked. Data were analysed using Statistical Package for Social Sciences (SPSS) version 23 for windows. Mean and the standard deviation (SD) for all the variables were calculated. Student's "t" test was performed to see the differences between mean values for each tested variable. Correlations between Vitamin D levels and TSH were shown by by correlation coefficient.

Odds Ratio was calculated to assess the strength of association between Vitamin D status and the Hypothyroidism. Results considered significant when $P < 0.05$.

RESULT

This study was done on 70 patients of either sex aged between 16 to 70 years of age. Thirty-five of these patients were considered the control group with normal thyroid levels. The other 35 cases were considered the case group who were newly diagnosed hypothyroid patients with increased serum TSH levels> 5.7 μU/ml.

Table I among the 70 evaluable patients, 55 were females, and 15 were males, with a male-female ratio of 1: 3.67. Among 70 studied cases, the mean age was 44.6 ± 11.69 years. Most of the patients were in-between 41 to 55 years (41%). The majority of cases were from rural areas (67%).

The socio-demographic profile was similar between both groups (P > 0.05).

Table I: Comparison of socio-demographic characteristics between case (35) and control (35) group (n=70)

Variable	Case group (Hypothyroid)	Control group (Euthyroid)	Total n (%)	p-value
Age group				
13-25 years	4	3	07 (10)	
26-40 years	8	9	17 (24)	0.791
41-55 years	16	13	29 (41)	
Above 55 years	7	10	17 (24)	
Sex				
(female)	29	26	55 (79)	0.382
Residence (Rural)	22	25	47 (67)	0.445
Monthly income				
< 15000 taka	12	16	28 (40)	
15000-40000 taka	17	15	32 (46)	0.578
> 40000 taka	6	4	10 (14)	
Academic qualification				
No formal education	6	8	14 (20)	
Primary	11	12	23 (33)	0.895
SSC	13	11	24 (34)	
HSC and above	5	4	09 (13)	

Table II shows serum 25(OH)D level was markedly reduced in hypothyroid cases compared to the euthyroid control group. T-test showed a significant decrease in vitamin D levels in hypothyroid patients (P-value < 0.005). The mean value of serum TSH and 25(OH)D in both groups are given

Table II: Comparison of the mean value of serum TSH and 25(OH)D in case and control group (n=70)

Study group	Case group (n=35) (Hypothyroid)	Control group (n=35) (Euthyroid)	Total (n=70)	p-value
Serum TSH value (Mean ± SD), μU/ml	10.89 ± 2.63	2.71 ± 0.98	6.81 ± 4.56	0.000
Serum 25(OH)D value (Mean ± SD), ng/ml	22.14 ± 8.02	26.22 ± 7.53	23.69 ± 8.1	0.032

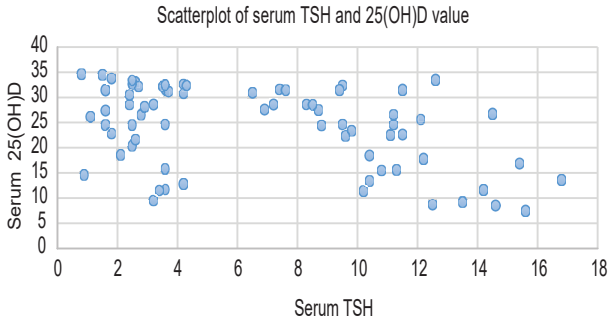

Figure 2. Scatterplot of serum TSH and 25 (OH) D value (n=70)

Figure-2 is a scatterplot of serum 25(OH)D and serum TSH of the studied cases (n=70) was done. Serum TSH values were plotted along with X-axis, and serum 25(OH)D values were plotted along Y-axis. It showed that serum 25(OH)D values decreased with the higher serum TSH values in most cases.

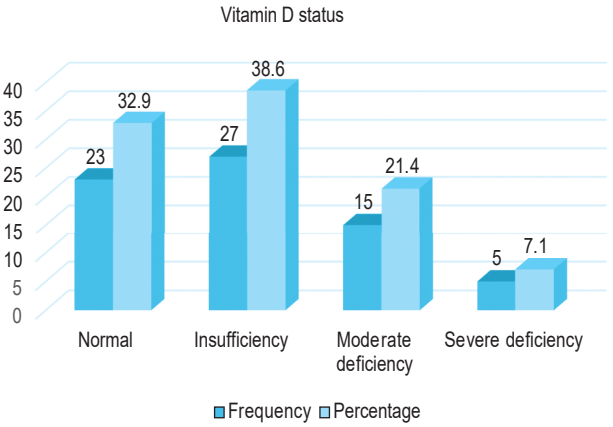

Figure 3. Vitamin D status of the cases according to serum 25 (OH) D level (n= 70)

Figure illustrate the Vitamin D status (assessed by serum 25(OH)D level) in both case and control groups. The mean value was 23.686 ± 8.1 ng/ml. Hypovitaminosis D was found in 67% of cases. Among them 39% had mild insufficiency (20-29 ng/ml), 21% had moderate deficiency (10-19 ng/ml) and 7% had severe deficiency (< 10 ng/ml). In 33% cases had normal value (≥ 30 ng/ml).

Table III shows socio-demographic profile of both case and control groups showed hypovitaminosis D was significantly found among elderly patients (P-value < 0.05). See details

Table III: Association of socio-demographic factors with hypovitaminosis D (n= 70)

Variable	Hypovitaminosis D (n= 47)	Normal Vit-D (n=23)	p value
Age group			
13-25 years	02	05	
26-40 years	10	07	0.041
41-55 years	21	08	
Above 55 years	14	03	
Sex (female)	39	16	0.199
Residence (Rural)	31	16	0.763
Monthly income			
< 15000 taka	19	09	
15000-40000 taka	22	10	0.871
> 40000 taka	06	04	
Academic qualification			
No formal education	10	04	
Primary	11	12	0.086
SSC	18	06	
HSC and above	08	01	

Table IV shows significant signs and symptoms observed in hypothyroid patients. Among the hypothyroid cases (n=35), fatigue (77%), cold intolerance (71%), and weight gain (69%) were more frequently found. Muscle pain was found in 65% of cases; on the contrary, muscle pain was present in 83% of cases (39 out of 47) of hypovitaminosis D

Table IV. Major signs and symptoms found among hypothyroid cases (n= 35)

Sign / symptom	Frequency	Percentage
Cold intolerance	25	71
Weight gain	24	69
Anorexia	22	63
Bradycardia	16	46
Delayed reflex	14	40
Fatigue	27	77
Muscle pain	23	65
Bone/joint pain	06	17

Table V shows in our study, hypovitaminosis D was more frequently found among the case group (hypothyroid cases) in comparison to the control group (euthyroid cases), and the result was statistically significant (χ^2 value = 5.245, P-value = 0.022, n = 70); shown

Table V. Association of hypovitaminosis D with hypothyroidism (n=70)

		Vitamin D status		Total	χ^2 value	p-value
		Hypovitaminosis D	**Normal vitamin D**			
Patient status	**Case group (hypothyroid)**	28	7	35	5.245	0.022
	Control group (euthyroid)	19	16	35		
Total		47	23	70		

DISCUSSION

Female predominance was observed in this study, which supports the study of Mehta M et al. in India, where female predominance was observed as out of 100 cases, 53 were female, and 47 were male[19]. Another study in a private medical college in Bangladesh by Hossain et al. Also found similar findings with female predominance where out of 212 patients, 73.6 % were female, and 26.4 % were male[20], which is identical to the results of this study.

Among 70 studied cases, the mean age was 44.6 ± 11.69 years between the case and control group. Most of the patients were in-between 41 to 55 years (41%). The majority of cases were from rural areas (67%), the monthly income of the majority, 46%, was 15000-40000 taka, and most of the respondents, 34%, had completed only SSC. The socio-demographic profile was similar between both groups (P > 0.05). Nevertheless, the socio-demographic profile of both case and control groups showed that hypovitaminosis D was significantly found among elderly patients (P-value < 0.05). A study about vitamin D levels in different socio-demographic populations in Bangladesh by Hossain et al. reported that the mean age of males was 49.7 (age range 18- 95) & females was 45.7 (range 18- 80). Regarding the level of education, 36.8% were graduate & post-graduate, level of education was not a strong determinant in that study, and occupation 61.7% of the study population was housewife, and socioeconomic status 85% were middle class[20]. Also, In other studies by Mehta M et al. [19]Koch et al.[21] Mackawy et al. [22] reported no relation or association between socio-demographic status and vitamin D and hypothyroidism. Benner et al.[23] also said no association between socio-demographic status and Vitamin D level and thyroid disease. Another study by Jääskeläinen et al.[24] among the adult population in mainland Finland reported a strong association between vitamin D level, age, and education level, which supports this study.

Among the hypothyroid cases (n=35), fatigue (77%), cold intolerance (71%), and weight gain (69%) were more frequently found. Muscle pain was found in 65% of cases; on the contrary, muscle pain was present in 83% of patients (39 out of 47) with hypovitaminosis D. In a study by Douchet et al.[25] reported clinical features were fatigue, weakness, mental slowness, drowsiness, chilliness, dry skin, constipation, deafness, depression, hoarseness, skin infiltration, anorexia, paleness, slowed reflexes, weight gain, cramps, snoring, paraesthesia, dizziness, bradycardia, disorientation. Out of these, fatigue and weakness were found in 50% of cases, and mental slowness, drowsiness, chilliness, dry skin, constipation, and deafness were found in % of the patients. In the young group, seven clinical signs were found in more than 50% of patients: fatigue, weakness, chilliness, paresthesia, weight gain, cramps, and depression. Seven other signs, mental slowness, dry skin, skin infiltration, drowsiness, constipation, dizziness, and slowed osteo-tendinous reflexes, were observed in more than 30% of patients. Some classical signs of hypothyroidism were not commonly observed. Another study by El-Shafie et al.[26] reported fatigue was the most typical symptom for 25%, followed by constipation which accounted for 20%. Rare symptoms such as dysarthria and dysphagia associated with a hoarse voice, and sleep apnea, all of which were localized in the oropharyngeal region, were observed in one patient. The patient had no goiter to explain these symptoms. Another rare presenting symptom was the swelling of the lower limbs, which was observed in another patient. Twenty-four patients (10 hypothyroid plus 14 subclinical hypothyroid) were asymptomatic, accounting for 38% of patients with hypothyroidism. Seven patients had only one symptom, and that was either constipation or fatigue. Three patients had two symptoms. Three had three symptoms, and one had four symptoms. Four patients had only one sign of hypothyroidism, either dry skin or the presence of a goiter. Only one patient had two signs. The remaining patients, i.e. 25 out of 30 patients with hypothyroidism, had no signs. Some classical signs of

hypothyroidism such as hoarseness of voice, hair loss, bradycardia, and confusion, were uncommon. These findings could be due to the place of study and inclusion criteria of the study population. Knutsen et al.[27] in a study of 572 patients reported that, in patients with nonspecific musculoskeletal pain, a total of 58% (334/572) patients had low vitamin D levels less than 50 nmol/L, which is supportive of the finding of this study.

