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Clinical Profile of Esophageal Varices among Children with Chronic Liver Disease; a Tertiary Care Hospital Experience in Dhaka, Bangladesh

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Abstract:

Background: *Chronic liver disease (CLD) in children is a complex condition, including various liver pathologies like NAFLD, autoimmune liver diseases, viral hepatitis, and metabolic disorders. Esophageal varices, dilated veins in the esophagus, are a severe complication, indicating advanced liver disease and an elevated risk of life-threatening bleeding. They are present in a significant percentage of children with CLD, with varying rates in different studies. Portal hypertension is the root cause of variceal formation, stemming from liver fibrosis and cirrhosis. Risk factors for varices in children include underlying liver disease, fibrosis extent, duration of illness, and genetic factors. Timely detection is crucial to prevent serious complications, but pediatric-specific data and research are limited compared to adults.*

Aim of the Study: *The study aimed to investigate the prevalence of esophageal varices among children with CLD and to identify the risk factors associated with their development.*

Methods: *This cross-sectional descriptive study was conducted at the Department of Pediatric Gastroenterology and Nutrition, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh. A total of 50 patients were enrolled and analyzed in this study from April 2019 to October 2021. All patients were diagnosed with Chronic Liver Disease (or Chronic Liver Cirrhosis), and they were divided into two groups. Child-Pugh is widely used for the assessment of prognosis in liver cirrhosis. It can help predict all-cause mortality risk and the development of other complications from liver dysfunction, such as variceal bleeding. The Ethical Committee of Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh, approved the study.*

Result: *This cross-sectional study involved 50 patients, with 76% having esophageal varices, while 24% did not. The patients' socio-demographic and disease history showed no significant differences between the groups in terms of age, gender, consanguinity, jaundice history, and liver disease history. However, more males were in Group B. Clinical characteristics revealed no significant difference in anemia prevalence between groups. However, stigmata were more common in Group B. Palpable spleens were significantly more common in Group B, and ascites were absent in Group A but present in 73.68% of Group B. Esophageal varices ranged from grades I to IV. Wilson's disease was the most common diagnosis, and there was a significant difference in Child-Pugh scores between the groups, with Group B showing more severe liver cirrhosis.*

Conclusion: *Esophageal varices pose a severe threat to children with chronic liver disease (CLD), carrying life-threatening risks. Identifying the prevalence and risk factors of pediatric CLD-related esophageal varices is crucial for early detection and improved care. This study aims to enhance knowledge in pediatric hepatology and inform evidence-based approaches for managing this condition in young patients.*

Keywords: *Prevalence, Esophageal Varices and Chronic Liver Disease (CLD).*

1. INTRODUCTION

Chronic liver disease (CLD) in children is a complex and often debilitating condition that poses significant challenges for both patients and healthcare providers. It encompasses a spectrum of liver pathologies, including non-alcoholic fatty liver disease (NAFLD), autoimmune liver diseases, viral hepatitis, and metabolic liver disorders, among others. One of the most severe complications of CLD in both adults and children is the development of esophageal varices [1]. Esophageal varices are dilated, tortuous veins that form in the esophagus due to increased pressure in the portal venous system, typically resulting from cirrhosis or advanced liver fibrosis [2]. The presence of esophageal varices in children with CLD not only signifies advanced liver disease but also places them at an increased risk of life-threatening bleeding episodes. Therefore, understanding the prevalence of esophageal varices among children with CLD is of paramount importance for timely diagnosis, risk stratification, and intervention to prevent complications. It was noted that esophageal varices were present in 71.4% of Bangladeshi children with CLD [3]. In a Canadian study by Gana et al. (2011), 69% of the studied children were found to have esophageal varices [4].

