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Research Article

A Study on Vitamin D Status and its Correlation with Severity in Children with Chronic Liver Disease Attending a Tertiary Care Hospital in Bangladesh

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Abstract

Background: Chronic liver disease (CLD) is a major cause of morbidity and mortality all over the world, it accounts for about 2% of all deaths in Europe (170,000/year) with increasing mortality rates in several countries. Vitamin D deficiency has been reported highly prevalent in chronic liver disease patients. The lower level of vitamin D is associated with severity of CLD, mortality and increased risk for infections. So, the aim of the present study was to evaluate the serum vitamin D status in patients with CLD**.**

Objective: To detect the serum Vitamin D status and its correlation with severity in children with CLD.

Methods: This cross-sectional analytical study was conducted at department of Paediatric Gastroenterology and Nutrition of Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh, from July 2019 through January 2021. A total of 20 cases diagnosed as CLD were studied who fulfilled inclusion and exclusion criteria. 20 patients other than CLD patients cough, common cold, constipation cases were included as controls. The detailed history, physical examination findings and investigation reports were recorded in a predesigned standard data sheet. Blood was collected from patients with chronic liver disease for investigation eg. s. albumin, prothrombin time, 25-hydroxyvitamin D and s. alkaline phosphatase. Blood was also collected from controls for 25-hydroxyvitamin D and s. alkaline phosphatase. 25-hydroxyvitamin D levels of <20, 21 to 30 and >31 ng/ml were defined as vitamin D ''deficiency'', ''insufficiency'' and "sufficiency" respectively. Severity was assessed by Child Pugh score.

Results: Twenty patients and 20 controls were evaluated. Mean age in cases and controls were 101.03 ± 67.31 months and 94.6 ± 50.15 months respectively. Wilson disease was found to be the commonest cause 10 (50.0%), followed by biliary cirrhosis 3 (15.0%) and 5 (25.0%) others .The mean PT was 24.49 ± 18.71 (sec) in cases and 12.35 ± 0.49 (sec) in controls. The mean INR was 2.35 ± 1.73 in cases and 1 ± 0 in controls. The mean serum albumin was 25.2 ± 6.24 (gm/dl) in cases and 39.95 ± 3.66 (gm/dl) in controls. Majority 17(85.0%) patients had deficiency of vitamin D level <20 ng/mL in cases and 16 (80.0%) in controls. The mean serum 25-hydroxy vitamin D level was 12.22 ± 6.21 (ng/mL) in cases and 16.91 ± 6.11 (ng/mL) in controls. The difference is statistically significant ($p < 0.05$) between two groups. The mean Child Pugh Score was 10.29 ± 2.08 in deficient, 10.67 ± 0.58 in insufficient group of vitamin D level. The difference were statistically not significant ($p > 0.05$) among three groups. The mean Vitamin D level was 11.52 ± 3.3 ng/mL in B class and 12.6 ± 7.43 ng/mL in C class. The difference was statistically not significant ($p > 0.05$) among two groups. There was negative not significant Pearson's correlation ($r = -0.148$; $p = 0.123$) between serum Vitamin D and Child Pugh Score and INR ($r = -0.316$; $p = 0.312$).

Conclusion: Blood levels of 25-hydroxyvitamin D in patients with chronic liver disease were found lower than those of controls. Serum Vitamin D had an inverse not significant correlation with Child Pugh Score and INR.