Out of 70 patients, serum 25(OH)D level was markedly reduced in hypothyroid cases compared to the euthyroid control group. T-test showed a significant decrease in vitamin D levels in hypothyroid patients (P-value < 0.005). Mean value of serum TSH for case group (n=35) was 10.89 ± 2.63 and control group (n=35) was 2.71 ± 0.98, Mean value of serum 25(OH)D in case group (n=35) 22.14 ± 8.02 ng/ml, and control group (n=35) was 26.22 ± 7.53 ng/ml and for the total study population (n=70) mean value was 23.69 ± 8.1 ng/ml. In this study, hypovitaminosis D was more frequently found among the case group (hypothyroid cases) in comparison to the control group (euthyroid cases), and the result was statistically significant (χ^2 value = 5.245, P-value = 0.022, n = 70). A study by Khare et al. [28] reported that Vitamin D levels were found to be significantly lower in TPOAb-positive hypothyroid patients (both male and female) (10.66 ± 18.34 ng/dL), And Serum TSH was higher in TPOAb-positive hypothyroid females (13.67 ± 74.56). Another study in Korea among 304 patients by Shin et al.[29] reported lower levels of 25(OH)D3 (12.6±5.5) in patients with AITD hypothyroidism. These findings are supportive of the findings of this study. Another study by Kivity et al. [30] reported that vitamin D deficiency was significantly higher in patients with AITDs than in healthy individuals (72% versus 30.6%; P,0.001). Another study by Koch et al.[21] reported the mean value of vitamin D in subclinical hypothyroid patients (16.73±12.46 ng/ml) and overt hypothyroid (13.23±10.08 ng/ml) were remarkably lower than the euthyroid (29.07±19.01 ng/ml) with P value<0.05. A significant negative correlation analysis between vitamin D and TSH (r=-0.314, P<0.01) has been seen in Pearson's correlation. Vitamin D deficiency negatively correlates with TSH. In this study's result in the scatter plot, it can be seen that Vitamin D deficiency negatively correlates with TSH, similar to the study of Koch et al. Also, a study by Mackay et al. reported that Serum 25(OH) Vitamin D was significantly lower in hypothyroid patients than in controls (t=-11.128, P =0.000). Its level was insignificantly decreased in females than in male patients (t=- 1.32, P >0.05). Moreover, serum calcium levels were significantly decreased in hypothyroid patients compared to controls (t= -5.69, P = 0.000), which is somewhat similar to this study with small differences found due to study site, sample criteria, and study population.

CONCLUSIONS

Study finds that, women of the fourth decade were frequently affected with hypothyroidism compared to their male counterparts. Overall, hypovitaminosis of D was present in three-fifths of the patients. Hypovitaminosis D is significantly more common in hypothyroid patients than in controls. Therefore, it may be concluded that in this population, hypovitaminosis D is associated with hypothyroidism. However, a multi centre study with larger sample simple size is thus recommended.

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Original Article

Evaluation of Ophthalmoscopic Findings in Type 2 Diabetic Patients at a Tertiary Level Hospital

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Abstract

Diabetes mellitus (DM) is a global burden of disease. Long standing disease causes macrovascular and microvascular complications. Diabetic retinopathy (DR) is the most common microvascular complication of diabetes and it remains a leading cause of blindness and visual impairment in the working-age population in both developing and developed world. Patients with diabetes often developed other ophthalmic complications, such as corneal abnormalities, glaucoma, iris neovascularization, cataracts, and maculopathy. The study was carried out to evaluate the ophthalmoscopic changes in type-2 diabetes mellitus (T2DM) patients. This hospital based cross-sectional study was conducted in the department of Medicine, Shaheed Suhrawardy Medical College Hospital, Dhaka, from September 2018 to March 2019. Patients with T2DM attended at the department of medicine within the mentioned period were enrolled after fulfilling the selection criteria. Patients with dense, lentalopacities and other media opacities which prevented posterior segment examination were excluded from the study. Sample was selected by purposive sampling method. Detail demographic data were collected from the patients and recorded in structured case report form. Clinical examination and relevant investigations were done meticulously. Then pupil was dilated and ophthalmoscopic examination was done. Among the 50 diabetic patient's male was 54%, middle aged (49-60 years) was 54% and sedentary workers was 84.0% with a positive family history of DM was 56.0%. Most of the patients were known hypertensive (64.0%) at the time of enrolment and almost all (94.0%) were taking antihypertensive drug. Retinal photography was performed in all patients and retinopathy was detected in 29 (58%) patients. Fundoscopic findings revealed that cotton-wool spots detected in 32.0% patients, Flame-shaped hemorrhages was 16.0% patients; Arteriovenous nipping was is 18.0% patients and opticdisc swelling (Papilloedema) in 26.0% patients. In this study 21 (42%) patients had normal fundoscopic findings. Retinopathy was more common in smoker (70.0%). Uncontrolled and long-standing diabetes and high HbA1c was major risk factors for the development of retinopathy (P < 0.001). In conclusion, diabetic retinopathy is more common in male smoker with uncontrolled and long-standing diabetic patients. T2DM is a major cause of blindness as it affects microvasculature of retina.

Keywords: *Diabetes mellitus, diabetic retinopathy, ophthalmoscopic.*

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INTRODUCTION

Diabetes mellitus (DM) is associated with reduced life expectancy, significant morbidity due to diabetes related microvascular and macrovascular complications.[1]

Diabetes mellitus (DM) is e of the oldest diseases known to man. It was first reported in Egyptian about 3000 years.[2]A study showed there were 171 million people in the world with diabetes in the year 2000 and this figure will be 366 million by 2030.[3] The American Diabetes association (ADA) assumed` the national costs of diabetes will be $192 billion in 2020.[4,5]

DM is linked with carbohydrate, protein and fat metabolism and results in microvascular, macrovascular and neuropathic complications.[6]The differentiation between type 1 and type 2 DM was clearly made in 1936.[7] Symptoms of marked hyperglycemia include polyuria, polydipsia, weight loss, sometimes with polyphagia, and blurred vision. Impairment of growth and susceptibility to certain infections may also accompany chronic hyperglycemia. Acute, life-threatening consequences of uncontrolled diabetes are hyperglycemia with ketoacidosis or the nonketotic hyperosmolar syndrome. Diabetes can be classified into the following general categories: [8] 1) Type 1 diabetes (due to β-cell destruction, usually leading to absolute insulin deficiency), 2) Type 2 diabetes (due to a progressive loss of insulin secretion on the background of insulin resistance), 3) Gestational diabetes mellitus (GDM) (diabetes diagnosed in the second or third trimester of pregnancy that is not clearly overt diabetes) and 4) specific types of diabetes due to other causes, e.g., monogenic diabetes syndromes (such as neonatal diabetes and maturity-onset diabetes of the young [MODY]), diseases of the exocrine pancreas (such as cystic fibrosis), and drug- or chemical-induced diabetes (such as with glucocorticoid use, in the treatment of HIV/AIDS or after organ transplantation).

Diabetes mellitusis a heterogeneous diseasein which clinical presentation and disease progression may vary considerably. Discrimination between type 1 or type 2 diabetes is important, but at the time of diagnosis clear classification is not possible in most of the cases.There is no age limitation of DM. Type 2 diabetes occurs only in adult and type 1 diabetes occurs in children is no longer accurate. Patients with type 2 diabetes may present with diabetic ketoacidosis and Children with type 1 diabetes typical symptoms of DM.[9]

Potential loss of vision, nephropathy, peripheral neuropathy, and autonomic neuropathy causing gastrointestinal, genitourinary, and cardiovascular symptoms and sexual dysfunction are recognized complications of DM. Hypertension and atherosclerotic events are more common in people with DM.

Diabetic Retinopathy (DR) is a chronic disease of the retina caused by microangiopathy due to long term effects of DM, leads to progressive damage of retina causing blindness. Diabetic Retinopathy (DR) is the leading cause of vision loss in adults aged 20–74 years.[10] From 1990–2010, DR ranked as the fifth most common cause of preventable blindness and fifth most common cause of moderate to severe visual impairment.[11] With diabetes now recognized as a global epidemic, the incidence of retinopathy, a common microvascular complication of diabetes, is expected to rise to alarming levels. Diabetic retinopathy is classified into non- proliferative diabetic retinopathy (NPDR) and proliferative diabetic retinopathy (PDR), characterized by the growth of new blood vessels (retinal neovascularization). NPDR is further divided into mild, moderate, and severe stages that may or may not involve the development of a macula diabetic macular oedema (DME).[12] The major causes of severe visual impairment are PDR and DME. Nearly all patients with Type 1 diabetes and >60% of patients with Type 2 diabetes are expected to have some form of retinopathy by the first decade of incidence of diabetes .[13,14]

DR, and severe non-proliferative DR or proliferative DR (PDR) or the presence of diabetic macular edema (DME) are more common in uncontrolled DM patients.[15]

The Diabetes Control and Complications Trial (DCCT) and United Kingdom Prospective Diabetes Study (UKPDS) clinical trials confirmed the strong relationship between chronic hyperglycemia and the development and progression of diabetic retinopathy, but the underlying mechanism that leads to the development of microvascular damage as a result of hyperglycemia remains unclear .[16,17]

PDR is the most common vision-threatening lesion particularly among patients with type 1 diabetes. However, DME is responsible for most of the visual loss experienced by patients with diabetes as it remains the major cause of vision loss in the highly prevalent type 2 diabetes[18] and is invariably present in patients with type 2 diabetes with PDR.[19] In addition to vision loss, DR and DME have also been shown to contribute to the development of other diabetes-related complications including nephropathy, peripheral neuropathy and cardiovascular events .[20,21,22,23]

The most clinically important risk factors for progression to vision loss include duration of diabetes, hyperglycemia and hypertension. Control of serum glucose and blood pressure have been shown to be effective in preventing vision loss due to DR. Prevalence and risk factors of DR have been studied widely in previous studies including regional and ethnic differences, but epidemiological data on DME are relatively scarce. In, Bangladesh there are only few study regarding this. So, this study was carried out to see the pattern of diabetic retinopathy and to evaluate the risk factors in type 2 diabetes patients in Bangladesh.

MATERIAL AND METHODS

This cross-sectional observational study was conducted in the Department of Medicine, Shaheed Suhrawardy Medical College Hospital, Dhaka, Bangladesh during the period of September 2018 to March 2019. Patients with diabetes mellitus attended indoor or emergency department of medicine within the mentioned period were enrolled after fulfilling the selection criteria. Patients with dense, lental opacities and other media opacities which prevented posterior segment examination were excluded from the study.

DATA COLLECTION

The study protocol included a thorough history taking regarding age, onset, duration of manifestation of DM, associated medical problem and complaintsrelated anycomplications were noted in detail. A thorough clinical examination including general physical examination, investigations was conducted meticulously. Risk factorsincluding HTN, smoking, dyslipidemia, obesity and family history of premature coronary artery disease were noted. Baseline laboratory investigation e.g., CBC, serum creatinine, HbA1C, fasting blood sugar, fasting lipid profile, ECG, was done in each patient. Then pupilswere dilated and direct as well as indirect ophthalmoscopic examinations were done. Note was made of any abnormalities in media, appearance of disc and blood vessels and of the presence and hemorrhages and exudates. Whenever possible, the retinal abnormalities were photographed.

STASTICAL ANALYSIS

Data for socio- demographic and clinical variables were obtained from all participants by the use of a pre- designed and easily understandable questionnaire. After collection of all information, these data were checked, verified for consistency and edited for finalized result. After editing and coding, the coded data were directly entered into the computer by using SPSS (Statistical Package for Social Sciences). Quantitative data will be expressed as mean and standard deviation and qualitative; data will be expressed as frequency and percentage. Comparison will be done by Chi-Square (χ^2) test and unpaired t-test where necessary. A probability (p) value of < 0.05 was considered statistically significant.

ETHICAL CONSIDERATION

Prior to the commencement of this study, the research protocol was approved by the ethical committee in Shaheed Suhrawardy Medical College Hospital. The aims and objectives of the study along with its procedure, method, risks & benefits of this study explained to the respondents in easily understandable local language and then informed written consent was taken from each patient or relatives or parents in case of minor. They were assured that all the information and records would be kept confidential and the procedure will be helpful for both the physician and the patients in making rational approach of the case management.

RESULTS

Table I shows distribution of socio-demographic variables among the study subjects. A total 50 patients were enrolled, male was slightly predominant (56%) and in age group 54.0% were within 40-60 years old age group.

Table I: Distribution of socio-demographic variables among the study subjects (n = 50)

Socio-demographic Variables		Frequency	Percentage
Age Group	≤ 40 Years	3	6.0
	40 – 60 Years	27	54.0
	≥ 60 Years	20	40.0
Sex	Male	27	54.0
	Female	23	46.0
Occupation	Sedentary	42	84.0
	Non-sedentary	8	16.0
Total		50	100.0

Table II shows distribution of risk factors among the study subjects. Known hypertensive was 64.0% and 94.0% was taking antihypertensive, where 40% had history of abnormal lipid profile and 88.0% were continuing treatment for that.

