ORIGINAL ARTICLE

The Correlation Between Cytopenia and Esophageal Varices in Patients With Liver Cirrhosis

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Summary

This retrospective study analysed the case records of 200 patients in the Department of Gastroenterology, Singapore General Hospital from February 2000 to January 2001who had liver cirrhosis and underwent gastroscopy for the detection of varices. The aim of this study was to determine any relationship between leucopenia, thrombocytopenia and the occurrence of esophageal varices in a cirrhotic population. Our results showed that the diagnostic yield of varices grade 2 and 3 was 6.3% if platelet count was > 150,000/mm^3, 25% if platelet count was 100,000 to 150,000/mm^3, 38.9% if platelet count was 50,000-99,000/mm^3 and 100% if platelet count was <50,000/mm^3. Similarly, the diagnostic yield of varices grade 2 and 3 was 19.4% if total white count was > 4,000/mm^3, 66.7% if total white count was 3,000- 4,000/mm^3 and 94.8% if total white count was < 3,000/mm^3. We conclude that thrombocytopenia and leucopenia can be used to stratify risk for occurrence of esophageal varices in cirrhotic patients and gastroscopy will have a high yield for varices when platelet count is < 150,000/mm^3 or total white is < 4,000/mm^3.

Key Words: Thrombocytopenia, Leucopenia, Esophageal varices

Introduction

Bleeding esophageal varices is a major complication of cirrhosis. The mortality of an episode of variceal bleeding varies from 30% - 50% depending on the Child Pugh grade and co-morbidities[1-2]. It is recognised that thrombocytopenia and leucopenia are secondary to hypersplenism and may predict the occurrence of esophageal varices. Prophylactic treatment to prevent variceal bleed can then be considered. A few studies have demonstrated correlation of thrombocytopenia and leucopenia with the occurrence of esophageal varices in Western countries. This observation requires verification in our local population where the etiology of cirrhosis is mainly due to viral hepatitis B. The aim of this study was to evaluate the correlation between platetelet and white cell counts and the occurrence of esophageal varices in a Singapore population with cirrhosis where the etiology of cirrhosis is mainly due to viral hepatitis B.

Materials and Methods

This was a retrospective review of case records of 200 consecutive patients with cirrhosis diagnosed in the Department of Gastroenterology, Singapore General Hospital from February 2000 to January 2001. The diagnosis of cirrhosis was based on biopsy in 22.5% or imaging (CT scan or Ultrasound) in 77.5%. Patients with sepsis were excluded and cell counts were taken before transfusion if this was required.

Patients with varices treated previously either with banding or beta blocker were not included in this study.

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379 patients with liver cirrhosis were diagnosed and 179 patients were excluded because either no gastrocopy was done or the patient presented with sepsis or the patients had varices treated previously.

Esophageal varices were graded as absent, grade 1, 2 and 3 according to De Franchis et al : Grade 1 esophageal varices occupied less than a third of the lumen and flatten with air insufflation. ; Grade 2 esophageal varices occupied less than a third and did not flatten with air insufflation. ; Grade 3 esophageal varices occupied at least a third of the lumen and did not flatten with air insufflation. Child's Pugh score was calculated according to the presence of ascites, encephalopathy, bilirubin level, albumin level and prothrombin time.

Data collection

A list of patients with cirrhosis based on histology or imaging who underwent gastroscopy was obtained from the medical records. The medical records of eligible patients were reviewed for baseline characteristics, clinical, laboratory and endoscopic data. Variables included age, sex, haemoglobin, white cell and platelet count, alanine and aspartate aminotransferase, serum bilirubin, albumin, and prothrombin time, etiology of liver cirrhosis and Child Pugh class.

The etiology of cirrhosis was established by Hepatitis B Surface antigen or Hepatitis B Core IgG, Anti HCV IgG (ELISA), ANA, Smooth Muscle antibody and caeruloplasmin assay.

Data Analysis:

Descriptive statistics of mean, standard deviation, percentage were obtained from the data. Association between predictive variables (platelet count, total white cell count) and esophageal varices were measured using Spearman's Rho correlation coefficient. Statistical analysis was by SPSS statistical package version 10.1.

Results

A total of 200 patients were included in this study. Baseline characteristics are shown in Table I. Hepatitis B (72 patients) and alcohol (52 patients) were the two commonest causes of cirrhosis in this study. The majority of cirrhotic patients, 112 over 200 patients (56.5%) had platelet count of 50,000/mm^3 to 99,000/mm^3, 48 over 200 patients (24%) had platelet count > 150,000/mm^3. 20 over 200 patients (10%) had platelet count of 100,000 to 150,000/mm^3 and only 19 over 200 patients (9.5%) had platelet count of < 50,000/mm^3.