Keywords: Vitamin D Status; Chronic Liver Disease; Bangladesh

Introduction

Chronic liver diseases (CLD) and its complications are becoming a major health problem. CLD can lead to cirrhosis in children and adolescents. Nutritional deficiencies are frequent in children and adults with chronic liver disease. The liver plays a central role in energy and nutrient metabolism. Liver disease results in complex pathophysiologic disturbances affecting nutrient digestion, absorption, distribution, storage, and utilization [1]. In chronic liver diseases, the decreased vitamin D levels are associated with both malnutrition and low exposure to sunlight. Moreover, liver disease is characterized by low intestinal absorption of vitamin D and low levels of binding proteins, which transfer the hormone to the liver and kidney, in order to be activated. In addition, hepatic hydroxylation of vitamin D is impaired leading to low production of the active hormone, whereas the catabolism of vitamin D is increased in CLD patients [2]. Liver cirrhosis forms a complex relationship between serum calcium, phosphate, parathyroid hormone and vitamin D levels, affecting the musculoskeletal system. Fat soluble vitamin deficiencies in children with cholestatic disease have been reported, but the prevalence and severity are not clearly documented [1]. The lower level of vitamin D is associated with the severity of CLD, mortality and increased risk for infections. These skeletal manifestations in liver disease are termed as hepatic osteodystrophy. Hepatic osteodystrophy results in a higher risk of fracture in cirrhotic patients, thus negatively affecting their morbidity. In general, optimal vitamin D status ranges from 30 to 50 ng/mL (i.e. 75-125 nmol/L). Vitamin D deficiency has been defined as serum 25(OH) D levels lower than 20 ng/mL (i.e. 50 nmol/L) and vitamin D insufficiency has been defined as serum levels between 20 and 30 ng/mL (i.e.50-75nmol/L) [2]. The Food and Nutrition Board committee also noted that serum concentrations greater than 125 nmol/L (50 ng/mL) can be associated with adverse effects (National institute of Health). There is still no definition regarding the optimal vitamin D levels for patients with chronic liver diseases. In a vitamin D deficient patient, the intestinal absorption of calcium and phosphorus is decreased. The parathyroid gland recognizes the low serum calcium concentrations and releases PTH to increase the serum calcium back into an adequate range. PTH increases the calcium reabsorption in the kidneys and the excretion of phosphorus, therefore decreasing the risk of complication from an elevated calcium phosphate product (e.g., kidney stones). While this reduction is protecting the body, it is also decreasing bone mineralization at the same time. Over weeks to months, osteomalacia, stunted growth and rickets may develop [3]. If vitamin D deficiency is present, oral vitamin D3 can be administered in a daily dose of 3–10 times the recommended dietary allowance (RDA) for age; however, close monitoring of serum calcitriol levels is required to prevent D deficiency disease [4].

Materials and Methods

- **Type of study**: Cross sectional analytical study.
- **Place of study**: Department of Pediatric Gastroenterology and Nutrition, BSMMU, Dhaka, Bangladesh.
- **Period of study**: July 2019 through January 2021.
- **Study population**: Patient with CLD who attended the Pediatric Gastroenterology and Nutrition department of BSMMU
- **Sample size:** Here, n = 20
- **Sampling technique:** Cases were collected purposively among children presented with features of CLD at the department seeking medical advice. Age and sex matched controls were collected from the children other than CLD (cough, common cold, constipation) who attended the outpatient department.

Inclusion criteria

- Patients of either gender, age less than 18 years diagnosed as CLD.
- Both cases and controls parents gave consent to participate in the study.

Exclusion criteria

- Patient taking medications which can affect the serum vitamin D levels, like vitamin A, calcium and vitamin D supplements, steroids, antiepileptic drugs and bisphosphonates.
- Patient suffering from chronic diseases that can impair calcium and vitamin D metabolism, like chronic kidney disease, malabsorption syndrome, tuberculosis, etc.
- Presence of hepatocellular carcinomas or other malignancies.
- Who took vit D supplementation in last 3 months.

Study procedure and sampling technique

- The present study was carried out at the Department of Paediatric Gastroenterology and Nutrition, BSMMU.
- Study protocol was approved by Institutional Review Board (IRB) of BSMMU.
- Patients attending Pediatric Gastroenterology and Nutrition department having chronic liver disease were initially enrolled for the study.
- During the study period, 35 CLD patients were admitted at the department. By method of exclusion 20 cases were included in this study regardless of sex and cause of CLD.
- 20 patients other than CLD patients cough, common cold, constipation attending outdoor of BSMMU were included as control.
- Initial evaluation by history and clinical examination of the patients were done and recorded in the preformed data collection sheet by the researcher herself.
- Data were collected using a structured questionnaire (research instrument) containing all the variables of interest and from investigation reports. Collected data were checked daily and edited.

Laboratory methods

With all aseptic precaution 3 ml of venous blood was drawn from anticubital vein and collected in a dry clean red capped glass tube, sent immediately to the department of Biochemistry, BSMMU. The technique used for the plasma assay of vitamin D was the ARCHITECT 25-OH Vitamin D, which is a chemiluminescent microparticle immunoassay (CMIA) for the quantitative determination of 25-hydroxyvitamin D in human serum and plasma, referred to as Chemiflex. Sample, assay diluent and paramagnetic anti-vitamin D coated microparticles were combined. 25-OH vitamin D present in the sample is displaced from the vitamin D binding protein and binds to anti-vitamin D coated microparticles, forming an antigen-antibody complex. After incubation, a conjugate containing acridinium-labeled vitamin D was added to the reaction mixture and binds to unoccupied binding sites of the anti-vitamin D coated microparticles. After further incubation and washing, pre-Trigger and Trigger solutions was added to the reaction mixture. The resulting chemiluminescent reaction was measured as relative light units (RLUs). There was a relationship between the amount of 25-OH vitamin D in the sample and RLUs detected by the ARCHITECT system optics. Results were calculated automatically based on the previously established calibration curve.