Table II: Distribution of risk factors among the study subjects (n = 50)

Risk Factors		Frequency	Percentage
Smoking Habit	Smoker	10	20.0
	Ex-smoker	7	14.0
	Non-smoker	33	66.0
Family History of Diabetes	Present	28	56.0
	Absent	22	44.0
Total		50	100.0

Table III shows distribution of risk factors among the study subjects. Fundoscopic findings revealed that cotton-wool spots detected in (32.0%) patients, Flame-shaped hemorrhages was 16.0% patients; arteriovenous nipping was 18.0% patients and disc oedema(Papilloedema) in 26.0% patients, where 42% patients had normal fundoscopic findings.

Table III: Distribution of risk factors among the study subjects (n = 50)

Risk Factors		Frequency	Percentage
History of Hypertension	Present	32	64.0
	Absent	18	36.0
History of Dyslipidemia	Present	20	40.0
	Absent	30	60.0
Total		50	100.0

Table IV contains eye examination and fundoscopic findings. Out of 50 patients, who had fulfilled the inclusion criteria, 29(58.0%) patients had ocular fundus abnormalities. The rest 41(42%) patients showed no ocular fundus abnormalities.

Table IV: Eye examination and fundoscopic findings (n=50)

Fundoscopic findings	Frequency*	Percentage
Cotton-wool spots	16	32.0
Flame-shaped hemorrhages	8	16.0
Arteriovenous nipping	9	18.0
Optic disc swelling(Papilloedema)	13	26.0
Hard exudates	6	12.0
Macular oedema/maculopathy	19	38.0
Dot and blot hemorrhages	5	10.0
Normal fundus	21	42.0

*Multiple respondents

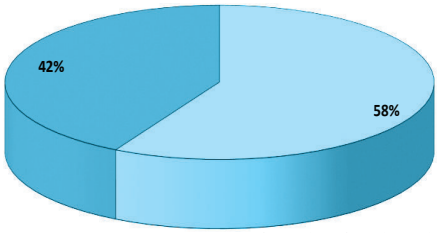

Figure I shows the Frequency of ocular fundus abnormality (n=50)

Table V shows spectrum of maculopathy amongst the patients with *retinopathy.* In this study 38.0% of total patient had maculopathy which complicate 65.5% of patients with retinopathy.

Table V: Spectrum of maculopathy amongst the patients with *retinopathy* (n = 29)

Maculopathy	Frequency	Percentage (%)
Absent	10	34.5
Present	19	65.5
Total	29	100.0

Table VI shows frequency of retinopathy among the study subjects**.** Retinopathy was present in 70.0% of the patients with a history of smoking. Ex-smokers had an increased incidence (57.1%).

Table VI: Frequency of retinopathy among the study subjects (n = 50)

Sex	Retinopathy		Total (n = 100%) n (%)
	Present (n = 29) n(%)	Absent (n = 21) n(%)	
Male	16 (59.26)	11 (41.74)	27 (54.0)
Female	13 (56.52)	10 (43.47)	23 (46.0)

Table VII shows duration of diabetes was found highly significant (p value <0.001) in the development of retinopathy but not in its progression and severity. Median duration with retinopathy was 10 (SD ±6.62).

Table VII: Evaluation of smoking habit as a risk factor of retinopathy among the study subjects.

Smoking Habit	Retinopathy		Total (n = 100%) n (%)
	Present (n = 29) n (%)	Absent (n = 21) n (%)	
Smoker	7 (70.0)	3 (30.0)	10 (20.0)
Ex-smoker	4 (57.1)	3 (42.8)	7 (14.0)
Non-smoker	18 (54.5)	15 (45.4)	33 (66.0)

Table VIII shows distribution of *duration of diabetes* according to presence and severity of retinopathy among the study subjects**.** Duration of DM was found to have non-significant role in the development of maculopathy (p>0.05).

Table VIII: Distribution of *duration of diabetes* according to presence and severity of retinopathy among the study subjects

Duration of DM(Years)	Retinopathy	N	MEAN	± SD	MEDIAN	RANGE	SIGN. *
	Present	29	10.91	6.620	10.00	30-1	P = 0.001^S
	Absent	21	6.89	5.346	5.50	25-1	
	Total	50	9.72	6.408	8.00	30-1	

* Independent samples t – test. S = Significant (P < 0.05)

Table IX shows association of glycemic status (*HbA1c*) with retinopathy among the study subjects .Median HbA1c was 8.90 (±2.17) in patients with retinopathy but 7.20 (±1.63) who did not have retinal change which is highly significant (P < 0.001).

Table IX: Association of glycemic status (*HbA1c*) with retinopathy among the study subjects

HbA1c (%)	Retinopathy	N	MEAN	± SD	MEDIAN	RANGE	SIGN. *
	Present	29	9.481	2.173	8.90	14.2-5.8	P = <0.001S
	Absent	21	7.750	1.633	7.20	12.3-5.6	
	Total	50	8.743	2.132	8.25	14.2-5.6	

* Independent samples t – test. S = Significant (P < 0.05)

Table X shows association of comorbidity of HTN with retinopathy among the study subjects

Table X :Association of comorbidity of HTN with retinopathy among the study subjects

HTN (n=32)	Retinopathy	N	MEAN	± SD	MEDIAN	RANGE	SIGN.*
	Present	25	9.652	2.25	8.90	14.2-5.8	P = <0.001S
	Absent	7	7.281	1.85	7.20	12.3-5.6	
	Total	32	8.743	2.132	8.25	14.2-5.6	

* Independent samples t – test. S = Significant (P < 0.05)

DISCUSSION

This hospital based cross-sectional study was done during a period of six months. Known diabetic patients confirmed by ADA criteria were enrolled in this study. A total of 50 patients after fulfilling the inclusion and exclusion criteria were included in the study. Out of 50, 27 (54%) were male. Age varied from 38-90 yrs., with majority (68%) from middle aged group (40-60 yrs). This was significant because the active population group suffering from diabetes most with risk of complications like retinopathy, nephropathy etc.

Most of the patients enjoyed sedentary life style. Out of 50, 42 (84.0%) fall in this category. Weight of the patients ranged from 38-93 kgs with Median 62 kg.

All patients enrolled in this study were known diabetic and on treatment. The duration of diabetes ranged from 1 yr. to 30 yrs. (median 8 yrs.). HbA1c was done in all patients to know the glycemic control. Median HbA1c 8.250 (14.2-5.6) which indicates poor control of diabetes in many patients.

In this study, retinopathy of any form was present in 29 patients (58.0%) and diabetic maculopathy detected in 19 patients which much more correlates with results of other study. A pooled individual participant meta-analysis involving 35 studies conducted worldwide from 1980 to 2008, estimated global prevalence of any DR and PDR among patients with diabetes to be 35.4 and 7.5 % respectively.[24] Diabetic retinopathy (DR) is a leading cause

of vision-loss globally. Of an estimated 285 million people with diabetes mellitus worldwide, approximately one third have signs of DR and of these, a further one third of DR is vision-threatening DR, including diabetic macular edema (DME).[24] A recent cross-sectional study at rural level found the prevalence was 21.6%[92]. Previous individual studies in other countries have shown considerable variability in DR prevalence estimates among individuals with both diagnosed and undiagnosed diabetes, with rates ranging from 17.6% in a study in India [25] to 19.9% in China[26] to 33.2% in a large U.S. study.[27] Differences in study methodologies, population characteristics, and ascertainment and classification of DR have made direct comparisons between studies difficult.

In this study 38.0% of total patient had maculopathy which complicate 65.5% of patients with retinopathy. Slight male predominance in the development of DR was observed (59.26% vs 55.07%) in this study. Male gender was observed to be associated a little more with the presence of any DR.[28] as this study. Similar observations were made by Pradeepa et al., in an urban Indian population and in the Los Angeles Latino Eye Study. [29,30] The reason for this may be gene or life style.

Smokers and ex-smokers, although small in number, showed increased prevalence of DR. 70.0% of smokers and 57.1% of x-smokers had DR in comparison to 54.5% of non-smoker who develop DR. This is supported by studies conducted by Cho NC et al,[31] where incidence of DM was increased in smokers. Same result were observed in Jee SH *et al*, Uchimoto S *et al* and Wannamethee SG *et al* [32,33.34] .

Duration of DM was seen to be important in the development of retinopathy. in this study, median duration was found 10 yrs in patients with DR and 5.5 yrs who did not develop (p<0.001). Many studies investigated and concluded that the duration of diabetes is a strong risk factor for development of DR supporting this study findings.[35,36,37] The Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR) had revealed the prevalence of any retinopathy was 8% at duration of 3 years diabetes, 25% at duration of 5 years diabetes, 60% at duration of 10 years diabetes, and 80% at duration of 15 years diabetes. The prevalence of PDR was 0% at duration of 3 years diabetes and increased to 25% at duration of 15 years diabetes. In the study conducted by Dandona et al in type 2 diabetes, it is reported that 87.5 per cent of those with >15 yr duration of diabetes had DR compared with 18.9 per cent of those who had <15 yr duration.[38] So annual retinal examination and early detection of DR could considerably reduce the risk of visual loss in diabetic individuals.

In many studies, severity of DR increased with the duration of diabetes and most of the moderate to severe NPDR cases were identified at 15 years after diagnosis.[39,40,41] Most of the diabetic retinopathy was of the mild or moderate NPDR and PDR type in India [38] as well as European population in ten years after diagnosis [41]. The prevalence of more severe grades of retinopathy was higher in Pima Indians with longer durations of diabetes [42]. Severe retinopathy (NPDR/PDR) however was more frequent in type 2 than type 1 diabetic patient has shown in European study [41]. In the Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR), the rate of PDR varied from 2% in patients who had DM for less than 5 years to 15.5% in diabetics who had DM for 15 or more years. All the above study findings were not consistent with this study. Though duration of DM was found highly significant for development of retinopathy, severity of DR was not found influencive by the duration of DM in this study (p>0.05).

There was strong evidence to suggest that the development and progression of DR was influenced by the level of hyperglycemia [43,44] It was observed in another study that glycosylated hemoglobin levels was a significant risk factor for the long-term progression of diabetic retinopathy.[45] This study showed here a similar result where HbA1c , the marker for glycemic control , had direct influence in the development of DR (Median 8.9 vs 7.2 for DR and NDR) and also in its severity (12.0 vs 8.3 for PDR and mild NPDR) with high significance (p value <0.001). European population with retinopathy had worse glycemic control than patients without retinopathy in ten years after diagnosis .[41] Development of Maculopathy also influenced by value of HbA1c in this study. Patients with maculopathy (DME) showed median HbA1c of 9.2 vs 8.3 who did not have maculopathy. (p<0.01)

CONCLUSIONS

Diabetic retinopathy is more common in uncontrolled diabetic patients and those with long duration of disease. Regular screening and eye examinations of diabetic patients may reduce the burden of visual impairment and blindness.