The distribution of patients according to white cell count was 80% with white cell count of > 4,000/mm^3 and 20% with white cell count of < 4,000/mm^3 . The distribution of patients with no varices, grade 1, grade 2, grade 3 were 30%, 33.5%, 31% and 5.5% respectively.

There was a statistically significant correlation between platelet count and variceal grade (Figure 1). A similar correlation was found between white cell count and varices (Figure 2).

Box plot of platelet count against grade of varices showed an inverse correlation of varices size and platelet count as shown in Figure 3 (Spearman Rho test – 0.583 p<0.001). Box plot of white cell count against grade of esophageal varices showed a similar inverse correlation of variceal size and total white cell count (Spearman Rho test – 0.436 p<0.001) (Figure 4).

The diagnostic yield of esophageal varices grade 2 and above for a given platelet count were :
> 150,000/mm^3 was 6.8%
100,000/mm^3 to 150,000/mm^3 was 25%
50,000/mm^3 to 99,000/mm^3 was 38.9%
< 50,000/mm^3 was 100%

The diagnostic yield of esophageal varices grade 2 or higher for a given white cell count were:
> 4,000/mm^3 was 19.4%
3,000/mm^3 to 4,000/mm^3 was 66.7%
< 3,000/mm^3 was 94.8%

Table I: Baseline Characteristics

Total number		200	
Sex:	Male	113	(56.5%)
	Female	87	(43.5%)
Child Pugh status			
	A	42	(21%)
	B	81	(40.5%)
	C	77	(38.5%)
		53	± 12 years
Age:			
Aetiology:			
	Hepatitis B	72	(36%)
	Alcohol	52	(26%)
	Cryptogenic	33	(16.5%)
	Others	43	(21.5%)