Other tests

Baseline laboratory investigations (CBC with PBF, prothombine time, international normalized ratio, LFT, S. ALT, S. ALP, S. albumin, S. bilirubin were done at Department of Hematology and Biochemistry of BSMMU respectively. Other tests such as screening for HBV, HEV, HAV were done at Virology Department of BSMMU. Autoimmune screening like ANA, SMA, LKM1 and Wilson disease screening by serum ceruloplasmin were done at Biochemistry department of BSMMU. 24 hours urinary copper estimation, baseline and after penicillamine was done at Atomic Energy of Dhaka University. Also Slit-lamp eye examination was done to identify causes of liver disease if necessary and results were recorded in a case record file.

Statistics analysis

Statistical analysis were done using Statistical Package for Social Science (SPSS 23; Chicago, Illinois) for Windows XP. Results were expressed as mean ± standard deviation (SD), or number or percentage. Independent 't' test was used for comparison of quantitative variables and to find out the relationship between two quantitative variables Pearson's correlation coefficient test was used. Qualitative data were analyzed by Chi-square test. For all statistical test p value of less than 0.05 was taken as significant.

Results

Age distribution of the studied patients

Total 40 patients were included in this study. 20 were cases and 20 were control. Their age range was ≥ 60 months to < 120 months. It was observed that nearly half (45.0%) belonged to age < 120 months in cases and 7 (35.0%) in control. The mean age was 101.03 ± 67.31 months in cases and 94.6 ± 50.15 months in controls. The difference is statistically not significant ($p > 0.05$) between two groups.

Among 20 patients 9 (45%) were male and 11 (55%) female.

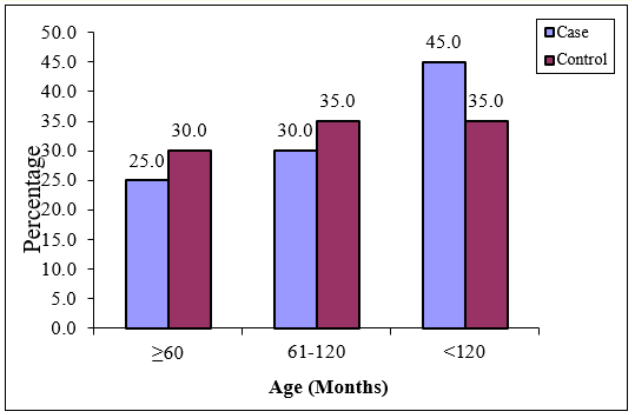

Figure 1: Bar-diagram showing age distribution of the studied patients Distribution of the studied patients by sex in case group (n = 20).

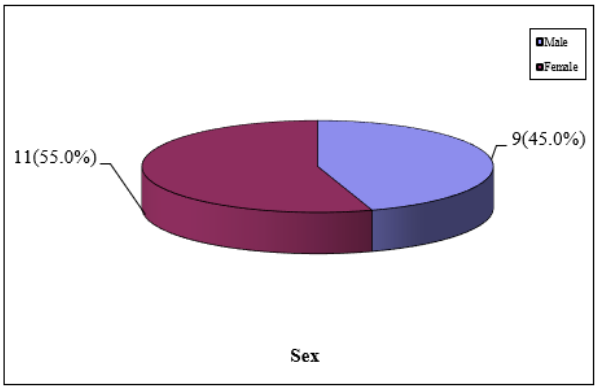

Figure 2: Pie-chart showing distribution of the study patients by sex in case group. Distribution of the studied patients by sex in control group (n = 20).

Among 20 patients 12 (60%) were male and 8 (40%) female.

Figure 3 and 7 shows the distribution of the studied patients by sex (N = 40). It was observed that more than half (55.0%) were female in cases and 8 (40.0%) in controls. The difference were statistically not significant (p > 0.05) between two groups.

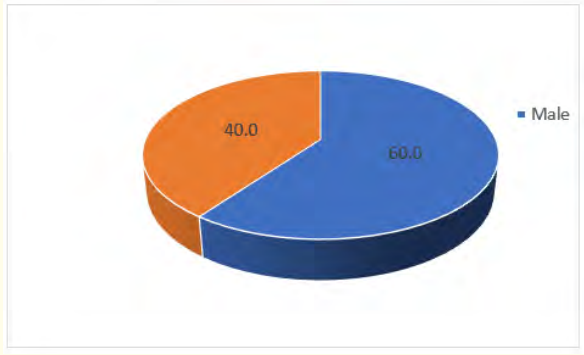

Figure 3: Pie-chart showing distribution of the study patients by sex in control group.