Limitation

This study did not cover all the aspects of diabetic retinopathy , carried out in a single center and in a short period of time which does not reflect the whole country

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Original Article

Computed Tomographic Evaluation of Renal Mass with Histopathological Correlation

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Abstract

Renal cell carcinoma (RCC) is the seventh most common cancer and the most common primary renal malignant neoplasm in adults. Computed Tomography (CT) is of a great value in differentiating malignant from benign masses of RCC. This cross-sectional study was conducted among 61 clinically suspected cases of renal mass at Sir Salimullah Medical College and Mitford Hospital (SSMC and Mitford Hospital) in the Department of Radiology and Imaging in collaboration with the Department of Urology and Pathology, from July '2011 to June' 2013. However, in 05 cases, histopathological reports were not available and 07 patients refused surgery after enrolling. Finally, histopathology reports were collected from 49 patients and they were considered as study subjects. Aim of the study was to evaluate the accuracy of CT scan findings in compere with the histopathological report for the diagnosis of renal mass and to differentiate its benign and malignant forms. The age range of the patients was 2 to 73 years, where more than two-third (69.38%) were male and rest of them were female. Maximum number of malignant cases observed in the age range of 50-59 years. In comparison, inflammatory and benign conditions dominate in early age group, mostly before 40 years. Among 49 cases, 41 (83.68%) cases were diagnosed as malignant renal mass by CT scan, 01 (2.04) case was missed, which was confirmed by histopathology. Rest 07 (14.28%) patients were diagnosed as benign both in CT scan and histopathology. The sensitivity of CT for malignant renal mass was found 97.62% and specificity was 100%. The positive and negative predictive values of CT were 87.5% and 97.59% respectively. Computed tomography is a valid diagnostic modality for differentiating benign and malignant renal mass.

Keywords: *Renal mass, computed tomography, histopathology, malignant, benign.*

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INTRODUCTION

Renal masses may be single or multiple or may be benign or malignant. Renal cysts are the most common mass lesions in the kidney. With ultrasonography 80% of detected renal masses are characterized as simple cysts thus ending their diagnostic evaluation. The remaining 20% of renal masses require further study with Computed tomography (CT) or Magnetic Resonance (MR) imaging.[1]

Renal cell carcinoma (RCC) is the seventh most common cancer as mentioned by Siddiqui et al (2005) and the most common primary renal malignant neoplasm in adults.[2] It accounts for approximately 90% of renal tumors and 2% of all adult malignancies. RCC is more common in men than in women (ratio, 1.6:1), and it most often occurs in patients aged 55-84 years.[3]

Approximately 87% of solid renal neoplasms in children are Wilms' tumors; Wilms' tumor is the most common primary pediatric malignant abdominal neoplasm; it is the third most common malignancy in children, after leukemia and brain tumors. It also is the third most common of all renal masses in childhood, after hydronephrosis and multicystic dysplastic kidney. Wilms' tumor occurs equally in males and females and occurs within 3 years.[4]

The accurate diagnosis of a renal mass is dependent on many factors, including the clinical history, the nature of the imaging findings, the experience of the radiologist, the quality of the examination, and the exclusion of conditions that can mimic a renal neoplasm.[5]

Ultrasonography (USG) is the first method in the diagnosis of renal malignancies. But staging is not possible with this modality. Multi detector Computed Tomography (MDCT) has ability to detect small renal lesions and to complete the examination a single breath hold. So Computed tomography have a great role in the evaluation of renal mass and also provide some clinical information regarding the lymphadenopathy & or the presence of metastatic lesion in the liver.[6]

High-resolution MDCT is accurate in the preoperative evaluation of patients with renal cell carcinoma. CT is the modality of choice for evaluating indeterminate renal lesions that are suspicious for Malignancy.[6]

USG has an advantage over CT in detection of nature of the lesion (solid/cystic) and evaluation of renal vein invasion by the lesion. CT including pattern of enhancement after contrast administration, presence of calcification and necrosis, perinephric extension, infiltration of adjacent organs, presence of thrombus in renal vein and inferior vena cava (IVC), retroperitoneal lymphadenopathy and distant metastasis. In addition, staging was done in patients with renal cell carcinoma according to Robson's staging criteria.

Although a variety of examinations (USG, MRI, and angiography) can be used in the workup of patients with suspected RCC, the preferred method of imaging these patients is dedicated renal computed tomography (CT). In most cases, this single examination can be used to detect and stage RCC and to provide information for surgical planning without additional imaging.[5]

MRI is comparable to helical CT for detection, diagnosis, and staging of renal masses. However, CT has the advantages of widespread availability, shorter examination time, and lower cost in comparison with MRI.[1]

The current use of CT scan and ultra-sonography for a wide variety of indications has led to the frequent incidental discovery of small (1.5-3.0 cm) and very small (< 1.5 cm) lesions in the renal parenchyma. These lesions are usually small benign cysts, complicated cysts, or small neoplasms.[7] CT is the most useful staging technique with accuracy ranging between 72% and 90%.[8] The present work has been carried out to assess the diagnostic accuracy of CT to evaluate renal mass.

MATERIALS AND METHODS

This cross sectional observational study was carried out in the Department of Radiology & Imaging, SSMC & Mitford Hospital, Dhaka in collaboration with the Department of Urology and Pathology to evaluate the diagnostic accuracy of computed tomography scan in the diagnosis of renal mass enrolling 61 patients who were referred by Urology department of SSMC & Mitford Hospital, Dhaka, as clinically suspected cases of renal mass for CT scan of whole abdomen. This study was conducted during July 2011 to June 2013. CT scan of abdomen was performed in all patients and after surgery specimen of renal masses were sent for histopathological diagnosis. Histopathological reports were collected and correlated with CT findings. However, in 5 cases, histopathological reports were not available and seven patients refused surgery after enrolling into the study. Finally, histopathology reports were collected from 49 patients and they were considered as study subjects. After taking informed consent, data was collected in a pre-tested questionnaire by taking history, examining the patients clinically, the finding and interpretation of the CT scan and histopathological reports. The data was expressed as frequency, percentage, mean (±SD) and range. For the validity of the study outcome sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy were calculated for CT scan using histopathological diagnosis as a gold standard of diagnostic criteria.

Results

Table I shows distribution of clinically suspected cases of renal mass; from total 61 clinically suspected cases of renal mass 49 patients were detected as renal tumors (benign and malignant conditions) and others 12 were normal condition.

Table I: Distribution of renal tumors and normal condition from clinically suspected cases of renal mass (N= 61)

No of patients with renal mass (clinically suspected)	Renal tumors (study subject)	Excluded cases from study	
		Refused surgery after enrolling	Histopathology report was not found
61	49	7	5

Table II contains the distribution of renal tumors (benign and malignant conditions) in different age groups; age range of the patients was 2 to 73 years. The distribution of benign condition was 16.32% and malignant condition was 83.68%. Among 49 patients with a renal tumors; 79.55% was in age group 40 ≥ 60 years, 12.24% was in age group 10-39 years and other 10.21% was in age group 2-9 years. Benign conditions were found 8.16% equally in both age group 10-39 years and 40 ≥ 60 years and no patient was found in age group 2-9 years. Malignant conditions were found 69.39% in age group 40 ≥ 60 years, 10.21% in age group 2-9 years, 4.08% in age group 30-39 years and no patients was found in age group 10-29 years.

Table II: Distribution of benign and malignant conditions according in different age groups (N=49)

Age group	Benign		Malignant		Benign + Malignant	
	No of patients	%	No of patients	%	No of total patients	%
2-9 Years	0	0	5	10.21	5	10.21
10-19 Years	2	4.08	0	0	2	4.08
20-29 Years	1	2.04	0	0	1	2.04
30-39 Years	1	2.04	2	4.08	3	6.12
40-49 Years	2	4.08	6	12.24	8	16.32
50-59 Years	1	2.04	16	32.66	17	34.70
≥ 60 Years	1	2.04	12	24.49	13	28.53
Total	8	16.32	41	83.68	49	100

Table III displays that 30.61% of patients were female and 69.36% were male. The male to female ratio was 2.27:1.

Table III: Distribution of patients by sex (N=49)

Gender	Number of Patients	Percentage	Male to female Ratio
Male	34	69.38	2.27:1
Female	15	30.62	

Table IV states the comparison of benign and malignant tumors of CT scan and histopathological examination. Here 35 (71.43%), 1 (2.04%) and 5 (10.21%) malignant tumors were detected as RCC, TCC and Wilms' Tumor respectively by CT scan; where 36 (73.45%), 1 (2.04%) and 5 (10.21%) were detected as RCC, TCC and Wilms' Tumor respectively by histopathological examination. Similarly 2 (4.08%), 4 (8.16%) and 2 (4.08%) benign tumors were detected as AML, Inflammatory and Cyst respectively by CT scan; on the other hand 3 (6.12%), 3 (6.12%) and 1 (2.04%) benign tumors were detected as AML, Inflammatory and Cyst respectively by histopathological examination.

Table IV: The distribution of different diagnosis of the renal mass made by CT scan and Histopathology (N=49)

	CT scan	Histopathology
Malignant		
Renal Cell carcinoma (RCC)	35 (71.43%)	36 (73.45%)
Transitional cell carcinoma (TCC)	1 (2.04%)	1 (2.04%)
Wilms' Tumor	5 (10.21%)	5 (10.21%)
Benign		
AML	2 (4.08%)	3 (6.12%)
Inflammatory	4 (8.16%)	3 (6.12%)
Cyst	2 (4.08%)	1 (2.04%)

Table V shows the comparison of CT-scan and histopathological diagnoses; 41 patients were both malignant on CT-scan and histopathology. In a CT scan of 42 patients with malignancy, 01 was found to have benign condition.

Table V: Comparison of CT scan with Histopathological Diagnosis of Malignant Renal Mass (N=49)

	Histopathological diagnosis		Total
CT scan	Malignant	Benign	
Malignant	41	0	41
Benign	1	7	8
Total	42	7	49

Table VI shows the comparison of CT-scan and histopathological diagnosis of benign renal tumor. CT scan detected 08 benign cases, of which 01 was histopathologically confirmed to be malignant.

Table VI: Comparison of CT scan with histopathological diagnosis of benign renal mass (N=49)

	Histopathological diagnosis		Total
CT diagnosis	Benign	Malignant	
Benign	7	1	08
Malignant	0	41	41
Total	7	42	49

Table VII shows comparison of CT-scan with histopathological diagnosis of inflammatory renal mass. Out of 04 inflammatory mass which are revealed on CT-scan, 03 were histo-pathologically detected.

Table VII: Comparison of CT scan with histopathological diagnosis of inflammatory renal mass (N=49)

CT scan	Histopathology		Total
	Inflammatory renal mass	Non-Inflammatory renal mass	
Inflammatory renal mass	3	1	4
Non-Inflammatory renal mass	0	45	45
Total	3	46	49

Table VIII shows that, out of 02 fat containing lesion which were detected by CT-scan, all were histopathologically same.

Table VIII: Comparison of CT scan with histopathological diagnosis of Fat containing lesion (N=49)

CT scan	Histopathology		Total
	Fat containing lesion	Non-fat containing lesion	
Fat containing lesion	2	0	2
Non-fat containing lesion	1	46	47
Total	3	46	49

Table IX shows margins of any lesion either well defined or ill-defined (for helps to diagnose type of pathology).

Table IX: Margin of lesion determined by CT scan (N=49)

Margin	Frequency	Percentage
Well defined	8	16.32
Ill defined	41	83.68

Table X shows density of the lesions by which characteristics of the lesion can be described. Mixed density, Hypo-dense, Iso-dense and Hyper-dense lesions were found in 48.98%, 42.86%, 6.12% and 2.04% of masses.

Table X: Distribution of patients by density of lesion in NECT (n=49)

Density	Frequency	Percentage
Iso-dense	3	6.12
Hypo-dense	21	42.86
Mixed density	24	48.98
Hyper-dense	1	2.04

Table XI shows the well-established indicator of benign and malignant lesion; pattern of enhancement (after IV contrast) in CT scan. Here 42 (85.71%) show minimal to moderate contrast enhancement. Large solid lesion with enhancement ranges between mild to moderate showed heterogeneous enhancements, where homogenous and no enhancement were 02 (4.09%) and 05 (10.20%).

Table XI: Distribution of patients by pattern of enhancement (N=49)

Enhancement	Frequency	Percentage
Heterogeneous	42	85.71
Homogenous	2	4.09
No enhancement	5	10.20

Table XII shows tumor characteristics staging of the lesions, especially malignant case. Presence of calcification, renal vein or IVC involvement, lymph node involvement, invasion of adjacent viscera and distant metastasis were found in 02 (4.08%), 03 (6.12%), 04 (8.16%), 03 (6.12%) and 01 (2.04%).

