Can platelet count/spleen diameter ratio be used for cirrhotic children to predict esophageal varices?

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Abstract

AIM
To determine the laboratory and radiologic parameters, including the platelet count (PC)-to-spleen diameter (SD) ratio as a non-invasive marker that may predict the presence of esophageal varices (EV) in children with cirrhosis.

METHODS
Eighty-nine patients with cirrhosis, but without a history of variceal bleeding were prospectively included. The children were grouped into 6-12 and 12-18 years of age groups. These groups were also divided into 2 subgroups (presence and absence of EV). All of the patients underwent a complete biochemical and radiologic evaluation. The PC (n/mm³)-to-SD (mm) ratio was calculated for each patient.

RESULTS
Sixty-nine of 98 (70.4%) patients had EV. The presence of ascites in all age groups was significantly associated
with the presence of EV. There were no differences in serum albumin levels, PC, SD and the PC-to-SD ratio between the presence and absence of EV groups in both age groups ($P > 0.05$).

**CONCLUSION**

Laboratory and radiologic parameters, including the PC-to-SD ratio as a non-invasive marker (except for the presence of ascites), was inappropriate for detecting EV in children with cirrhosis.

Key words: Esophageal varices; Variceal bleeding; Platelet count-to-spleen diameter ratio; Children

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Core tip: Laboratory and radiologic parameters, including the platelet count (PC)-to-spleen diameter (SD) ratio were investigated in children with cirrhosis as a non-invasive marker that may predict the presence of esophageal varices (EV). This study is the first study to assess the PC-to-SD ratio in children with cirrhosis for detecting EV according to age groups. This study demonstrated that the parameters, other than the presence of ascites, were inappropriate for detecting EV in children with cirrhosis.

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**INTRODUCTION**

Esophageal variceal bleeding is among the most serious consequences of chronic liver disease. Approximately two-thirds of children with cirrhosis have esophageal varices (EV), and the mortality associated with a variceal bleeding episode is 20%-35%. Prevention of bleeding from a ruptured EV has become one of the main goals in the follow-up of these patients. Although a consensus has been reached for adults, there is no formal recommendation for endoscopic screening in children with cirrhosis.

Esophagogastroduodenoscopy (EGD) is the present reference standard diagnostic test for EV. Nevertheless, only 50%-70% of cirrhotic children have varices on the first EGD and < 30% have large varices and/or the red wale sign (high-risk EV for bleeding) in adults and children. Because of the relatively low prevalence of varices that require primary prophylaxis, the cost, inconvenience, and morbidity associated with endoscopic surveillance may not be justified for all patients with cirrhosis. To reduce the increasing burden on endoscopy units and prevent unnecessary harm to patients, researchers have attempted to identify parameters for non-invasive prediction of EV. Several reports have identified non-invasive variables that may predict the presence of EV in childhood and have shown predictive factors for bleeding risk, such as hypoalbuminemia, the Child-Pugh score, an increased spleen diameter (SD), a low platelet count (PC), the PC-to-SD ratio, the clinical prediction rule, and the aspartateaminotransferase-to-platelet ratio index.

For this purpose, the PC-to-SD ratio was investigated to predict the presence of EV in adult patients with cirrhosis. Chawla et al. concluded that the PC-to-SD ratio is elegant, simple and inexpensive, and it may become a helpful tool to limit the number of endoscopies for primary prophylaxis in adult patients with portal hypertension. Therefore, we conducted this study to investigate laboratory and radiologic parameters, including the PC-to-SD ratio, as predictors of EV in children with cirrhosis.

**MATERIALS AND METHODS**

All children (6-18 years of age) who had been diagnosed with cirrhosis in the outpatient clinics of the Paediatric Gastroenterology Hepatology and Nutrition at Baskent University, Ankara, Turkey, were included in this prospective study. The diagnosis of cirrhosis was made based on laboratory, radiologic, and physical examination findings or by liver histology in the absence of clear clinical signs of liver cirrhosis. Demographic characteristics (age, gender and underlying disease), blood chemistry evaluations, international normalized ratio, and Child-Pugh scores were recorded for each patient.

Patients with a clinical history of upper digestive hemorrhage, band ligation, sclerosing therapy, transjugular intrahepatic portosystemic shunt stent, surgery for portal hypertension, hepatic encephalopathy, and use of beta-blockers or other vasoactive drugs were excluded from the study.

The children were further grouped into 6-12 and 12-18 year age groups. These groups were divided into two sub-groups (EV-present and -absent) based on the EGD. The EGD was performed by the same paediatric endoscopists in our endoscopy unit using a video endoscope (Olympus GIF-XP 240; Tokyo, Japan or Fujinon EG 590W videoendoscopy; Tokyo, Japan). EV were classified according to the Baveno IV criteria and American Association for the Study of Liver Diseases practice guidelines as no, small, and large varices. EV were also classified according to the bleeding risk as high risk and non-high risk using varices diameters and red sign parameters.