Physical Findings	Case (n = 20)		Control (n = 20)		p value
	N	%	n	%	
Anaemia					
Mild	13	65.0	9	45.0	[a]0.010[s]
Moderate	5	25.0	3	15.0	
Severe	2	10.0	0	0.0	
Jaundice	19	95.0	0	0.0	
Stigmata of CLD	20	100.0	0	0.0	
KF ring	6	30.0	0	0.0	
Edema	17	85.0	0	0.0	-
Abdominal tenderness	4	20.0	0	0.0	-
Palpable liver	18	90.0	0	0.0	-
Palpable spleen	16	80.0	0	0.0	-
Ascites	20	100.0	0	0.0	-

Table 1: Physical findings of the studied subjects (N = 40).

s = significant, ns = not significant, [a]p value reached from Chi-square test, [b]p value reached from Unpaired t-test.

Table 1 shows physical findings of the studied subjects. It was observed that almost 13 (65.0%) patients had anaemia in cases and 9 (45.0%) in control. The difference of anaemia was statistically significant (p < 0.05) between two groups. Majority (95.0%) patients had jaundice in cases. All 20 (100.0%) patients had stigmata of CLD in cases. Almost one third 6 (30.0%) patients

had KF ring in cases. Majority 17 (85.0%) patients had edema in cases. Four (20.0%) patients had abdominal tenderness. Majority 18(90.0%) patients had palpable liver. Majority 16 (80.0%) patients had palpable spleen. All (100.0%) patients had ascites.

Physical Findings	Case (n = 20)	Control (n = 20)	p value
	N %	N %	
Current Weight (Kg)			
Mean ± SD	9.21 ± 1.37	11.21 ± 1.65	[a]0.001[s]
Range (min-max)	6.5-12	8-13.5	
Height (cm)			
Mean ± SD	7913.5 ± 4377	9650 ± 1821.65	[a]0.109[ns]
Range (min-max)	3000-20300	7500-14000	

Table 2: Physical findings of the studied subjects (N = 40).

s = significant.

ns = not significant.

[a]p value reached from Chi-square test.

[b]p value reached from Unpaired t-test.

Current Weight (Kg)			
Mean ± SD	24.15 ± 13.89	25.8 ± 11.28	[b]0.682[ns]
Range (min-max)	3.5-49	4.5-52	
Height (cm)			
Mean ± SD	118.3 ± 33.92	118.2 ± 25.87	[b]0.991[ns]
Range (min-max)	51-158	58-154	

The mean current weight was 24.15 ± 13.89 (Kg) in cases and 25.8 ± 11.28 (Kg) in controls. The mean height was 118.3 ± 33.92 (cm) in cases and 118.2 ± 25.87 (cm) in controls. The difference were statistically not significant (p > 0.05) between two groups.

Laboratory test blood	Case (n = 20)		Control (n = 20)		p value
	n	%	n	%	
Hb (gm/dl)					
Mean ± SD	9.21 ± 1.37		11.21 ± 1.65		[a]0.001[s]
Range (min-max)	6.5-12		8-13.5		
TC (cu/mm)					
Mean ± SD	7913.5 ± 4377		9650 ± 1821.65		[a]0.109[ns]
Range (min-max)	3000-20300		7500-14000		
Platelet count (/cumm)					
Mean ± SD	186500 ± 126946.5		311450 ± 85686		[a]0.001[s]
Ranged (min-max)	43000-420000		165000-445000		
ESR					
Mean ± SD	22.4 ± 20.28		12.15 ± 7.6		[a]0.040[s]
Range (min-max)	5-80		5-30		
PBF–(Hemo-lysis)					
Present	4	20.0	0	0.0	[b]0.035[s]
Absent	16	80.0	20	100.0	
PT (sec)					
Mean ± SD	24.49 ± 18.71		12.35 ± 0.49		[a]0.006[s]
Range (min-max)	11-91.7		12-13		
INR					
Mean ± SD	2.35 ± 1.73		1 ± 0		-
Range (min-max)	1-2.3		1-1		
Serum ALP (U/L)					
Mean ± SD	449.15 ± 347.98		211.05 ± 86.64		[a]0.005[s]
Range (min-max)	67-1390		77-468		
Serum bilirubin: Total (mg/dl)					

Mean ± SD	7.73 ± 7.25	0.16 ± 0.06	[a]0.001[s]
Range (min-max)	0.5-27.8	0.1-0.25	
Serum ALT (U/L)			
Mean ± SD	103.15 ± 73.43	29.1 ± 10.96	[a]0.001[s]
Range (min-max)	18-326	15-49	
Serum albumin (gm/dl)			
Mean ± SD	25.2 ± 6.24	39.95 ± 3.66	[a]0.001[s]
Range (min-max)	16-36	35-48	

Table 3: Laboratory parameter of the studied patients (N = 40)

ns = not significant, [a]p value reached from Unpaired t-test, [b]p value reached from Chi-square test.