Table XII: Distribution of patients by presence of calcification, renal vein or IVC involvement (N=49)

Tumor characteristics	Frequency	Percentage
Calcification	2	4.08
Renal vein or IVC involvement	3	6.12
Lymph node involvement	4	8.16
Invasion of adjacent viscera	3	6.12
Distant metastasis	1	2.04

Table XIII contains the frequency of benign or malignant mass lesions by CT diagnosis. Benign mass like angiomyolipoma and other benign mass were found in 02 (4.08%) and 06 (12.24%) masses. Malignant mass like Renal cell carcinoma, Wilms' tumor and TCC were found in 35 (71.43%), 05 (10.21%). and 01 (2.04%) masses.

Table XIII: Distributions of patients by type of renal mass by CT diagnosis (N=49)

Type		Frequency	Percentage
Benign mass			
	Angiomyolipoma	2	4.08
	Other Benign mass	6	12.24
	Renal cell carcinoma (RCC)	35	71.43
Malignant mass			
	Wilms' tumor	5	10.20
	Transitional cell carcinoma (TCC)	1	2.04

DISCUSSION

The study was conducted among 61 clinically suspected cases of renal mass from where 49 patients were detected as renal tumors (benign and malignant conditions) and others 12 were normal condition. These 49 patients were selected as study subjects. The age range of 49 patients with renal masses was 2 to 73 years. Malignant lesion were found mostly on the 5th and 6th decades and thereafter, with malignant lesion seen most frequently during 5th decade. Wilms' tumor was found between 0 to 5 years. Benign lesions were found in earlier ages i.e. before 40 years. In this study, 30 (61.22%) patients aged 50 years or more and 17 (34.69%) patients were in between 50 to 59 years, while 13 (26.53%) patients were aged more than 60 years. The peak incidence of malignant lesions was found in the age group of 50 years and older. Sutton D (2003) reported that Renal cell carcinoma most commonly after 40 years of age and most cases arise spontaneously from 5th to 7th decade of life, as presented by Grainger RG (2008).[9,10]Helenon et al (2002) in a series of 125 cases of renal masses, found highest incidence in the age group of 50 years and older.[11] Deborah A, 2011 found RCC most often occurs in patients aged 55-84 years. Their observation was similar to our study.[6]

In this present study it was observed that male was predominant, where male and female patients were found 69.38% and 30.61% respectively with a male to female ratio of 2.27:1. Sutton D (2003) reported that RCC has a male to female predominance of 2.5:1.[9]

Asymptomatic renal tumors are increasingly detected incidentally (more than 50%) with the routine use of CT scanning evaluation of nonspecific findings. A manifestation of classically triad of gross hematuria, flank pain and a palpable mass occurs only 7-10% of patients.[12] We found 10 patients (20.40%) presented with abdominal pain and hematuria and 10 patients (20.40%) presented with abdominal pain and lump, 3 patients (6.12%) presented with symptoms of uraemia. The reliable symptoms, "classical triad" (pain, hematuria and flank mass was found in few cases (5 cases = 10.2%) and it generally indicates advanced diseases, Helenon et al (2002) found the percentage of classical triad (10%) which was almost close to our study.[11]

In our study most of the lesions (83.68%) showed ill-defined or poorly defined margin. Benign lesion (16.32%) showed well defined margin that correlates with the findings of Zagoria et al, 1990.[13]

In this study, Sensitivity and specificity, PPV, NPV and accuracy of CT scan diagnosing malignant renal mass were 97.62%, 100%, 100%, 87.5%, 97.59%. Sensitivity and specificity, PPV, NPV and accuracy of CT scan diagnosing renal cell carcinoma were 97.22%, 100%, 100.00 %, 92.86%, 97.59%. Sensitivity and specificity, PPV, NPV and accuracy of CT scan diagnosing benign renal mass were 100.00%, 97.62%, 87.5%, 100.00 %, 97.59%. Sensitivity and specificity, PPV, NPV and accuracy of CT scan diagnosing inflammatory renal mass were 100.00%, 97.83%, 75.00%, 100.0%, 97.59%.These findings are more or less closer to the findings of Silvermann SG (1994) the sensitivity and specificity of spiral CT in detecting renal mass less than 3 cm in size was 78% and 86% and Biswas NP (2007), sensitivity,specificity and accuracy of CT scan in the diagnosis of renal tumors were 100%,66.66% and 97.43% respectively.[1,14] Sensitivity and specificity, PPV, NPV and accuracy of CT scan diagnosing fat containing lesion were 66.67%, 100%, 100.0%, 97.87%, 97.57%. This study was conducted in only one tertiary care hospital at Dhaka, using non probability sampling technique (purposive sampling), which might not represent the whole country scenario. So, further study with large sample size involving multiple centers is recommended.

CONCLUSIONS

CT scan is useful diagnostic modality in pre-operative discrimination of renal mass and it should be worthy to note here that CT can help the patients and doctors in the rational approach of patient management. CT has definite value in the diagnosis of renal mass and can be regarded as a sensitive and specific imaging modality for pre-operative discrimination of the tumor.

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Original Article

Comparison of Pulse Rate and Blood Pressure between Obese and Non-Obese Young Adults

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Abstract

Obesity has been reported to be associated with a number of cardiovascular diseases. Some researchers forecast that obesity may contribute to increase prevalence of high blood pressure in young adults. To compare pulse rate and blood pressure between young obese and non-obese subjects, this cross-sectional analytical study was done in the Department of Physiology, Sylhet MAG Osmani Medical College from January to December 2017. Fifty obese (BMI ≥27.5 kg/m2) and age-sex matched non-obese (BMI 18.5-22.9 kg/m2) young adult were selected. The age (35.56 ± 3.02 years versus 32.40 ± 4.20 years; p=0.116) and sex 26 (52.0%) male versus 31 (62.0%) male; p=0.313) were not differ between obese and non-obese subjects. The mean resting pulse rate (82.98 ± 3.50 beats /minute versus 72.64 ± 3.58 beats/minute; p<0.001), systolic blood pressure (130.20 ± 10.00 mm Hg versus 107.30 ± 10.60 mm Hg; p<0.001) and diastolic blood pressure (80.90 ± 7.19 mm Hg versus 67.90 ± 7.22 mm Hg; p<0.001) were higher in obese compared to non-obese participants. Obesity increases pulse rate and blood pressure in young adults.

Keywords: *Obesity, pulse rate, systolic blood pressure, diastolic blood pressure*

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INTRODUCTION

Obesity may be defined as excessive accumulation of body fat resulting from the positive energy balance.[1] Globally it has become a serious public health challenge. Obesity becomes nearly doubled in past decade worldwide and its incidence continues to be rising rapidly in many countries, leading the World Health Organization to coin the word 'globesity' to explain the worldwide situation.[2] Obesity is become endemic and is approximately tripled worldwide between 1975 and 2016. In 2016 World Health Organization (WHO) reported that over 1.9 billion adult people were overweight and more than 650 million were obese globally. Overall, about 13% of the adult global population (11% and 15% of male and female respectively) was obese in 2016.[3]

Physiologically, obesity is an excess of body fat leading to weight gain.[4] Body Mass Index (BMI) gives the most efficient measure of obesity in population level because it is identical for all ages of adults and also for both sexes. BMI is calculated as weight (kg) divided by height in meters square (BMI=kg/m^2 - Quetelet's Equation).[5] WHO has set standards for normal weight, overweight and obesity by BMI (BMI 18.5-24.9), (BMI 25-29.9) and ≥30kg/m^2 respectively. But, the BMI cut off point for normal weight, overweight and obesity for Asian population are lower than the WHO criteria which are (BMI 18.5-22.9), (BMI 23-27.5) and ≥27.5 kg/m^2 respectively.[6]

Obesity is linked to with a number of cardiovascular (CV) diseases, pro-inflammatory state, coagulation abnormalities and metabolic disturbances like lipid abnormalities, altered glucose metabolism, insulin resistance and development of type 2 diabetes mellitus.[7]

Weight of a person depends on the balance between one's energy intake and energy expenditure. Autonomic nervous system (ANS) encompasses a major part in the adjustment of intake of food with involvement in controlling signals for satiety and expenditure of energy; thus, dysregulation of ANS is a factor for weight gain. Dysregulation of ANS incorporates a bi-directional connection to obesity; ANS alterations may initiate obesity whereas excess weight gain induces dysfunction of ANS.[8] The altered ANS function in obesity consequently results in cardiovascular disorders.

Hence in obesity the study on ANS function is of considerable clinical interest.[9] Disturbed sympathetic nervous system (SNS) function is also of significance in obesity.[10] SNS is the primary regulator of cardiovascular system activity; obesity might trigger alteration within the sympathetic regulation of cardiovascular function, thus favouring the rise in cardiovascular complications and morbidity.[5]

Blood pressure (BP) is regulated by activity within the autonomic nervous system.[11] Obesity is related to sympathetic activation and is the leading explanation of development of hypertension.[12] However, a recent report indicated that the extent of BP did not increase despite a rise in obesity.[13] In an exceedingly large cross sectional study, BMI has been shown to be a stronger index of body fatness compared to waist-hip ratio.[14] Therefore, it is important to assess the effect of obesity on BP and pulse rate, and to clarify to what extent this prevalence of high BP are often accounted for by the presence obesity measured by BMI among young adults.

MATERIALS AND METHODS

This was a cross sectional analytical study was conducted in the Department of Physiology, Sylhet MAG Osmani Medical College from January to December 2017. Fifty obese (BMI ≥27.5 kg/m^2) and 50 non-obese (BMI 18.5-22.9 kg/m^2) persons aged between 18-40 years were selected from staffs, attendants of admitted and outdoor patients in Sylhet MAG Osmani medical College and Hospital were selected. Individuals with diabetes mellitus, chronic kidney diseases, stroke and other neurological disorders, any obvious cardiovascular diseases, chronic obstructive lung diseases, thyroid disorders and hypertension were excluded. Non probability convenient sampling was applied to sampling.

Informed written consent was taken from all the participants after full explanation of the aim of the study. They were informed of their right to withdraw from the study at any stage without any consequences.

All the participants were assessed from history, physical examination. Those who fulfilled the inclusion criteria were enrolled and those fulfilled the exclusion criteria were excluded in this study.

Assessment of Weight and Height: Weight was recorded in kilograms with the participant standing on the weighing balance without shoes and minimum clothing. Weight of the patients and controls were recorded in the same weighing balance. Height was recorded in meter with the subject barefooted, feet together, back and heels against the upright bar of the height scale; head upright in Frankfort horizontal plane – look straight ahead. The height measuring scale has a vertical bar and a horizontal bar of wood which was brought down comfortably on participants' head.

Calculation of Body Mass Index: Body Mass Index (BMI) was estimated using the formula, BMI=Weight in Kilogram's/Height in meters^2.

Grouping of the sample: The participants were divided into two groups by their body mass index. Group A consisted of obese subjects with BMI ≥27.5 kg/m^2 and Group B consisted of non-obese subjects with BMI between 18.5-22.9 kg/m^2 each consisting 50 sample.

Measurement of blood pressure and pulse rate: Blood pressure was measured on right arm by auscultation method with a standardized clinical sphygmomanometer using an appropriate cuff. A stethoscope was placed over the brachial artery pulse, proximal and medial to the cubital fossa, and below the underside fringe of the cuff. BP measurements were taken 5 min after resting with the subject in sitting position. The cuff was rapidly inflated to pressure above the extent at which the radial pulse could now not be felt. According to appearance of Korotkoff sound was recorded as systolic BP, then the mercury was allowed to fall further till the sound ceased to be tapping in quality, became muffled and then disappeared was noted as diastolic BP. A mean of two recordings (each one minute apart) was taken. Pulse rate was calculated by palpation of radial pulse for one minute.

Statistical Analysis: Collected data were processed and analyzed with the assistance of Statistical Package for Social Science (SPSS) Version 22.0. Quantitative data were expressed as mean and standard deviation; and comparison was done using Chi-quare (χ^2) test. Qualitative data were expressed as frequency and percentages; comparison was done using unpaired t test. P value of <0.05 was taken as significant.

