

Association between severity of chronic liver disease with grading of oesophageal varices in children

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Article Info

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Abstract

Chronic liver disease is a uncommon manifestation in the children and many of them presents with oesophageal varices. The aim of this study was to observe the association between severity of chronic liver diseases determined by Child- Pugh score with grading of oesophageal varices. 62 cases (male, 34) were included in the present study. Mean age of the study population was 9.5 ± 3.3 years. Male to female ratio was 1.2:1. Wilson's disease was the most common etiology of chronic liver disease (64.5%). Of the 62 children, 30.7% had Child class A, 16.1% had Child class B and the remaining 53.2% had Child class C cirrhosis. Oesophageal varices were found in 43 (69.3%) children. On univariate analysis low platelet count and splenomegaly were found to be associated with the presence of esophageal varices. Splenomegaly was found as independent predictor for presence of varices on multivariate analysis (OR; 15.51, 95% CI, 3.7-63.5). Furthermore, splenomegaly was also independent risk factor for large esophageal varices. No association was found between Child-Pugh classification (child A, B, C) with grading of oesophageal varices (Grade - I, II, III, IV). Our study showed no positive association between Child-Pugh classifications with grading of esophageal varices. Splenomegaly predicts the presence of oesophageal varices as well as the presence of large esophageal varices.

Introduction

Chronic liver disease (CLD) is not so uncommon among children. Cirrhosis is referred as the most advanced stage of CLD. Several complications may occur at advanced liver disease. Development of oesophageal varices is one of them and variceal bleeding is one of the most dreadful complications of CLD because of its high mortality. Oesophageal varices are present in about 40% of patients with the compensated CLD when diagnosed for the first time and in about 60% of patients with decompensated disease with ascites.¹ When varices develop, the occurrence of subsequent variceal bleeding in the next two years is 25-35%. Mortality rate is as high as up to 50% from index haemorrhage.² The incidence of oesophageal varices rises by approximately 5% per year in patients with CLD. The progression rate from small to large varices are about 5-10% per year.³ American College of Gastroenterology advocates screening all CLD patients for the early pick up of esophageal varices. The society also suggests to treating patients with

beta-blockers to reduce the incidence of first variceal haemorrhage who developed large varices.⁴ Thus performing an upper GI endoscopy for detection of varices in all CLD patients implies a large number of unnecessary endoscopies especially in children. It also increases the workload of endoscopy units as well as an economic burden to the patients and this is more difficult in a resource-limited country like ours. It would be beneficial if patients with higher chances of oesophageal varices could be diagnosed by meticulous clinical examination and by less invasive laboratory tests. Then they would be submitted to upper GI endoscopy, which is an invasive and expensive examination that may have complications, especially in children.

Various scoring systems are used to determine the severity and the prognosis in patients with CLD. The Child-Pugh score, which predicts disease severity and survival rate on the basis of physical signs and the findings of liver function tests. Based on the total point score, patients are categorized into one of three stages. Those with Child class A



may survive as long as 15 to 20 years, whereas those with Child class C may survive only 1 to 3 years.⁵ However, endoscopic screening in children and adolescents diagnosed as chronic liver disease results in up to 50% normal endoscopies.⁶ In addition to patients undergoing an invasive procedure unnecessarily, general anaesthesia is necessary to perform the procedure in most of the children. Considering the overpopulation in medical services and the high cost to the health system we need to restrict endoscopy to those patients who have ultrasonographic or laboratory indicators. There are several indicators that can predict the presence and severity of varices would result in a better risk/ benefit ratio for the endoscopic study. In recent years, several studies^{2,5,6} have demonstrated the relation between presence of esophageal varices and various clinical, laboratory, and/or ultrasonographic parameters mostly in adult population. This study was conducted to observe the association between severity of CLD determined by Child-Pugh score with the grading of oesophageal varices in children.