Esophageal varices usually arise at a rate of 7-8% every year and progress from small to large varices at a rate of 10-12% every year [5]. When liver cirrhosis is diagnosed for the first time, esophageal varices are present in about 40% of patients with the compensated disease and about 60% of patients with the decompensated disease [6]. Pediatric CLD is a growing concern worldwide, with increasing incidence and prevalence rates observed over recent decades. Portal hypertension is the underlying pathophysiological process that leads to the formation of portosystemic collaterals and heralds the onset of severe complications: variceal hemorrhage. It is estimated that approximately 50% of pediatric patients with chronic liver disease experience gastrointestinal bleeding [7].The etiology of CLD in children varies across geographic regions, with NAFLD becoming a major contributor in many Western countries, while viral hepatitis, autoimmune liver diseases, and metabolic liver disorders remain significant causes in various populations [8,9]. Regardless of the underlying etiology, the progression of CLD in children can lead to liver fibrosis, cirrhosis, and, ultimately, the development of esophageal varices. Esophageal varices are a consequence of portal hypertension, a condition characterized by elevated pressure in the portal venous system, primarily due to impaired blood flow through the liver. As CLD advances, architectural changes in the liver, including fibrosis and cirrhosis, disrupt normal blood flow, leading to increased portal pressure [10]. This elevated pressure causes collateral vessels to form, including esophageal varices, which are particularly prone to rupture, resulting in severe bleeding and its associated morbidity and mortality. Several factors influence the development of esophageal varices in children with CLD. These include the underlying etiology of liver disease, the extent of liver fibrosis or cirrhosis, and the duration of liver disease [11, 12]. Additionally, genetic predisposition, such as specific gene polymorphisms, may contribute to variceal formation [13]. Understanding these risk factors is essential for identifying children at higher risk of developing esophageal varices and tailoring their clinical management accordingly. The presence of esophageal varices in children with CLD has significant clinical implications. Not only do varices signal advanced liver disease, but they also place children at an increased risk of potentially life-threatening bleeding episodes. Variceal hemorrhage can result in severe morbidity, including anemia, shock, and hepatic encephalopathy, and can be fatal if not promptly treated [14]. Consequently, early detection and monitoring of esophageal varices are crucial for preventing these complications. While esophageal varices are well-studied in adults with CLD, there remains a notable gap in our understanding of the prevalence and risk factors associated with variceal formation in pediatric CLD. Most research in this area has focused on adult populations, and pediatric-specific data are limited. Moreover, the available studies vary in methodology and patient populations, making it challenging to draw definitive conclusions.

2. METHODOLOGY AND MATERIALS

This is a cross-sectional descriptive study; a total of 50 patients were enrolled and analyzed in this study. The study was conducted at the Department of Pediatric Gastroenterology & Nutrition, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh. The study duration was two years, from April 2019

to October 2021. All patients were diagnosed with Chronic Liver Disease (or Chronic Liver Cirrhosis), and they were divided into two groups. Before collecting data, an informed consent form was taken from every patient, and the data were kept very confidential. The study was approved by the Ethical Committee of Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh.

Group A: Patients without Esophageal Varices.

Group B: Patients with Esophageal Varices.

- **Inclusion Criteria:**
- Patients under 18 years.
- Both male and female.
- Patients with Chronic Liver Disease (Either Chronic Hepatitis or Chronic Liver Cirrhosis).
- **Exclusion Criteria:**
- Patients with previous or active gastrointestinal bleeding
- Patients who previously had undergone injection sclerotherapy, band ligation, or surgery for esophageal varices
- Patients with tense ascites.

Child-Pugh is widely used for the assessment of prognosis in liver cirrhosis. It can help predict all-cause mortality risk and the development of other complications from liver dysfunction, such as variceal bleeding. The score is composed of several categories. e.g., total bilirubin, serum albumin, INR, presence of ascites, and hepatic encephalopathy [15].

All data were presented in a suitable table or graph according to their affinity. A description of each table and graph was given to understand them clearly. All statistical analysis was performed using the statistical package for social science (SPSS) program and Windows. Continuous parameters were expressed as mean±SD and categorical parameters as frequency and percentage. Student's t-test made comparisons between groups (continuous parameters). Categorical parameters compared by Chi-Square test. The significance of the results, as determined by a 95.0% confidence interval and a value of $P<0.05$, was considered statistically significant.