The spleen bipolar diameter and presence of ascites were evaluated by ultrasonography (Siemens Sonoline Antares 4.1 MHz or 9.4 MHz probe; Siemens Medical Solutions United States, Inc., Issaquah, WA, United States) by the same radiologist.

The study design was approved by the Ethics Committee of our hospital (Study No. KA11/11252). Before enrollment, written informed consent was obtained from the primary caretaker of each patient.

We used SPSS software (version 16.0; SPSS, Inc.,...
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**Table 1** Laboratory and ultrasonographic data in the age group of 6-12 years

|                      | Patient with varices ($n = 29$) | Control ($n = 13$) | $P$ value |
|----------------------|---------------------------------|-------------------|-----------|
| Mean age (yr)        | 9.7 ± 2.0                       | 10.0 ± 1.9        | 0.595     |
| Gender (% female)    | 45                              | 38.5              | 0.384     |
| INR                  | 1.5 ± 0.5                       | 1.4 ± 0.5         | 0.860     |
| ALT (IU/L)           | 573 ± 50.8                      | 443 ± 29.3        | 0.210     |
| AST (IU/L)           | 791 ± 71.5                      | 53.1 ± 32.9       | 0.241     |
| Total bilirubin (mg/dL) | 3.5 ± 6.0                     | 2.5 ± 4.7         | 0.618     |
| Albumin (mg/dL)      | 3.9 ± 0.6                       | 4.2 ± 0.6         | 0.231     |
| Ultrasonographic ascites (%) | 27.5%                        | 0%                | 0.037     |
| Spleen diameter (mm) | 167.3 ± 39.1                    | 151.3 ± 32.4      | 0.206     |
| Platelet count (thousand/mm$^3$) | 129000 ± 53519              | 153000 ± 9798     | 0.312     |
| Platelet count/spleen diameter | 976.6 ± 793.5               | 1062.4 ± 718.0    | 0.741     |
| Child-Pugh score     | 6.3 ± 1.5                       | 5.7 ± 1.4         | 0.193     |

INR: International normalized ratio; ALT: Alanine transaminase; AST: Aspartate transaminase.

**Table 2** Laboratory and ultrasonographic data in the age group of 12-18 years

|                      | Patient with varices ($n = 40$) | Control ($n = 16$) | $P$ value |
|----------------------|---------------------------------|-------------------|-----------|
| Mean age (yr)        | 14.2 ± 1.7                      | 13.5 ± 1.2        | 0.161     |
| Gender (% female)    | 48                              | 56                | 0.591     |
| INR                  | 1.3 ± 0.3                       | 1.4 ± 0.6         | 0.347     |
| ALT (IU/L)           | 86.5 ± 76.1                     | 60.5 ± 67.2       | 0.250     |
| AST (IU/L)           | 115.2 ± 124.2                   | 105.5 ± 231.8     | 0.842     |
| Total bilirubin (mg/dL) | 5.0 ± 10.4                   | 5.3 ± 12.5        | 0.931     |
| Albumin (mg/dL)      | 3.8 ± 0.7                       | 3.9 ± 0.7         | 0.797     |
| Ultrasonographic ascites (%) | 35%                           | 6%                | 0.028     |
| Spleen diameter (mm) | 181.4 ± 37.2                    | 150.3 ± 34.2      | 0.389     |
| Platelet count (thousand/mm$^3$) | 103000 ± 55867              | 115000 ± 65472    | 0.499     |
| Platelet count/spleen diameter | 733.9 ± 737.4               | 830.78 ± 553.5    | 0.637     |
| Child-Pugh score     | 6.9 ± 1.9                       | 6.2 ± 1.8         | 0.214     |

INR: International normalized ratio; ALT: Alanine transaminase; AST: Aspartate transaminase.

...percentage of ascites was observed among the EV-present group than the EV-absent group (Tables 1 and 2). We did not find a statistically significant difference in the PC-to-SD ratio between patients with large and small varices (636.9 ± 256.5 and 894.1 ± 844.4, respectively; $P = 0.89$).

We did not find a significant difference for serum albumin, PC, SD and the PC-to-SD ratio between the EV-present and -absent varices sub-groups in both age groups ($P > 0.05$; Tables 1 and 2).

**DISCUSSION**

Despite advances in diagnosis and treatment, bleeding from EV is one of the major causes of morbidity and mortality among patients with cirrhosis. Hence, preventing the first episode of variceal bleeding may reduce mortality and morbidity.