Ethical Consideration: After explaining the aim of study, informed written consent was taken from each subject. The consent form clearly described the aim, objectives and method of study, confidentiality of the interview, risk and good things of participating in the study, their right to participate voluntarily and refuse at any point of time from the study were explained to the respondents .

Prior to the starting of the study, the research protocol was submitted to the ethical review committee of Sylhet M.A.G Osmani Medical College, Sylhet and an approval was obtained.

RESULTS

Table I shows the age (mean ± SD) was 35.56 ± 3.02 (range, 22-38) years in obese participants and was 32.40 ± 4.20 (range, 22-38) years in non-obese participants. The age difference of obese participants and non-obese participants did not reach the level of significance (t=1.585; p=0.116).

There were 26 (52.0%) male and 24 (48.0%) female in obese group; whereas 31 (62.0%) male and 19 (38.0%) female in non-obese group. The sex difference between the participants of obese and non-obese group failed to show any statistically significant difference (χ^2=1.020; p=0.313).

Table I. Comparison of Participants According to Demographic Characteristics

Demographic characteristics		Study group		p value
		Group-A (n=50)	Group-B (n=50)	
Age (mean ± SD) years		35.56 ± 3.02	32.40 ± 4.20	†p=0.116
Sex	Male	26 (52.0%)	31 (62.0%)	*p=0.313
	Female	24 (48.0%)	19 (38.0%)	

*Chi-Square (χ^2) Test and †unpaired't' test were applied to analyze the data. SD: Standard deviation.

Table II shows the height (mean ± SD) of the obese participants was 1.61 ± 0.07 (range 1.47-1.78) meters; whereas the height of the non-obese participants was 1.63 ± 0.08 (range 1.42-1.73) meters. The height of obese and non-obese participants failed to differ significantly (t=-1.599; p=0.113).

The weight (mean ± SD) of the obese participants was 76.39 ± 10.08 (range 42-181) Kg; whereas the weight of the non-obese participants was 57.14 ± 6.56 (range 42-85) Kg. The weight of the obese participants was higher significantly compared to non-obese participants (t=11.316; p<0.001). The BMI (mean ± SD) of the obese participants was 29.39 ± 2.27 (range 18.3-31.9) Kg/M^2; whereas the BMI of the non- obese participants was 21.34 ± 1.02 (range 18.7-38.0) Kg/M^2. The BMI of obese was higher significantly compared to non-obese participants (t=22.885; p<0.001).

Table II. Comparison of participants by anthropometric status

Anthropometric status	Study subjects		p value
	Group-A (n=50)	Group-B (n=50)	
Height (Cm)	1.61 ± 0.07	1.63 ± 0.08	*p=0.133
Weight (Kg)	76.39 ± 10.08	57.14 ± 6.56	*p<0.001
BMI (Kg/M2)	29.39 ± 2.27	21.34 ± 1.02	*p<0.001

*Unpaired t test was employed to analyse the data.
Data were presented as mean ± SD (standard deviation).

Table III shows the resting pulse rate (mean ± SD) was 82.98 ± 3.50 (range 76-90) beats /minute in obese participants and 72.64 ± 3.58 (range 68-80) beats/minute in non-obese participants; the resting pulse rate was higher significantly in obese compared to non-obese participants (t=14.602; p<0.001).

The resting systolic blood pressure (mean ± SD) was 130.20 ± 10.00 (range 100-150) mm Hg in obese participants and was 107.30 ± 10.60 (range 90-140) mm Hg in non-obese participants; the SBP was higher significantly in obese compared to non-obese participants (t=11.110; p<0.001).

The resting diastolic blood pressure (mean ± SD) was 80.90 ± 7.19 (range 60-90) mm Hg in obese participants and was 67.90 ± 7.22 (range 60-85) mm Hg in non-obese participants; the DBP was higher significantly in obese compared to non-obese participants (t=9.020; p<0.001).

Table III. Comparison of participants according to resting pulse and blood pressure

Parameters	Study subjects		p value
	Group-A (n=50)	Group-B (n=50)	
Pulse (beats/min)	82.98 ± 3.50	72.64 ± 3.58	*p<0.001
SBP (mm Hg)	130.20 ± 10.00	107.30 ± 10.60	*p<0.001
DBP (mm Hg)	80.90 ± 7.19	67.90 ± 7.22	*p<0.001

*Unpaired t test was employed to analyse the data.

Data were presented as mean ± SD (standard deviation).

DISCUSSION

In this study, subjects with BMI greater than 27.5 were categorized into obese and those with BMI 18.5 to 22.9 kg/m^2 as non-obese.[15]

This study revealed that the mean age was 35.56 ± 3.02 and 32.40 ± 4.20 years (p=0.116); sex 52.0% male versus 62.0% male (p=0.313) did not differ significantly between two groups of participants. Akhter et al.[10] supported this result that obese and non-obese participant were matched for age and sex. Shibao et al.[16] also reported that the mean age was 35 ± 3.0 and 32 ± 3.0 years (p=0.256); and equal number of male and female obese and non-obese respectively.

This study showed that the height of the obese participants was 1.61 ± 0.07 meters and non-obese participants was 1.63 ± 0.08 meters. The height of obese and non-obese participants failed to differ significantly (p=0.113). This result correlated with Shenoy et al.[17] that the height of both obese and non-obese participants failed to differ significantly (p=0.50). This result was also concordance with the study of Akhter et al.[10] that the height of both obese and non-obese participants failed to differ significantly (p>0.05).

This study showed that the weight of the obese participants was 76.39 ± 10.08 Kg; and the non- obese participants was 57.14 ± 6.56 Kg. The weight of the obese participants was higher than that of non-obese participants (p<0.001). This finding was consistent with the study of Akhter et al.[10] that the weight of obese was greater than that of non-obese. Shetty et al.[18] also reported that the weight of the obese was greater than that of non-obese (p<0.001).

In the current study BMI of the obese participants was 29.39 ± 2.27 and the non- obese participants was 21.34 ± 1.02 Kg/M^2. BMI of obese was greater than that of non-obese participants (p<0.001). This result was consistent with Chaudhuri et al.[19] that BMI of the obese participants was greater compared to non-obese participants. This result was also supported by Akhter et al.[10] that BMI of the obese participants was greater compared to non-obese participants.

The resting pulse rate was 82.98 ± 3.50 beats /minute in obese participants and 72.64 ± 3.58 beats/minute in non-obese participants. The resting pulse rate of the obese participants was greater the non-obese participants (p<0.001). This result correlated with the study of Chaudhuri et al.[19] that the resting pulse rate of the obese participants was greater than that of non-obese participants. This result was also supported by Das and Mondal,[8] that resting pulse rate of obese group was greater compared to that of non-obese group (p = 0.01). But Shenoy et al.[17] failed to find significant disparity in the resting pulse rate between obese group participants and non-obese participants (p= 0.67).

In the current study the resting SBP (mm Hg) was 130.20 ± 10.00 in obese participants and was 107.30 ± 10.60 in non-obese participants. The SBP of the obese participants was greater significantly compared to that of non-obese participants (p<0.001). Das and Mondal,[8] supported this result that resting SBP of obese group was greater significantly compared to the SBP of non-obese group. But Chaudhuri et al.[19] failed to find significant discrimination between the SBP of obese group and non-obese group (p=0.22).

This study demonstrated that the resting DBP (mm Hg) was 80.90 ± 7.19 in obese participants and 67.90 ± 7.22 in non-obese participants. The DBP of the obese participants was greater significantly than that of non-obese participants (p<0.001). Das and Mondal,[8] supported this result that resting DBP of obese group was greater

significantly than the DBP of non-obese group. But Kalpana et al.[20] found no significant disparity in the DBP between obese group and non-obese group (p>0.05).

Limitations of the study were (1) This study was done in a single tertiary care hospital, (2) sample size was small due to time constrain and (3) sampling was non-random.

CONCLUSIONS

Obesity is related to increased pulse rate and blood pressure in young obese subjects. Therefore, young obese subjects are more prone for risk of development of hypertension or other cardiovascular disorders in later stages of their life. Hence further studies involving multicenter and large sample are of utmost needed to succeed in a legitimate conclusion.

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Original Article

Prevalence of Post-traumatic stress disorder among Physicians during the COVID-19 Pandemic

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Abstract

The healthcare professionals endured a major physical as well as psychological burden against the coronavirus disease (COVID-19) global catastrophe. Owing to their role in the frontline, they were the most exposed group who faced the deadly virus head-on which increased their mental health problems during this pandemic. The study was designed as a cross-sectional study to assess the prevalence of PTSD among 314 working physicians from the purposively selected government and private hospitals during the COVID-19 pandemic in Dhaka city. 'Impact of Event Scale-Revised' (IES-R) was used to construct the questionnaire. The mean age of the physician was 32.2±4.7 years. One-fifth of them (21.0%) diagnosed COVID-19 positive by the rt-PCR test. The most prevalent co-morbidities were found bronchial asthma (74.2%), hypertension (32.3%) and diabetes mellitus (19.4%). About half of the physicians (48.6%) had mild PTSD. The test of significance denotes the significant associations of the prevalence of mild PTSD level with physician's age, gender, marital state, work settings, results of COVID-19 positive and had co-morbidities in physicians ($p<0.05$). The prevalence of mild PTSD was higher in the age group of 25-35 years (49.1%), in females (49.8%), unmarried (50.0%), work in private settings (51.5%), ever been COVID-19 positive (59.1%) and had co-morbidities (51.6%). This study reveals that about half the physicians are suffering from mild PTSD. A high encumbrance of COVID-19 related mental disorders and fear among frontline physicians' entreaties to government and policymakers' prompt regard for taking appropriate preventive measures.

Keywords: *COVID-19, prevalence, IES-R, PTSD levels, physicians, Bangladesh.*

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INTRODUCTION

At the end of December 2019, the Chinese city of Wuhan was notified regarding some cases of pneumonia of unknown etiology.[1]China, was caused by a novel betacoronavirus, the 2019 novel coronavirus (2019-nCoV It was termed COVID-19, and later this rapid global spread of disease led to its declaration as a pandemic by the WHO.[2] Worldwide, this pandemic is highly shattering with more than 92.51 million confirmed cases and around 2 million fatalities to date.[3] Bangladesh also beheld nearly fifteen thousand five hundred deaths among more than 0.5 million confirmed cases to date.[4] The current pandemic has upraised uncertainty over the economic stability, employment, savings, and relationships as well as over physical and mental health.

Healthcare professionals are at the frontline in the pandemic, a profession that has proved to be correlated with heightened mental health disorders amid pandemic emergencies.[5,6] Precisely, these workers are more susceptible to developing PTSD. It is a psychological condition of individuals who have been subject to possibly traumatic experiences. Health professionals are subject to a heightened risk of infection, loss of patience, liability for complex medication retention decisions, and alteration of usual supportive structures.[7] Estimates of PTSD effects in healthcare staff are higher than in the general public and vary from 6-10% in a recent COVID-19 study conducted in Singapore[8], 18% from hospital nurses in general[9], and 20% from the SARS outbreak.[10] Thus, during pandemics, PTSD effects incline to be higher compared to times

without unusual conditions. As documented in earlier pandemics, like SARS and MERS, interacting closely with infectious individuals was correlated with high levels of PTSD symptoms.[11–13]

In Bangladesh, healthcare professionals face extreme resource shortages. Because of a lack of PPE's as well as a heavy workload and apprehension of illness, physical fatigue, caseload, responsibilities, and active participation in the epidemic predisposes them to be anxious, stressed, and insomniac. Studies found that half of the healthcare staff had stress, anxiety, and sleep disorder.[14] The possibility of infection and professional burden is speculated to have steadily exacerbated doctors' mental health status in Bangladesh as they face stigma, fear of conveying the infection to family members, and fear of alienation.