Methods

This cross-sectional prospective study was conducted at the Department of Paediatric Gastroenterology & Nutrition, BSMMU, from January 2016 through July 2017. Consecutive 62 children diagnosed as chronic liver disease were included in the study after fulfilling the inclusion criteria. Chronic liver disease was considered when any stigmata of chronic liver disease were present irrespective of duration of liver disease with elevated alanine aminotransferase or presence of jaundice for a long period with elevated alanine aminotransferase or those diseases which are chronic in nature like Wilson's disease, autoimmune hepatitis, Alpha 1 antitrypsin deficiency or histologically diagnosed as a case of chronic hepatitis or cirrhosis.^{7,8} A complete history, physical examination findings, and investigation reports were recorded in a standard datasheet. Children who had continuing upper GI bleeding or recent history of GI bleeding (within two weeks) or who were on beta-blocker therapy or history of endoscopic treatment (band ligation or sclerotherapy) for oesophageal varices or previous history of surgical intervention for portal hypertension, were excluded from the study.

Children were classified into three groups: Child-Pugh class A, Child- Pugh class B, and Child- Pugh class C according to score⁹. Complete blood count (CBC), prothrombin time (PT), blood glucose, serum creatinine, serum electrolytes, liver function tests (serum bilirubin, Alanine aminotransaminase, aspartate aminotransferase, serum albumin) were done in all the patients. Viral markers (HBsAg, anti-HCV), slit-lamp examination for Kayser- Fleischer (KF) ring and sunflower cataract, serum ceruloplasmin, 24 hour urinary copper estimation, serum IgG level, antinuclear antibody (ANA),

anti-liver-kidney microsomal antibody (anti LKM), anti-smooth muscle antibody (anti SMA) were done to find out the aetiology of CLD. All children went through upper GI endoscopy to rule out oesophageal varices and associated findings. Endoscopy was done by two experienced endoscopist in the department by Olympus video endoscope GIF 160 endoscopy machine. Children were grouped as without varices, with small varices and with large varices. Varices were further graded as small (grades I-II) and large (grades III-IV) according to Paquet's grading system during procedure.¹⁰ Informed written consent was taken from every parents or guardians.

For statistical analysis all data were expressed as mean \pm standard deviation (SD) or median (range) or number or percent. Chi-square test and Fisher's exact test were used for categorical variables. Student *t*-test and Mann whitney test were done for continuous variables. *p* value < 0.05 was considered as statistically significant for all statistical tests. Variables that were found significant in univariate analysis were included as candidate for regression analysis to identify predictors for the presence of varices. All calculations were made by using SPSS software (Statistical package for social science, version 20).

Results

Among the sixty-two subjects, 19 children (30.7%) were in Child A group, 10 children (16.1%) in Child B and 33 children (53.2%) were in the Child C group. Among them, the minimum age was one year, whereas the maximum age was 15 years. Majority cases, 30 (48.3%) belonged to the 5-10 years age group. According to Child classification, 11 (57.8%) cases were in Child A group who belonged to the age group > 10 years. 19 cases (57.5%) were in Child Class C and belonged to the age group 5-10 years. In Child class B, 5 (50 %) cases were in both age group 5-10 years and >10 years. This difference was statistically not significant (*p* = 0.271). Out of 62 patients 34 (54.8%) were male and 28 (45.2%) female. Male-female ratio was 1.2:1. Statistically, no significant difference was found in sex distribution between Child A, B, and C group (*p* = 0.942). Wilson disease is the predominant aetiology among the known causes of CLD. Of the 62 patients, 43 patients (69.3%) had oesophageal varices, and varices were absent in 19 patients (30.7%). Among 43 patients who had oesophageal varices, 12 patients (28%) had grade I varices, six patients (14%) had grade II varices, seven patients (16.2%) had Grade III varices and 18 patients (41.8%) had grade IV varices. Twelve patients who had grade I oesophageal varices, most (66.7%) of them, 8 out of 12 were in child C group. Six patients had grade II varices among them, 50% were in the child C group. Five patients (71.4%) out of 7 patients of grade III varices were also in the child C group. Among 18 patients of grade IV varices, eight patients (44.4%) were in child C group

and seven patients (38.9%) were in child A group. The association between child A, B, C group and different grades of esophageal varices is statistically not significant ($p=0.901$). (Table-I). On univariate analysis, low platelet count and splenomegaly were found significantly associated with the presence of esophageal varices ($p=0.02$ and $p<0.001$ respectively) among different demographic, laboratory

and clinical parameters and also for large esophageal varices ($p=0.041$ and $p=0.002$ respectively) (Table-II and III). Splenomegaly was significantly associated with the presence of any grades of esophageal varices (OR; 15.51, 95% CI, 3.79-63.58) and also for presence of large varices (OR; 10.21, 95% CI, 1.8-58.05) on multivariate analysis.