Table 3 shows the distribution of the studied patients by laboratory test. The mean Hb was 9.21 ± 1.37 (gm/dl) in cases and 11.21 ± 1.65 (gm/dl) in controls. The mean TC was 7913.5 ± 4377 (cu/mm) in cases and 9650 ± 1821.65 (cu/mm) in controls. The mean platelet count was 186500 ± 126946.5 (/cumm) in cases and 311450 ± 85686 (/cumm) in controls. The mean ESR was 22.4 ± 20.28 in cases and 12.15 ± 7.6 in controls. Four (20.0%) patients had feature of hemolysis in cases. The mean serum bilirubin: total was 7.73 ± 7.25 mg/dl in cases and 0.16 ± 0.06 mg/dl in controls. The mean serum ALT was 103.15 ± 73.43 U/L in cases and 29.1 ± 10.96 U/L in controls. The mean serum ALP was 449.15 ± 347.98 U/L in cases and 211.05 ± 86.64 U/L in controls. The mean PT was 24.49 ± 18.71 sec in cases and 12.35 ± 0.49 sec in controls. The mean INR was 2.35 ± 1.73 in cases and 1 ± 0 in controls. The mean serum albumin was 25.2 ± 6.24 gm/dl in cases and 39.95 ± 3.66 gm/dl in controls and the difference is statistically significant ($p < 0.05$) between two groups.

Table 4 shows the distribution of the studied patients by serum 25-hydroxy vitamin D. It was observed that majority (85.0%) patients had deficiency (<20 ng/mL) in cases and 16 (80.0%) in control group.

Serum 25-hydroxy vitamin D: (ng/mL)	Case (n = 20)		Control (n = 20)	
	n	%	n	%
Deficient, <20 ng/ml	17	85.0	16	80.0
Insufficient, 21 to 30 ng/ml	3	15.0	3	15.0
Sufficient, >31 ng/mL	0	0.0	1	5.0

Table 4: Distribution of the studied patients by serum 25-hydroxy vitamin D (N = 40).

	Case (n = 20)	Control (n = 20)	p value
	Mean ± SD	Mean ± SD	
Serum 25-hydroxy vitamin D: (ng/mL)	12.22 ± 6.21	16.91 ± 6.11	0.021[s]
Range (min-max)	4.2-25.9	8.37-33.04	

Table 5: Distribution of the study patients by serum 25-hydroxy vitamin D (N = 40).

s = significant, p value reached from Unpaired t-test

The mean serum 25-hydroxy vitamin D was 12.22 ± 6.21 (ng/mL) in case and 16.91 ± 6.11 (ng/mL) in control. The difference was statistically significant ($p < 0.05$) between two groups.

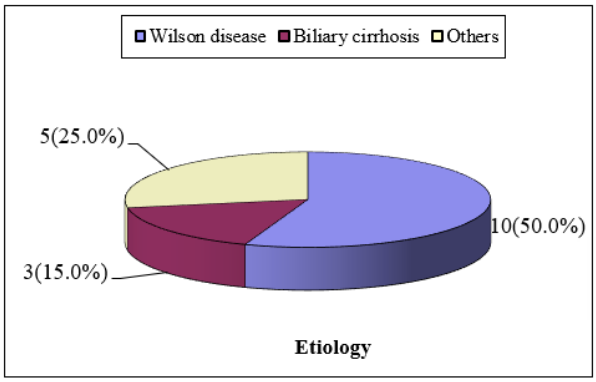

Figure 4: Etiologies of CLD in studied population (n = 20).

Pie chart (Figure 4) shows the etiology of CLD in studied patients. Half 10 (50.0%) patients had Wilson disease in studied cases, 3 (15.0%) were biliary cirrhosis and 5 (25.0%) had other diagnoses.

	Grade of CP Score			
	A Class (n = 0)	B Class (n = 7)	C Class (n = 13)	p value
	Mean ± SD	Mean ± SD	Mean ± SD	
Vitamin D level(ng/ml)	-	11.52 ± 3.3	12.6 ± 7.43	0.721^{ns}

Table 6: Relationship of vitamin D levels with Child Pugh class of cirrhosis of the liver only case group (n = 20).