Fig. 1: Platelet Count and Grade of Varices

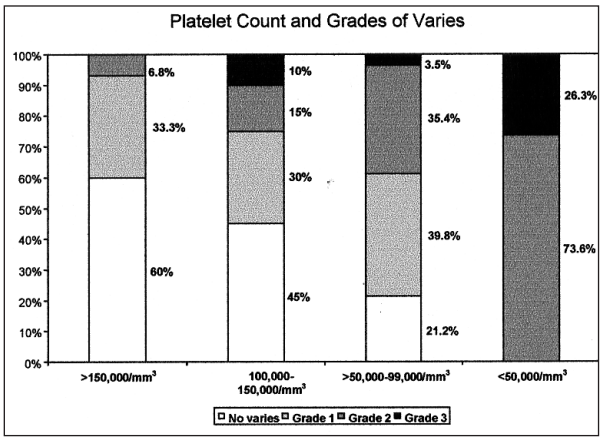


Fig. 2: White Cell Count and Grade of Varices

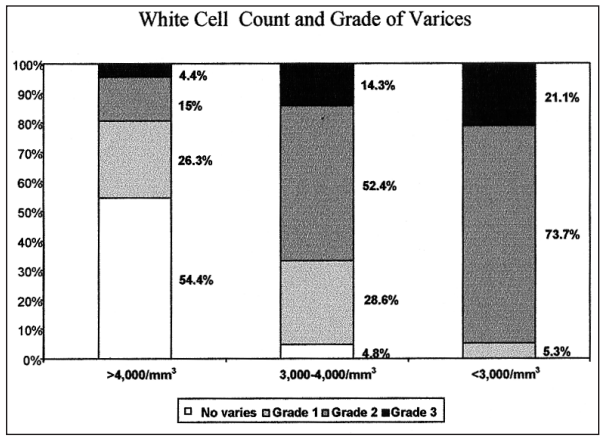


Fig. 3: Box Plot of Platelet Count Against Grade of Varices

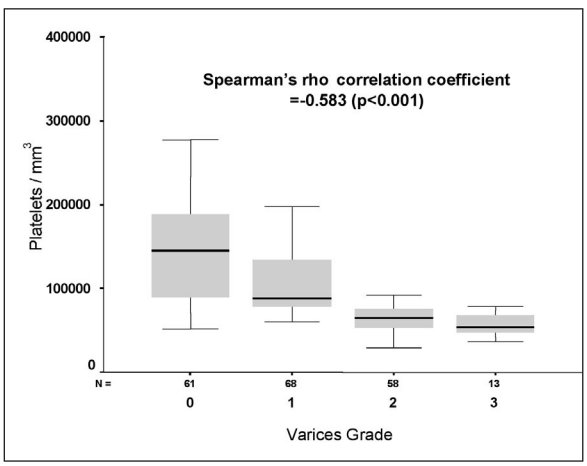
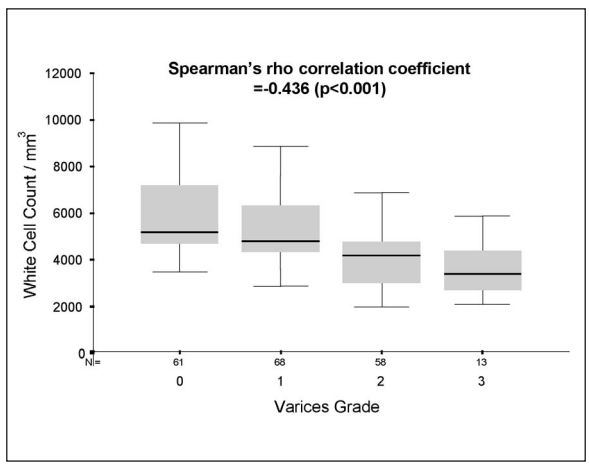


Fig. 4: Box Plot of White Cell Count Against Grade of Varices



Simple parameters like platelet count and white cell count can be used to stratify the risk for esophageal varices in cirrhotic patients. Gastroscopy has a high yield for varices when platelet count is less than 150,000/mm^3 or total white cell count < 4,000/mm^3. In this study 100% had grade 2 or higher varices when platelet was <50,000/mm^3.

Discussion

Variceal bleeding in cirrhotic patients is associated with high morbidity, mortality and health care costs[3]. Primary prophylaxis can reduce the risk of bleeding and it is recommended that all cirrhotic patients should have endoscopy to detect varices. If significant esophageal varices are found (grade 2 and above) a beta blocker or endoscopic variceal ligation are effective prophylactic measures[4-11]. The prevalence of esophageal varices in cirrhosis is estimated at 9-36%[12-13] and a non-invasive method to select patients at risk of esophageal varices is desireable compared to screening all patients with endoscopy.

The relationship between Child-Pugh score and esophageal varices is not consistent. Some studies fail to show a relationship between esophageal varices and Child-Pugh score[13]. Parameters like platelet count and white cell count can predict the presence of significant esophageal varices and therefore increase the yield of

endoscopy [14-16]. Our results show a significant correlation between low platelet count and white cell count with the occurrence of significant esophageal varices grade 2 or above. The cause of thrombocytopenia and leucopenia have been attributed to splenic sequestration or antibody mediated destruction of platelet[17]. Recent studies have shown a reduce d hepatic production of the liver derived thrombocytopoietic growth factor as a major factor for thrombocytopenia in liver cirrhosis[18-19]. Therefore reduced platelet count in cirrhosis may be due to both hypersplenism secondary to portal hypertension and impaired hepatic derived platelet growth factor.

There are several biases in the retrospective design of this study. Firstly, the grading of varices may be subject to inter-observer variability. We reviewed all endoscopic reports and pictures to minimise the bias. When the grade of varices was reported as a range of variceal grade, the upper grade was taken. Cryptogenic cirrhosis contributed a significant proportion of patients. The evaluation of etiology may be incomplete and cryptic hepatitis B (anti HBc IgG positive) was not tested in every case. (Nine out of thirty-three cryptogenic cirrhotic patients did not have anti HBc lg G done) There are limited studies on the relationship between cytopenia and varices occurrence. These studies were mainly done in Western countries. A few studies have identified predictive factors for esophageal varices in cirrhotic patients. Schepis et al [14] reported screening by gastroscopy when platelet count <100, 000/mm^3 resulted in a significant yield of esophageal varices. Zaman A , et al [15] evaluated 89 patients without a history of varices bleeding who underwent gastroscopy as part of a liver transplant evaluation and found a platelet count of < 88,000/mm^3 associated with the presence of large varices. Similarly Chalasani N et al [16] retrospectively evaluated 346 liver transplant candidates and factors predicting the presence of large varices. He reported 28% cirrhotic patients with a platelet count of <88,000/mm^3 had large esophageal varices.

In conclusion, this retrospective study corroborates previous studies that platelet count and / or white cell count can be used to predict the presence of significant esophageal varices in cirrhotic patients. By stratifying the risk for significant varices, it may be possible to reduce the number of gastroscopies needed to identify patients for prophylactic treatment with beta blocker.

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