Table-I

Association between Child classification with grading of esophageal varices (N=62)

Variable	Grade I n (%)	Grade II n (%)	Grade III n (%)	Grade IV n (%)	p value
Child A	2	2	2	7	0.901
Child B	2	1	0	3	
Child C	8	3	5	8	

*Fisher's exact test

Table-II

Association between Child classification with grading of esophageal varices (N=62)

Variable	Varices present (n=43)	Varices absent (n=19)	p value
Ascites, n (%)	28(65.1)	11(57.9)	0.587*
Splenomegaly, n (%)	32(74.4)	3(15.8)	<0.001¶
Hepatic encephalopathy, n (%)	2(4.7)	0(0.0)	0.339 ¶
Child pugh class (A vs B/C)	13(30.2)	6(31.6)	0.915*
Class A Class B & Class C	30(69.8)	13(68.4)	
Hemoglobin (g/dl)			
Mean±SD	8.72±1.67	9.57±1.54	0.06±
Platelet count (per cumm)			
Mean±SD	123581±85069	179055±77015	0.02 ±
S. Bilirubin (mg/dl)	2	2.6	
Median (range)	(0.4-31.6)	(0.4- 36.2)	0.47£
S. Albumin (g/dl)			
Mean±SD	2.62±0.91	2.81±0.91	0.45±
INR			
Mean±SD	2.03±1.04	1.84±0.73	0.46±

*Chi square test

¶ Fisher's exact test

± Independent t-test

£ Mann Whitney U-test

Table-III

Association between clinical and laboratory parameters with the presence of large oesophageal varices(N=43)

Variable	Varices present (n=43)	Varices absent (n=19)	p value
Ascites, n (%)	28(65.1)	11(57.9)	0.587*
Splenomegaly, n (%)	32(74.4)	3(15.8)	<0.001¶
Hepatic encephalopathy, n (%)	2(4.7)	0(0.0)	0.339 ¶
Child pugh class (A vs B/C)	13(30.2)	6(31.6)	0.915*
Class A Class B & Class C	30(69.8)	13(68.4)	
Hemoglobin (g/dl)			
Mean±SD	8.72±1.67	9.57±1.54	0.06±
Platelet count (per cumm)			
Mean±SD	123581±85069	179055±77015	0.02 ±
S. Bilirubin (mg/dl)	2	2.6	
Median (range)	(0.4-31.6)	(0.4- 36.2)	0.47£
S. Albumin (g/dl)			
Mean±SD	2.62±0.91	2.81±0.91	0.45±
INR			
Mean±SD	2.03±1.04	1.84±0.73	0.46±

*Chi square test

¶ Fisher's exact test

± Independent t-test

£ Mann Whitney U-test

Discussion

In the present study, among 62 patients, 69.4% had oesophageal varices, 58% of these were grade III and IV and thus bearing a higher chance of variceal bleeding. Gana et al¹¹ also demonstrated almost similar findings. They found 69% of studied children had oesophageal varices, among them large varices were found in 32% children. Of the 62 studied children, 30.6% were in Child-Pugh A, 16.1% in Child-Pugh B, and 53.2% in Child-Pugh C group. These findings don't match with the results of Alcantara et al¹³, who found 82.4% in child A, 14.7% in child B, and 2.9% children in the child C group. The difference most probably is because most of the patients came to us with advanced liver disease as this is a tertiary care hospital and may also be due to late reporting because of poor socio-economic background.