MATERIALS AND METHODS

Study design and settings

This was a cross-sectional study conducted to assess the prevalence of PTSD among physicians working in the different government and private hospitals during the COVID-19 pandemic in Dhaka city, Bangladesh.

Study population

The study was conducted among 314 physicians working in the purposively selected three government hospitals (Dhaka Medical College Hospital, Bangladesh Kuwait Moitree Hospital and Mugda Medical College Hospital) and three private hospitals (Anwer Khan Modern Medical College Hospital, Universal Medical College Hospital and United Hospital Limited), within the last 11 months of the COVID-19 pandemic situation were included. The non-working doctor in the COVID unit was excluded from this study.

Data sources and tools

Participants were interviewed face-to-face and over the phone according to their convenience from January 2021 to June 2021. Data were collected through a pretested semi-structured questionnaire. This questionnaire was developed through-

A. A semi-structured questionnaire was used to evaluate the sociodemographic characteristics.

B. The 'Impact of Event Scale-Revised' (IES-R) was used to diagnose PTSD among physicians.

A. **Semi-structured questionnaire for sociodemographic characteristics:**

The questionnaire had sociodemographic variables such as age, gender, marital status, education level, monthly income, family history and COVID-19 infection state.

B. **The 'Impact of Event Scale- Revised' (IES-R):**

The IES-R has 22 items and a cut-off score of 33 or above. It is recommended that the provisional diagnosis of PTSD. Patients select numbers from 0=not at all, 1=a little bit or mild and 2=severely to indicate how frequently particular comments have been true during the past seven days. The total scores, which range from 0 to 44, provide a measure of the severity of PTSD. As well as providing total scores, the IES-R also contains sub-scales for avoidance, intrusions and hyperarousal.

Statistical analysis

Data were coded, entered, edited, and cleaned cautiously and then exported into SPSS v25. Exploratory analysis was carried out to describe the study population and categorical variables will be summarized using frequency tables. Continuous variables were summarized using measures of central tendency and dispersion such as mean, percentile, and standard deviation. For significance, both Chi-square ($\chi 2$) test and Fisher exact test were used to see the associations with a 95% confidence level computed and the p-value <0.05 was considered as having a significant association. The results were presented in tables and chart.

Ethical aspects

The study was approved by the department of the ethical committee of North-South University. Informed written consent was obtained from the participating doctors and data were collected anonymously. Confidentiality of data was ensured and unauthorized access to data was not allowed.

RESULTS

Table I state that among 314 doctors; 88.2% were in the 25-35 years of age group with mean age of 32.2±4.7 years. Here females were 64.0% and married 63.4%. Among the physician 57.0% had consisting of family size less than 4 members others 29.0% of physicians were post-graduate and 66.3% were working in private settings; where 71.0% didn't disclose their monthly household income and 12.1% had earned more than 1,00,000 BDT each month.

Table I: Socio-demographic characteristics of the physicians (n=314)

Characteristics		N (%)
Age group (years)		
	25-35	277(88.2)
	36-50	37(11.8)
	Mean±SD	32.2±4.7
Gender		
	Female	201(64.0)
	Male	113(36.0)
Marital status		
	Married	199(63.4)
	Unmarried	110(35.0)
	Divorced	5(1.6)
Education		
	Graduation	223(71.0)
	Post-graduation	91(29.0)
Family member		
	≤4	179(57.0)
	>4	135(43.0)
Work settings		
	Government	112(35.7)
	Private	202(66.3)
Monthly household income (BDT)		
	Didn't said	223(71.0)
	≤1,00,000	53(16.9)
	>1,00,000	38(12.1)

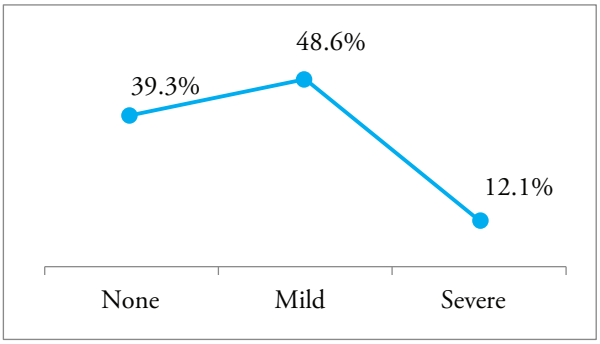

Figure 1: *Prevalence of PTSD levels among physicians by IES-R scores*

Figure 1 portrays the prevalence of PTSD levels among the physicians by IES-R scores. About half (48.6%) of physicians had mild PTSD and 12.1% of physicians had severe PTSD.

Table II demonstrates the prevalence of COVID-19 infection among physicians. Here 21.0% were diagnosed as COVID-19 positive by the rt-PCR test and 19.7% had any sort of co-morbidity and among them. Bronchial asthma (74.2%), hypertension (32.3%) and diabetes mellitus (19.4%) were found in study population.

Table II: Prevalence of COVID-19 infection (n=314)

Traits		N (%)
Ever COVID-19 positive by the rt-PCR		
	Yes	66(21.0)
	No	248(79.0)
Co-morbidities among physicians		
	Yes	62(19.7)
	No	252(80.3)
Co-morbidities conditions (n=62)		
	Bronchial asthma	46(74.2)
	Cardiac diseases	7(11.9)
	Hypertension	20(32.3)
	Diabetes mellitus	12(19.4)

*Multiple responses

Table III interprets significant associations were found in the prevalence of mild PTSD level among the physicians with their age (p=0.010), gender (p=0.025), marital state (p=0.006), work settings (p=0.005), results of COVID-19 positive by the rt-PCR (p=0.027) and had co-morbidities in physicians (p=0.020). The prevalence of mild PTSD was 49.1% in the age group of 25-35 years, in females 49.8%, unmarried 50.0%, work in private settings 51.5%, ever been COVID-19 positive 59.1% and co-morbidities was 51.6%.

Table III: Association of different variables with the prevalence of PTSD levels among physicians

Variables	PTSD levels among physicians				χ2	p-
	None N (%)	Mild N (%)	Severe N (%)	Total N (%)	value	value
Age group (years)						
25-35	107(38.6)	136(49.1)	34(12.3)	277(100)	66.870	*0.010
36-50	16(43.2)	17(46.0)	4(10.8)	37(100)		
Gender						
Female	78(38.8)	100(49.8)	23(11.4)	201(100)	49.321	*0.025
Male	46(40.7)	53(47.0)	14(12.3)	113(100)		
Marital state						
Married	81(40.7)	95(47.7)	23(11.6)	199(100)	†74.822	*0.006
Unmarried	39(35.5)	55(50.0)	16(14.5)	110(100)		
Divorced	1(20.0)	2(40.0)	2(40.0)	5(100)		
Education						
Graduation	88(39.5)	107(48.0)	28(12.6)	223(100)	87.154	0.761
Post-graduation	36(39.6)	46(50.5)	9(9.9)	91(100)		
Family members						
≤4	71(39.7)	89(49.7)	19(10.6)	179(100)	76.586	0.924
>4	53(39.3)	64(47.4)	18(13.3)	135(100)		
Work settings						
Government	38(33.9)	54(48.2)	20(17.9)	112(100)	27.211	*0.005
Private	78(38.6)	104(51.5)	20(9.9)	202(100)		
Ever COVID-19 positive by the rt-PCR						
Yes	18(27.3)	39(59.1)	9(13.6)	66(100)	18.530	*0.027
No	118(47.6)	102(41.1)	28(11.3)	248(100)		
Co-morbidities among physicians						
Yes	22(35.5)	32(51.6)	8(12.9)	62(100)	21.164	*0.020
No	110(43.7)	103(40.9)	39(15.5)	252(100)		
Co-morbidities conditions (n=62)						
Bronchial asthma	7(15.2)	20(43.5)	19(41.3)	46(100)	†28.561	0.062
Cardiac diseases	1(14.3)	3(42.9)	3(42.9)	7(100)		
Hypertension	3(15.0)	8(40.0)	9(45.0)	20(100)		
Diabetes mellitus	1(8.3)	6(50.0)	5(41.7)	12(100)		

*Statistically significant value †Fisher exact test

DISCUSSION

Most of the research on PTSD reports lifespan prevalence, which provides higher figures for the number of individuals with PTSD. In these researches performed on American and Canadian populations, the lifespan prevalence ranged from 6.1 to 9.2%.[15-19] The level is undoubtedly underestimated and attributable to under-reporting. However, based on the WHO data, it is estimated that in upper to lower-middle-income countries, the lifetime incidence of PTSD is about 2.3% to 2.1%.[19,20]

The present study reveals that the prevalence of PTSD among physicians in the age group of 25-35 years, physicians suffered from mild PTSD (49.1%) which was higher than the age group of 36-50 years who suffered from mild PTSD (46.0%). According to gender, females were suffering from PTSD at 49.8% which was higher than males 47.0%. An epidemiological study was conducted in Canada to assess PTSD and related comorbid conditions; there the prevalence of PTSD in the age group of 18-35 is 40.3% than the age group of 35-60 is 42.8% and females are more affected by PTSD 51.7% than in males 48.3%, which is consistent with this study.[16]

According to marital status, married persons had 47.7% PTSD unmarried persons had 50.0% and divorced had 40.0% PTSD levels. These findings are similar to the studies.[21,22] Lack of marital and other types of social support might result in negative consequences. The relationship between marital status and PTSD had a significant association. It was found that single persons had the largest number of referrals, followed closely by married persons, which is similar to these study findings.[8,12,21]

The study demonstrates that one-fifth of physicians (19.7%) had co-morbidities like bronchial asthma (74.2%), hypertension (32.3%) and diabetes mellitus (19.4%). A study found that about (24.8%) of doctors had been suffering from at least one chronic disease. The most commonly reported chronic disease was chronic bronchial asthma.[22]

In both settings, about half (48.6%) were suffering from mild PTSD and 12.1% were suffering from severe PTSD. The test of significance denotes the significant associations of physician's age, gender, marital state, work settings, results of COVID-19 positive by the rt-PCR and had co-morbidities in physicians ($p<0.05$). The prevalence of mild PTSD was higher in the age group of 25-35 years (49.1%), in females (49.8%), unmarried (50.0%), work in private settings (51.5%), ever been COVID-19 positive (59.1%) and had co-morbidities (51.6%).

CONCLUSION

Our study reveals that nearly half the physicians are suffering from mild PTSD, which is a concerning health issue for our country in pandemic situation. An appropriate risk reduction technique should be bent and carried out to condense the risk of getting mental disorders. The supply of sufficient PPE's and the advancement of a trained workforce with contamination control abilities also should be considered to reduce the mental effects.

Abbreviations: BDT: Bangladeshi taka, COVID-19: Coronavirus disease, MERS: Middle-east respiratory syndrome, PTSD: Post-traumatic stress disorder, SARS: Severe acute respiratory symptoms, SPSS: Statistical Package for the Social Sciences and WHO: World Health Organization,

Author's contributions: Conceptualization, methods and literature review: Nurunnabi M, Nazia A, and Kakoly NS; Data acquisition: Nurunnabi M and Nazia A; Statistical analysis: Nurunnabi M; Draft of manuscript: Nurunnabi M, Nazia A, Chowdhury N, Alam MB and Islam MM; Finalization of manuscript: Nurunnabi M, Nazia A, Chowdhury N, Alam MB, Islam MM and Kakoly NS. All the authors approved the final manuscript.

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Competing interests: The authors declared no competing interests.

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Case Report

Parry Romberg Syndrome: A Rare Entity from a Primary Care Center in Bangladesh

*Podder CS [1], Chowdhury N[2]

Abstract

Parry Romberg syndrome (PRS) is an acquired, rare, neurocutaneous disorder presenting most commonly as hemiatrophy of face with characteristic involvement of skin, subcutis, bone and denture with or without neurological manifestations [1]. Here we present a case of 16 year old girl, who presented with characteristic insidious, progressive, selflimited hemifacial atrophy accompanied with headache and facial pain.