3. RESULT

In this cross-sectional investigation, 50 patients were included and subjected to thorough analysis. Among these 50 patients, 38 individuals (76.0%) exhibited the presence of esophageal varices, while the remaining 12 patients (24.0%) did not display any signs of esophageal varices (as illustrated in Figure 1). A comprehensive overview of the socio-demographic and medical histories of the study population is presented in Table 1. The analysis revealed that age distribution among the patients indicated that eight individuals (62.5%) in Group A and 19 individuals (50.0%) in Group B fell within the age group of over ten years. Consanguinity was observed in 8 patients, all of whom were part of Group B. A history of jaundice was identified in 10 patients (83.33%) in Group A and 35 patients (92.11%) in Group B. Furthermore, a history of liver disease was noted in 3 patients (25.0%) in Group A and two patients (5.26%) in Group B. Importantly, there were no statistically significant differences between the two groups with regard to age, gender, consanguinity, history of jaundice, and history of liver disease, as the p-values exceeded 0.05 (as shown in Table 1). The gender distribution of the patients indicated that eight individuals (66.67%) in Group A and 30 individuals (78.95%) in Group B were male. However, there was no significant statistical difference in age between the two groups, with a p-value of 0.378 (as depicted in Figure 2). A comprehensive summary of the clinical characteristics of the study population is provided in Table 2. Of the 12 patients in Group A, four individuals (33.33%) had anemia, while in Group B, 22 patients (57.89%) were diagnosed with anemia. The statistical analysis indicated no significant difference between the two groups regarding anemia, with a p-value of 0.423. Stigmata was present in half of the patients (50.0%) in Group A, while in Group B, 35 patients (92.11%) exhibited stigmata. There was a significant statistical difference between the two groups regarding the presence of stigmata, with a p-value of 0.023. In both groups, 75.0% of the patients had a palpable liver. However, the presence of a palpable spleen was significantly more common in Group B (36 patients, 94.74%) compared to Group A (2 patients, 5.26%) ($p < 0.001$). Notably, no patients (0.0%) in Group A had ascites, while 28 patients (73.68%) in Group B were diagnosed with ascites. A highly significant statistical difference was observed between the two groups regarding the presence of ascites, with a p-value

of < 0.001 (as outlined in Table 2). Among the 50 patients with esophageal varices, 10 patients (20.0%) had grade I esophageal varices, 19 patients (38%) had grade II, 13 patients (26.0%) had grade III, and eight patients (16%) had grade IV esophageal varices (as presented in Figure 3). In terms of diagnosis, half of the patients (n=25, 50.0%) were diagnosed with Wilson's disease, nine patients (18%) were diagnosed with Chronic hepatitis B, and six patients (12%) were diagnosed with Autoimmune hepatitis. Other diagnoses included Cryptogenic cirrhosis (5 patients, 10%), Biliary cirrhosis (3 patients, 6%), and Glycogen storage disease (GSD) (2patients, 4%) (as detailed in Table 3). Regarding the severity of liver cirrhosis, all patients in Group A were classified as Class A, while in Group B, only five patients (13.16%) were classified as Class A. In Group B, Class B and Class C were identified in 19 patients (50%) and 14 patients (36.84%), respectively. A highly significant difference was found between the two groups in terms of Child-Pugh score (p < 0.001), as indicated in Table 4.

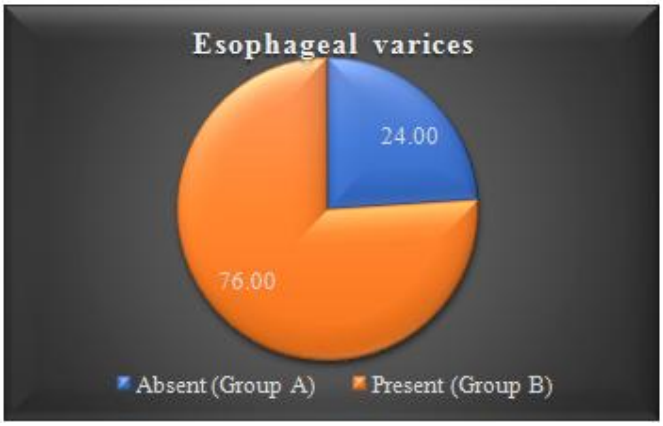

Figure1. *Distribution of patients by esophagealvarices (N=50)*

Table1.*Socio-demographic and disease history of the studied population (N=32).*

Variables	Group A (N=12)		Group B (N=38)		P-value
	n	%	n	%	
Age group (in years)					
Up to 10	4	37.50	19.00	50.00	0.691^{NS}
>10	8	62.50	19.00	50.00	
Consanguinity					
Absent	12	100.00	30.00	78.95	0.296^{NS}
Present	0	0.00	8.00	20.83	
History of jaundice					
Absent	2	16.67	3.00	7.89	0.999^{NS}
Present	10	83.33	35.00	92.11	
History of liver disease					
Absent	9	75.00	36.00	94.74	0.147^{NS}
Present	3	25.00	2.00	5.26	