The mean Vitamin D level was 11.52 ± 3.3 ng/mL in B class and 12.6 ± 7.43 ng/mL in C class. The difference was statistically not significant (p > 0.05) among three groups.

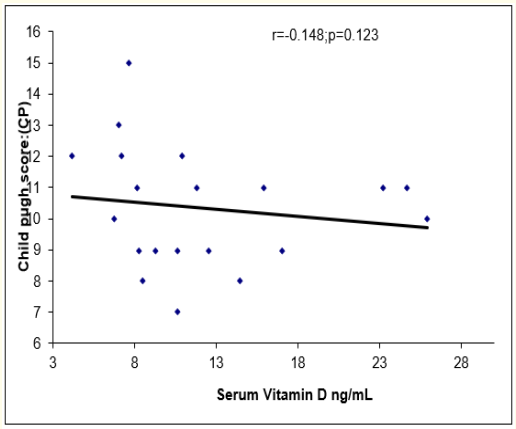

Figure 5: Scatter diagram showing negative correlation (r = -0.148; p = 0.123) between serum Vitamin D and Child Pugh Score. p value is not significant.

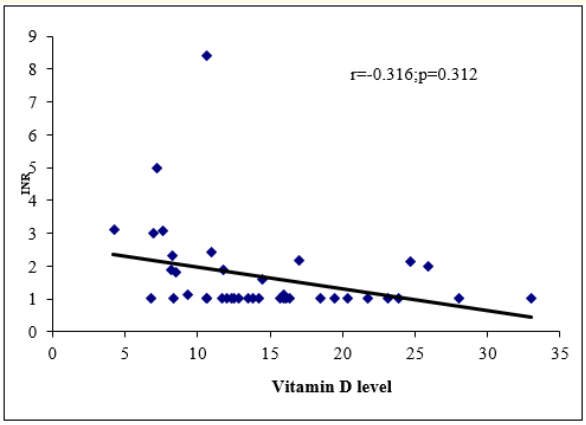

Figure 6: Scatter diagram showing negative correlation (r = -0.316; p = 0.312) between serum Vitamin D and INR. p value is not significant.

Discussion

This cross sectional study was carried out with an aim to quantify serum Vitamin D level in children suffering from Chronic Liver Disease and to identify the relationship of vitamin D levels with Child Pugh class of cirrhosis of the liver as well as to assess the relationship between INR and serum vitamin D level. A total of 40 patients who attended the Pediatric Gastroenterology and Nutrition department, of BSMMU were included in this study. Among them 20 patient with CLD and 20 patient without CLD were considered as cases and control group respectively. Patients of either gender, age less than 18 years diagnosed as CLD, were enrolled in this study. The present study findings were discussed and compared with previously published relevant studies. In this present study, Wilson disease was found to be the commonest cause 10 (50.0%), followed by biliary cirrhosis 3 (15.0%) and 5 (25.0%) others. Regarding diagnosis of chronic liver disease, Behairy., *et al.* [5] found that 6.7% had Wilson disease, 43.4% were diagnosed with chronic hepatitis of unknown etiology (11.7%). In this present study it was observed that 45.0% belonged to age <120 months in case and 35.0% in control. The mean age was 101.03 ± 67.31 months in case and 94.6 ± 50.15 months in control. The mean age was almost similar between two groups, no statistically significant difference (p > 0.05) was observed between two groups. Behairy., *et al.* [5] study found the mean age was 144 ± 36 months of the studied 60 children suffering from chronic liver disease of different etiologies. Five patients were infants aged younger than one year while 60.0% were aged 60 months or older. In this current study it was observed that 55.0% were female in case and 40.0% in control. The difference was statistically not significant (p > 0.05) between two groups. This can explain by not equal number of male and female patients in this present study. Jamil., *et al.* [6] study observed most of the patients in the study were females, 125 participants, 92.0% were females and only 8.0% were males, which support with the present study. Behairy., *et al.*