The present study showed statistically no significance in age ($p = 0.27$) and sex ($p = 0.94$) distribution among child A, B, and C group and also patients with or without oesophageal varices. Among the different aetiologies¹⁴, Wilson's disease (64.5%) was the predominant cause of chronic liver disease in

the present study followed by biliary cirrhosis (8%) and chronic hepatitis B infection (6.5%). In 13% of cases, aetiology could not be identified due to poor socio-economic conditions of the patient and lack of investigation facilities at the center. A study was done by Hanif et al.¹⁵ among Pakistani children to find out the etiology of chronic liver disease. It was found that 24% had chronic hepatitis B infection, 16% autoimmune hepatitis, and 16% Wilson's disease. Aetiology remained unknown in 44% of cases. The findings of the present study partially matched with Hanif et al.¹⁵ and the difference most probably is because the two studies were conducted at different geographical location and time frame and also vaccination against hepatitis B virus was included in EPI schedule since 2005 in our country. Oesophageal varices were present in 69.4% (43 out of 62) patients. This result is close to the findings of Fagundes et al.⁶, where it was reported that the prevalence of oesophageal varices among cirrhotic children was 52% and prevalence of varices was higher (68.6%) in patients with Child-Pugh score B or C when compared with Child A score (40%). These findings closely resemble to the present study, where 69.4% of patients with varices were in Child B and C group and 30.6% patients in the Child A group.

In the present study, splenomegaly independently identified the presence of oesophageal varices ($p = <0.001$) as well as the presence of large varices (Grade III & IV) ($p = 0.002$). Splenomegaly found as significant predictor for the presence of any grade of varices and also for the presence of large varices on multivariate analysis. Splenomegaly was also reported by various studies as an independent risk factor for esophageal varices.^{1,6,13,16-19} Among the laboratory parameters, thrombocytopenia (platelet count $<100000/\text{mm}^3$) independently identified the presence of oesophageal varices ($p = 0.02$). Platelet count $<100000/\text{mm}^3$ also identified the presence of large varices (Grade III & IV) ($p = 0.04$). But on multivariate analysis, thrombocytopenia (platelet count $<100000/\text{mm}^3$) was not found significant for the presence of any varices (OR; 8.45, 95% CI, 0.89-80.07) or for the presence of large varices (OR 1.8; 95% CI, 0.53-6.47).

In this study, no association was found between child A/ B/ C group with the different grading of oesophageal varices (Grade I, II, III, IV) ($p = 0.901$). As there were not sufficient children in Child B class, Child-Pugh class was further labelled into two groups: Child-Pugh class A vs. Child-Pugh class B and C. Variceal grading was also recategorized as small (Grade I and II) and large (Grade III and IV). But this version also showed no positive association between advanced child-pugh class (B and C) with the presence or absence of varices ($p = 0.915$) or presence of large varices ($p = 0.331$). These findings were consistent with few other studies.^{11,12,18,20,21} It was hypothesized Child-Pugh classification would be a good marker of the presence of varices as it takes into account the results of liver function tests (prothrombin time and albumin). Use of two subjective criteria (ascites and staging of hepatic encephalopathy) may be the cause of lack of correlation, which may under or overscore some patients.

Oesophageal varices have become a huge burden in a patient with CLD. The individuality and clarity of this study are based on the fact that examinations and scores can be easily done at the patient's bedside that can be compared. In the present study, only simple, easily performable and available markers were considered that may guide the physicians in remote areas where endoscopy facilities are not available, or patients are too poor to do it, in helping them to initiate appropriate primary pharmacological prophylaxis. Moreover in places where the endoscopy workload is high, a non-invasive marker, as in this study, can help one to initiate drug therapy while waiting for the endoscopy procedure.

Conclusion

Splenomegaly was found as an independent predictor for the presence of oesophageal varices and also for the presence of large varices. Splenomegaly showed nearly 15 times and 10

times more likely to have any varices and large varices respectively. But no association was found between severity of chronic liver disease according to Child-Pugh classifications and the grading of oesophageal varices.

Prior to the commencement of this study, ethical clearance was taken from the Institutional Review Board of the Bangabandhu Sheikh Mujib Medical University. Approval paper was given by 106th Institutional Review Board, Bangabandhu Sheikh Mujib Medical University, meeting which was held on 14th February 2016 (No. BSMMU/2016/2124).

Conflict of Interest: None

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