In this prospective study involving children 6-18 years of age with cirrhosis, we found that only the presence of ascites is associated with the presence of EV. There have been several studies identifying non-invasive variables that may predict the presence of EV in children. The first study, in which the predictive risk factors were evaluated by Fagundes et al. in a pediatric group [median age at the time of first EGD was 6 years (age range, 0.7-17.6 years)], showed that children with cirrhosis and splenomegaly were nearly 15-fold more likely to have EV compared with children with cirrhosis but without splenomegaly. Fagundes et al. concluded that hypoalbuminemia, splenomegaly, and a PC < 130000/mm$^3$ were predictors for the presence of EV, spleen size was not measured by ultrasonography. The second study, conducted by Gana et al., derived a non-invasive clinical prediction rule capable of identifying children with EV. In this study, 17 of 51 children (< 18 years of age) with liver disease or portal vein thromboses were shown...
to have EV, and hypoalbuminemia was shown to be an independent variable for the presence of EV. In the same study[7], a higher percentage of ascites, increased spleen length, and lower PC (cut-off value = 115000/mm$^3$) were reported among children with EV. Further, the PC-to-spleen length-for-age Z score ratio was significantly lower among the EV-present group[7].

Fagundes et al[6] and Gana et al[7] reported lower albumin levels among children with EV. Our results were not in agreement with the findings of these two studies. A possible explanation may be the difference in etiologic factors in our patients.

A recent study involving 103 patients with a diagnosis of chronic liver disease or extrahepatic portal vein obstruction (mean age, 8.9 ± 4.7 years) showed a significantly higher spleen length and lower PC (cut-off value = 115000/mm$^3$) among children with EV than children without EV[10]. In the same study, it was reported that a PC-to-spleen size (cm) ratio < 1.0 discriminated between patients with and without EV, despite a lack of statistical significance based on logistic regression. The authors suggested the lack of statistical significance was explained by the age and gender differences in spleen size.

Based on the findings of these three studies[6,7,10], low PC and increased spleen length are logical parameters by which to determine EV in children with cirrhosis. In addition, Gana et al[7] and Adami et al[10] reported that PC (cut-off value = 115000/mm$^3$) was the best predictor of EV.

In the current study, we did not find a significant difference for PC, SD and the PC-to-SD ratio between the EV-present and -absent sub-groups in both age groups. A possible explanation is the heterogeneity of patients studied. Another explanation is the lack of children with portal vein thromboses in the current study. The three studies investigating risk factors for EV included children with cirrhosis and portal vein thromboses[6,7,10]. It is well-known that portal vein thrombosis is a risk factor for splenomegaly and thrombocytopenia. The PC loses discriminatory power because of multi-causality (such as autoimmune events, myelotoxic effects of viruses, or reduced synthesis of thrombopoietin) as a consequence of progressive liver dysfunction; however, in children with portal vein thromboses, thrombocytopenia is directly related to portal hypertension, as well as the development of varices[10].

One of the most important limitations of our study was the small number of patients; however, this study was the first study to assess the PC-to-SD ratio in children in two age groups with cirrhosis as a means to detect EV. We consider the PC, SD and PC-to-SD ratio to lack suitability as non-invasive markers for detecting EV in children with cirrhosis. Further studies on this subject with larger sample sizes are required to assess the importance of the PC, SD and PC-to-SD ratio in cirrhotic children with or without portal vein thrombosis.

**COMMENTS**

**Background**

Esophageal variceal (EV) bleeding is among the most serious consequences of chronic liver disease. Approximately two-thirds of children with cirrhosis have EV and the mortality associated with a variceal bleeding episode is 20%-35%. Identification of children with cirrhosis who are at high risk for EV using a non-invasive test is important to reduce the need for endoscopy. The authors’ goal was to investigate laboratory and radiologic parameters, including the platelet count (PC)-to-spleen diameter (SD) ratio to predict the presence of EV in children with cirrhosis.

**Research frontiers**

To reduce the increasing burden on endoscopy units and prevent unnecessary harm to patients with cirrhosis, researchers have attempted to identify parameters for the non-invasive prediction of EV.

**Innovations and breakthroughs**

A few studies have shown that a low PC and PC-to-SD ratio may predict the presence of EV in patients with cirrhosis. In their study, the authors did not find a significant difference in the PC, SD and PC-to-SD ratio between the EV-present and -absent sub-groups in both age groups of children.

**Applications**

The PC-to-SD ratio is not an appropriate index with which to predict EV in children with cirrhosis. This may indicate that endoscopy remains the ideal choice for detecting EV in children with cirrhosis.

**Terminology**

Esophageal varices are abnormal, enlarged veins which generally occur in patients with serious liver diseases. The vessels can leak blood, or even rupture, thus causing life-threatening bleeding.

**Peer-review**

It is helpful for clinical doctors to perform endoscopic examination promptly.

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