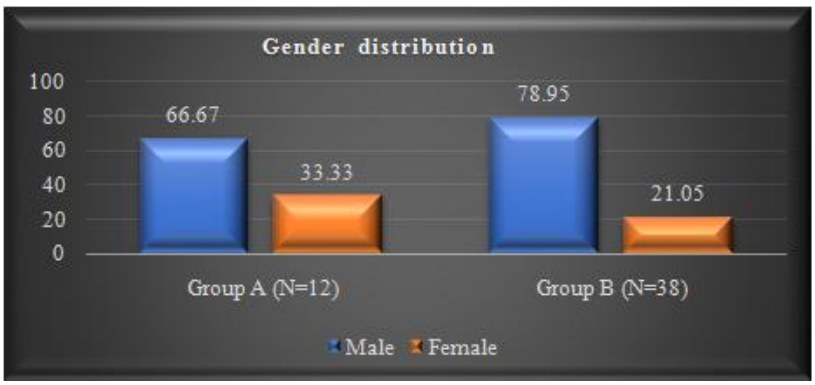

Figure2. *Distribution of the study population based on the groups*

Table2. *Clinical characteristics of the studied population (N=50)*

Clinical characteristics	Group A (N=12)		Group B (N=38)		P-value
	n	%	n	%	
Anaemia					
Absent	8	66.67	16.00	42.11	0.423^{NS}
Present	4	33.33	22.00	57.89	
Stigmata					
Absent	6	50.00	3.00	7.89	0.023^{S}
Present	6	50.00	35.00	92.11	
Liver					
Palpable	9	75.00	29.00	76.32	0.999^{NS}
Not Palpable	3	25.00	9.00	23.68	
Spleen					
Palpable	3	25.00	36.00	94.74	<0.001^{S}
Not Palpable	9	75.00	2.00	5.26	
Ascites					
Absent	12	100.00	10.00	26.32	<0.001^{S}
Present	0	0.00	28.00	73.68	

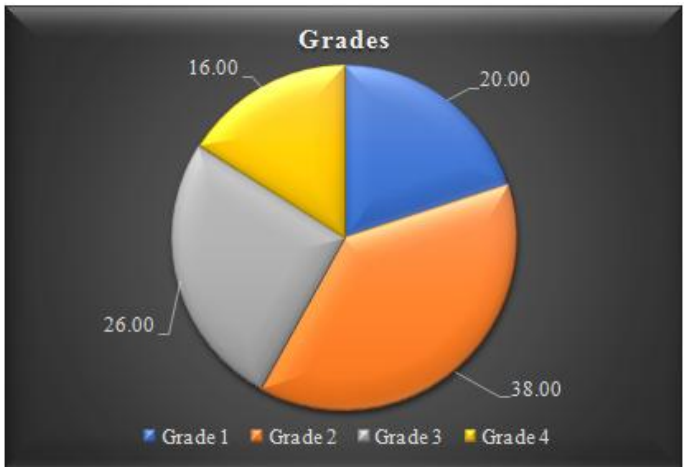

Figure3. *Distribution of patients by grading of esophageal varices (N=50)*

Table3. *Diagnosis of the studied population (N=50).*

Causes	Frequency (n)	Percentage(%)
Wilson's disease	25	50.00
Biliary cirrhosis	3	6.00
Glycogen storage disease (GSD)	2	4.00
Autoimmune hepatitis	6	12.00
Chronic hepatitis B	9	18.00
Cryptogenic cirrhosis	5	10.00

Table4. *Child-Pugh score of the studied population (N=50).*

Child-Pugh score	Group A (N=12)		Group B (N=38)		P-value
	n	%	n	%	
Class A	12	100.00	5.00	13.16	<0.001
Class B	0	0.00	19.00	50.00	
Class C	0	0.00	14.00	36.84	

4. DISCUSSION

Esophageal varices refer to the dilation of veins within the esophagus, the muscular tube linking the throat to the stomach. These varices primarily manifest in individuals afflicted by severe liver conditions. The genesis of esophageal varices is associated with the obstruction of normal blood circulation to the liver, typically stemming from either the formation of blood clots or the presence of scar tissue within the liver. In this cross-section study, we found 38 (76.0%) with esophageal varices, while the remaining 12 (24.0%) did not