Key words: *Parry Romberg syndrome, Hemifacial atrophy*

INTRODUCTION:

Parry Romberg syndrome or, Progressive hemifacial atrophy is a rare disorder of unknown origin. First delineated by Parry in 1825 and Romberg in 1846[2] the term Progressive hemifacial atrophy (PHA) was Introduced by Ellen berg in 1871. The syndrome is characterized by slowly progressive hemifacial atrophy and subcutaneous structures such as fat, fascia, cartilage, bones and others of the affected side. After a progressive phase, which may continue upto 20 years, the process settles down. Usually the disfiguartions are permanent Seen most commonly among females, it is also associated with ocular, neurological and oral manifestations and associated with some common autoimmune diseases. Chronic vascular disturbance, autoimmunity, prior trauma and genetic causes have been postulated for development of PHA.Diagnosis is based on history and clinical features. Histopathology and imaging aids in diagnosis. Immunosuppressants, steroids, plastic & reconstructive surgery are some of the treatment options. Here we present a case of Parry Romberg syndrome in a 16 year old girl with trigeminal neuralgia**.**

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2. Dr. Nandini Chowdhury, MD Resident, Phase A, Paediatrics, Bangladesh Institute of Child Health

* For correspondence

CASE REPORT:

A, 16 years old girl presented to Debidwar UHC OPD with complaints of progressive atrophy of left side of the face for last 10 years. Her mother mentioned this shrinking started at the age of 6 and following recovery from a febrile illness which persisted for about 2 weeks. It was progressive and gradually increasing over the years and for last 3 years it has settled down and there is no noticeable progress. She also complained of recurrent episodic pain in the left side of the face.

She had no diminished sensations on affected side hearing or speech difficulties, no convulsions or, noticeable denture abnormalities.

On examination, there was asymmetry of left side of the face, with atrophy of cheek and mandibular region. leftside of tongue was also atrophied. There was no sensory deficit of left side, paraesthesia, auditory or speech disturbance. Other cranial nerves & motor system examination also revealed no abnormality.

Table 1: Patient's baseline reports

Investigations	Results
Hb%	11.9 gm/dl
WBC count	7,800/cumm
Neutrophil	67%
Lymphocyte	28%
Monocyte	3%
Eosinophil	2%
Platelet count	1,75,000/cumm
TSH	2 25 mIU/L
ANA	Negative

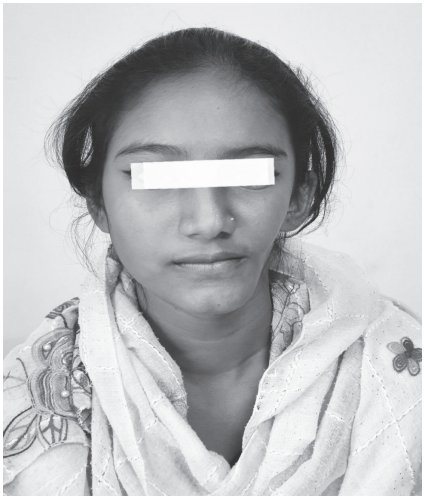

Fig 1: *Patients photograph showing left sided hemifacial atrophy*

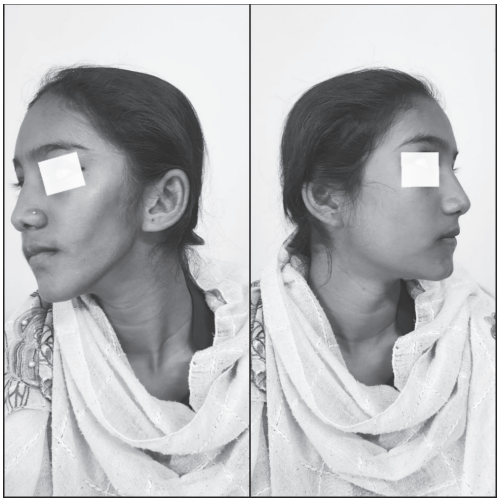

Fig 2: *Showing marked facial Asymmetry*

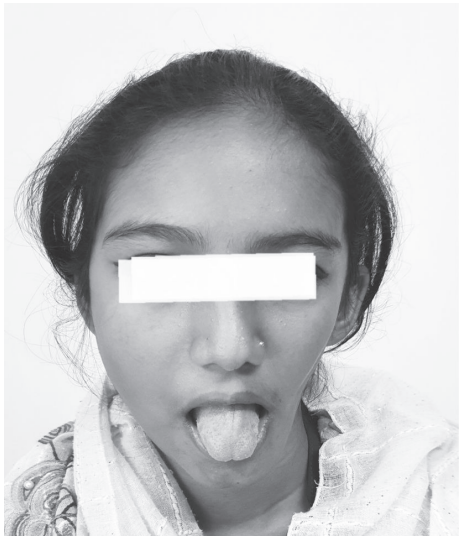

Fig 3: *Showing atrophy of left half of tongue*

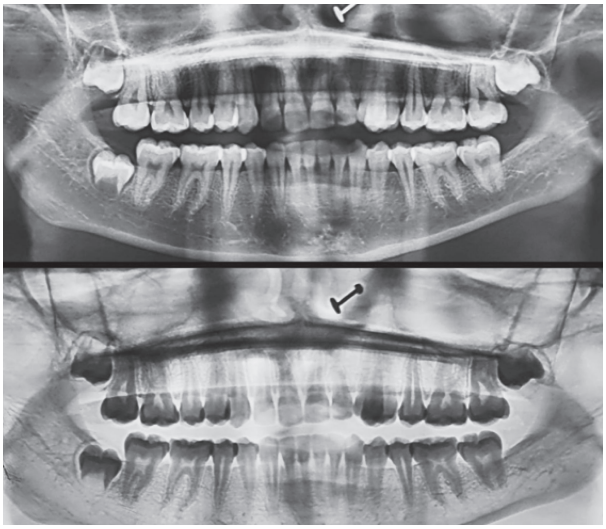

Fig 4: *The orthopantomography shows decreased vertical height of ramus along with loss of gonial angle prominence on the affected side. There is also Class 3 malocclusion in right side, left side class 1*

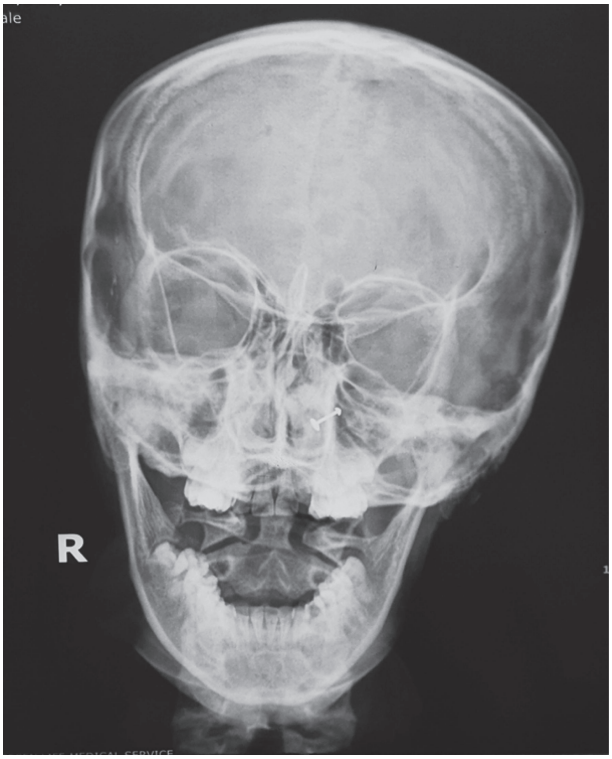

Fig 5: *X ray Skull showing no obvious bony deformity*

DISCUSSION:

Parry Romberg syndrome is a rare disorder of unknown aetiology and pathogenesis. It has been propositioned to be related to prior trauma, genetics, infection, vascular

malformation, cervical sympathetic overactivity and autoimmunity.[3,4,7,8,9]

Parry Romberg syndrome has a female prelidiction, presenting more commonly in 1st and 2nd decades and average age of onset is 13.7 year. [3,4] Interestingly left side of the face most common involved. [5] After initial presentation, the course is insidious, slowly progressive and is selflimiting.[13] Characterized by hemifacial atrophy, absence of underlying skin induration, atrophy of subcutaneous tissue, fat, skin, muscle, bone (100%), dental abnormalities (50%), migraine/facial pain (45%), hemimasticatory spasm (35%), tongue atrophy (25%), vitiligo (20%), hemiatrophy of ipsilateral/contralateral arm/trunk/leg (20%)[6]. Trigeminal neuralgia, facial paraesthesia, severe headache and epilepsy are most common neurological manifestations. Our patient presented at the age of 6, was progressive and later on halted on its own, had left hemifacial atrophy and subcutis, but no obvious involvement of bone. The mentioned OPG findings are corelatable with PRS. Notably, she was complaining of episodic sharp lancinating pain, which was very much typical of trigeminal neuralgia. She had no history of epilepsy. she had a preceding history of fever but, the it's aetiology was unknown. She had no history of trauma to affected side or positive family history for any autoimmune diseases. Closest differential of it is linear scleroderma,"en coup de sabre" (ECDS).But, distinctive clinical features and histopathological findings help to differentiate between these two entities., due to financial constrains and lack of resource, histopathology had not been done. However, 28-42% of patients have been reported to have concurrence of these two diseases [8,14]

Overall prognosis of PRS is unpredictable. Usually there is only cosmetic effect rather than any life threatening disability. Treatment for PRS is very challenging. Methotrexate is the standard therapy for active disease. Methotrexate is often combined with oral prednisolone in tapering dosage. For prolonged remission a 12-24 month course of methotrexate is recommended [9,10,11] .Other immunosuppressive agents have variable response. Surgey has been recommended when the disease process halts. It needs a multidisciplinary approach and autologous fat grafting, injectable fillers, lipoinjection, dermal fat grafts, adipofascial flash, bone grafts are some of the treatment options for aesthetic augmentation [11,12] .As, our patient when presented to us, had no evidence of active disease, no treatment was offered. However, she was counselled about available possible treatment options, but she refused. She had been counselled about the disease course, prognosis and possible complications and had been asked for periodic followup.

AUTHORS CONTRIBUTION:

CSP was involved in diagnosing the case and management of the patient. NC was involved in literature review and manuscript writing.

Conflict of interest: Nothing to declare

Consent: Informed written consent was taken from the patient for publication of this case report with accompanying images.

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Obituary news September-2022

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

Sl. No.	Name	Date of Death
1	Professor Dr. Mamun Ur Rashid	21/10/2021
2	Dr. Shamsul Arif Musa	02/10/2021
3	Dr. Mousumi Mou	08/10/2021
4	Dr. Sinha Monsur	14/10/2021
5	Dr. Sharmin Hossain Nila	18/10/2021
6	Dr. Bishakha Ghosh	19/10/2021
7	Professor Dr. Chowdhury Wahidur Rouf	21/10/2021
8	Dr. Mashrikur Razzak	21/10/2021
9	Dr. Md. Abdul Halim	26/10/2021
10	Dr. Niaz Morshed	05/11/2021
11	Dr. Golam Sarwar	23/11/2021
12	Dr. Shaharin Sohely Sumi	12/12/2021
13	Associate Professor Dr. Anup Kumar Saha	15/12/2021
14	Dr. Ashis Kumar Datta	18/12/2021
15	Dr. Abul Kashem	19/12/2021
16	Dr. Md. Walid Latif Kamal	21/12/2021

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.

Call for paper

To reach the doctors throughout the country and ensure their participation as author, contents and presentation of the Bangladesh Medical Journal have been updated & changed to some extent. In addition to original articles, review articles and case reports; we are going to publish following sections regularly.

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With a view to increase the bondage with the readers, we encourage to write letters to the editor. Letters may include original research presented in a research letter format or case reports or series. Alternatively, readers may express their ideas, opinions on important national or international issues related to doctors, medical science or medical profession.

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