[5] studied 60 children suffering from chronic liver disease of different etiologies they were 55.0% male and 45.0% female. In control children were 50.0% females and 50.0% males with no statistically significant difference between both groups. Lee., *et al*. [7] study found 54.0% males and 46.0% female. Similarly, male predominant also observed by Jha., *et al*. [8], Buonomo., *et al*. [9], Yazdanpanah., *et al*. [10] (2017) and Gupta., *et al.* [11]. In this current study it was observed that 65.0% patients had anaemia in case and 45.0% in control. The anaemia was statistically significant ($p < 0.05$) between two groups. Majority 95.0% patients had jaundice in case. All 100.0% patients had stigmata of CLD in case. Behairy., *et al*. [5] observed the CLD patients presented clinically with jaundice 66.6%. In another study Jha., *et al*. [8] showed that majority (80.0%) patients had jaundice, however Buonomo., *et al*. [9] study observed that 39.5% patients with cirrhosis and ascites. In this current study it was observed that almost one third 30.0% patients had slit lamp examination of eyes (KF ring) in case. Majority 85.0% patients had edema in case. The mean current weight was 24.15 ± 13.89 (Kg) in case and 25.8 ± 11.28 (Kg) in control. The mean height was 118.3 ± 33.92 (cm) in case and 118.2 ± 25.87 (cm) in control. In this current study it was observed that 20.0% patients had abdomen examination tenderness, 90.0% had liver palpable, 80.0% spleen palpable and all 100.0% patients had ascites. Behairy., *et al*. [5] study found ascites 6.6% in CLD patients and Jha., *et al*. [8] study showed almost all patients (100%) had ascites in patients with CLD, which support with the current study. In this present study it was observed that the mean Hb was 9.21 ± 1.37 (gm/dl) in case and 11.21 ± 1.65 (gm/dl) in control. The mean Hb was significantly ($p < 0.05$) lower in case group. Behairy., *et al*. [5] and Jamil., *et al*. (2018) study found the mean Hb was 10.7 ± 1.5 g/dl with ranged from 7.4 to 13 g/dl and 9.43 ± 2.15 g/dL with ranged from 7.80 to 15.60 g/dl respectively, which are comparable with CLD patients in the present study. In this present study it was observed that the mean ESR was 22.4 ± 20.28 in case and 12.15 ± 7.6 in control. Four (20.0%) patients had PBF–(Hemolysis) in case. In this current study it was observed that the mean serum ALT was 103.15 ± 73.43 (U/L) in case and 29.1 ± 10.96 (U/L) in control. The mean serum ALP was 449.15 ± 347.98 (U/L) in case and 211.05 ± 86.64 (U/L) in control. The mean ALT and ALP were significantly ($p < 0.05$) higher in case group. Behairy., *et al*. [5] study found the mean ALT was 115 ± 93 U/L with ranged from 75 to 483 U/L and the mean ALP was 371.47 ± 218.52 IU/L with ranged from 91 to 1022 IU/L. Jamil., *et al*. [12] study showed that the mean ALT was 55.53 ± 38.37 U/L with ranged from 20 to 302 U/L and the mean ALP was 218.50 ± 88.68 U/L with ranged from 102 to 575 U/L, which support with the present study. In this current study it was observed that the mean TC was 7913.5 ± 4377 (cu/mm) in case and 9650 ± 1821.65 (cu/mm) in control. The mean platelet count was186500 ± 126946.5 (/cumm) in case and 311450 ± 85686 (/cumm) in control. In this present study it was observed that the mean PT was 24.49 ± 18.71 sec in case and 12.35 ± 0.49 sec in controls. The mean PT was significantly ($p < 0.05$) higher in case group. Behairy., *et al*. (2020) found the mean PT was 14.5 ± 2.6 sec with ranged from 11 to 25 sec, which is lesser then the present study. In this current study it was observed that the mean INR was 2.35 ± 1.73 in cases and 1 ± 0 in controls. Behairy., *et al*. [5] observed the mean INR was 1.33 ± 0.31 ranged from 1 to 2.9. Jha., *et al*. [8] observed that the mean PT-INR was 1.43 in case group and 1.50 in control group, which differ with the current study. vitamin D deficiency was found higher in cirrhotic patients in Child-Pugh class C than in patients in Child-Pugh class A. Similar results were demonstrated from studies that evaluated vitamin D levels in patients with NAFLD and non-alcoholic steatohepatitis (NASH) [13,14]. In this current study it was observed that 85.0% patients belonged to deficient (<20 ng/mL) in cases and 80.0% (<20 ng/mL) in controls. The mean serum 25-hydroxy vitamin D was 12.22 ± 6.21 (ng/mL) in cases and 16.91 ± 6.11 (ng/mL) in controls. The mean serum 25-hydroxy vitamin D was found significantly ($p < 0.05$) lower in case group. Behairy., *et al*. [5] showed that there was a statistically significant difference between the studied groups as regards to the level of serum 25-(OH)-vitamin D as it was statistically lower in the hepatic group. Seventy-five percent of the control group had sufficient, and 25% had insufficiency of 25-OH-vitamin D. While in the hepatic group, 38.3% had sufficient 25-OH-vitamin D, 41.7% insufficiency, and 20% had deficient 25-OHvitamin D. Such findings are consistent with the status of Lee., *et al*. [7] who found that vitamin D deficiency was prevalent in children with CLD despite supplementation of vitamin D. Overall, 28.0% of the subjects were either vitamin D deficient or insufficient. Also, Jamil., *et al*. [12] found that 88.0% had either insufficient or deficient levels of vitamin D, while only 12.0% had sufficient levels of vitamin D. Thus, a total of 28.0% were either deficient or insufficient vit D status. In addition, more than one in five children (20.0%) with CLD had at least one physical sign of vitamin D deficiency.