exhibit esophageal varices. It is noteworthy that esophageal varices were present in 71.4% of Bangladeshi children with CLD [3]. A Canadian study conducted by Gana et al. (2011) reported that 69% of the children they studied had esophageal varices [4]. Conversely, a study conducted in Brazil by Fuguendes et al. (2008) revealed that 60% of children displayed esophageal varices during their initial upper GI endoscopy. Of the 24 patients with esophageal varices in our research, 10 (41.7%) had large esophageal varices [16]. These findings align with those from other studies, indicating that 32% to 55% of children had large esophageal varices, thereby supporting our current study's results. Importantly, in our research, most of the children were male, and there was no statistically significant difference in gender distribution between children with or without esophageal varices (p=0.378) [4,16]. A similar male predominance was observed in other studies [3,17], although Gana et al. (2011) reported a majority of female children in their study [4]. Another study found no gender difference in this regard [18]. The average age of the children in our study was 10.7±4.2 years. In a study by Rukunuzzaman (2015) that assessed the clinical and laboratory profile of Wilson's disease (WD) in children, the mean age of the children was 8.5±4.5 years, while Alam et al. (2019) observed a mean age of 9.7±3.2 years in children with CLD, consistent with our study's findings [3,17]. Notably, consanguinity in marriage was observed in 5 patients, all of whom were in Group B. Consanguinity in marriage is a feature of WD because it is an autosomal recessive condition. Rukunuzzaman (2015) found consanguinity in marriage in 30% of patients in their study [17], and Tryambak et al. (2009) identified WD to be more prevalent among children born to consanguineous parents in Japan [19]. Regarding clinical manifestations, stigmata were present in 50.0% of patients without esophageal varices, while most patients (91.7%) with esophageal varices had stigmata. Among the patients with esophageal varices, 13 (54.2%) had clubbing, 6 (25.0%) had leuconychia, 8 (33.3%) exhibited thenar and hypothenar wasting, 2 (8.3%) had gynecomastia, and 6 (25.0%) had Palmar erythema. The prevalence of gynecomastia in cirrhotic adult patients has been reported in one study to be 44% [20]. Spider angioma was found in 33% of cases, and clubbing was observed in 24% of cirrhosis cases [21,22]. In Rukunuzzaman's study (2015), thenar and hypothenar wasting were found in 8%, spider angioma in 2%, and clubbing and gynecomastia in 1% of cases each [17]. Spider angioma and gynecomastia are attributed to impaired estradiol metabolism in the liver [21], while clubbing develops due to the release of platelet-derived growth factors from aggregated platelets in the nail bed [22]. In Groups A and B, 75.0% and 76.32% of patients had a palpable liver. However, the presence of a palpable spleen was significantly higher in children with esophageal varices (36 out of 50, 94.74%) compared to children without esophageal varices (2 out of 8, 25.0%) ($p < 0.001$). This finding is consistent with other studies [4,7,&23]. Regarding the underlying causes among the patients in our study, half were diagnosed with Wilson's disease, 9 (18%) with Chronic hepatitis B, and 6 (12%) with Autoimmune hepatitis. Others had Cryptogenic cirrhosis (5 out of 50, 10%), Biliary cirrhosis (3 out of 50, 6%), and Glycogen storage disease (GSD) (2 out of 50, 4%). A prospective study by Alam et al. (2019) reported that the predominant etiology of CLD was Wilson's disease (65.5%), with other causes including chronic hepatitis B (6%), autoimmune hepatitis (7.1%), biliary atresia (6%), celiac disease-associated liver disease (1.2%), glycogen storage disease (1.2%), hepatitis C virus infection (1.2%), and cryptogenic (11.9%) [3]. The Child-Pugh scoring system, designed to predict mortality in cirrhosis patients, classified all patients without esophageal varices as Class A, while among patients with esophageal varices, only 5 (13.16%) were classified as Class A. Class B and Class C were found in 19 (50%) and 14 (36.84%) patients, respectively. A highly significant difference was found between the groups regarding the Child-Pugh score ($p < 0.001$). This scoring system employs five clinical and laboratory criteria to categorize patients: serum bilirubin, serum albumin, ascites, neurological disorder, and prothrombin time [24]. Given that all these parameters were significantly elevated in patients with esophageal varices, a significant difference in Child-Pugh scores between the groups was anticipated.

Limitations of the study: The limitations of the study on the "Frequency of esophageal varices among children with chronic liver disease" include a relatively small sample size, which

may not fully represent the entire pediatric population with chronic liver disease. Additionally, the study's cross-sectional design limits the ability to establish causation or assess the progression of esophageal varices over time. Data collection may rely on medical records, introducing potential inaccuracies or missing information. Variability in diagnostic methods and interobserver variability in identifying esophageal varices could also impact the study's accuracy. Furthermore, the study's geographic or institutional focus may limit generalizability to broader populations of children with chronic liver disease.

5. Conclusion and Recommendations

In conclusion, esophageal varices represent a critical complication of chronic liver disease in children, with potentially life-threatening consequences. Understanding the prevalence and risk factors associated with esophageal varices in pediatric CLD is essential for early detection and intervention, ultimately improving the quality of care and outcomes for affected children. This study aims to bridge the knowledge gap in pediatric hepatology and contribute to evidence-based strategies for the management of esophageal varices in this unique patient population.

Ethical approval

The study was approved by the Institutional Ethics Committee.

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