Biochemical evidence of hyperparathyroidism, characterized by an elevated level of PTH, was seen in 8.5% of the patients. Many studies showed that many patients suffering from cirrhosis of liver had either deficient or insufficient vitamin D levels [8-11]. In this present study it was observed that 65.0% patients had Class C, (10-15) and 35.0% Class B, (7-9). Buonomo., *et al*. [9] reported that patients with decompensated cirrhosis (Child- Pugh classification B or C) were higher among those with infections compared with patients with no evidence of infection. Lee., *et al*. [7] showed there was no significant difference between the prevalence of vitamin D sufficiency and gender, age and progression of liver disease (progressive vs. stable). There was a significant relationship between INR and different vitamin D levels ($p < 0.05$), where the highest vitamin D levels were in mild deficiency form with a frequency of 39.0% for normal patients and in mild deficiency form with a frequency of 56.0% for abnormal ones. Gupta., *et al*. (2016) observed that the mean vitamin D level was 25.58 ± 7.19 ng/dl with bilirubin level of <2 mg/dl, 21.99 ± 4.08 ng/dl with bilirubin level of 2-3 mg/dl and 19.16 ± 7.42 ng/dl with bilirubin level of >3 mg/dl. The mean vitamin D level decreases with increase in bilirubin level ($p < 0.05$). It was observed that majority (85.0%) of patients belonged to deficient, <20 ng/mL in cases and 16(80.0%) in controls. The mean serum 25-hydroxy vitamin D was 12.22 ± 6.21 (ng/mL) in cases and 16.91 ± 6.11 ng/mL in controls. The difference are statistically significant ($p < 0.05$) between two groups. Jamil., *et al*. [12] observed Vitamin D levels in CLD patients lower than vitamin D levels in the control group but, statistically, this difference was not significant ($p > 0.05$). Thus, patients with higher scores in the Child Pugh classification notably had lower vitamin D levels compared to patients with lower Child Pugh scores. Buonomo., *et al*. [9] mentioned in their study that Vitamin D levels were lower in patients with more advanced cirrhosis. Such differences are also significant when it was assessed among the three Child-Pugh classes ($p < 0.001$). In this current study it was observed that there was a negative but not significant Pearson's correlation ($r = -0.148$; $p = 0.123$) between serum Vitamin D and Child Pugh Score. Jamil., *et al*. [12] showed Child Pugh score with vitamin D levels had significant negative correlation coefficient = −0.556, ($p = 0.001$). Gupta., *et al*. [11] observed significant negative correlation with Child-Pugh score ($r = –0.7382$, $p < 0.001$). Konstantakis., *et al*. [15] found an inverse correlation of 25(OH)D levels with the Child-Pugh score. The present study also showed negative correlation but the correlation was not significant ($p > 0.05$), which may be due to lower sample size. In this present study it was observed that there was inverse but not significant Pearson's correlation ($r = -0.316$; $p = 0.312$) between serum Vitamin D and INR. Similarly, Behairy., *et al*. [5] also found there was a statistically not significant inverse correlation ($r = -0.97$; $p > 0.05$) between 25-OH-vitamin D and INR which is consistent with the current study.

Conclusion

This study was undertaken to detect the serum Vitamin D status in patients with chronic liver disease. Most of the patients age belonged to >120 month and female predominant in patients with chronic liver disease. History of Jaundice, gradual abdominal destination, hepatitis-B vaccination and history of anorexia were more common and anaemia and PBF were significantly more frequent in patients with chronic liver disease. Ascites, Liver and Edema were more common in these patients. Hb and Serum albumin, were significantly lower in patients with chronic liver disease, however, ESR, Serum bilirubin: Total, Serum ALT, Serum ALP, PT significantly higher in patients with chronic liver disease. Wilson disease was more common etiology in CLS patients. The mean serum 25-hydroxy vitamin D was significantly ($p < 0.05$) lower in case group. There was negative not significant correlation showed between serum Vitamin D with child pugh score with Prothom bin time. Vitamin D deficiency is documented in the majority of patients afflicted by CLD, particularly those having advanced disease. As the disease advances, the levels become more deficient.

Conflict of Interest

None.

Source of Fund

Nil.

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