INTRODUCTION

Esophageal and para-esophageal varices are abnormally dilated collateral veins within the wall of the esophagus that project directly into the lumen and are prone to haemorrhage. These are a result of portal hypertension secondary to cirrhosis.1,2 Bleeding from gastro-esophageal varices is the most serious and life threatening complication of cirrhosis.3 Major causes of cirrhosis were hepatitis C (n=79, 77.5%), hepatitis B (n=12, 11.8%), mixed hepatitis B and C infection (n=8, 7.8%) and Wilson's disease (n=3, 2.9%). Seven patients had esophageal grade I, 24 had grade II, 35 had grade III, and 36 had grade IV.

RESULTS

One hundred and two patients with thrombocytopenia and esophageal varices were included in the study. There were 62 (60.8%) males and 40 (39.2%) females. The mean age of onset of the disease in these patients was 49.49±14.3 years with range of 11-85 years. Major causes of cirrhosis were hepatitis C (n=79, 77.5%), hepatitis B (n=12, 11.8%), mixed hepatitis B and C infection (n=8, 7.8%) and Wilson's disease (n=3, 2.9%). Seven patients had esophageal grade I, 24 had grade II, 35 had grade III, and 36 had grade IV. Porta hypertensive gastropathy were detected in 87 patients. There was an inverse correlation of platelet count with grading of esophageal varices (r=-0.321, p < 0.001).

CONCLUSION

The severity of thrombocytopenia increased as the grading of esophageal varices increased. Thrombocyte count was significantly and inversely correlated with the grade of esophageal varices.

Key words: Thrombocytopenia. Grading. Esophageal varices. Correlation. Chronic liver disease. Hepatitis C.

OriGinal Article

Correlation of Thrombocytopenia with Grading of Esophageal Varices in Chronic Liver Disease Patients

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ABSTRACT

Objective: To determine the severity of thrombocytopenia in different grades of esophageal varices. Study Design: Cross-sectional analytical study. Place and Duration of Study: Jinnah Postgraduate Medical Centre, Karachi, Medical Unit-III, Ward-7 from January to December 2008. Methodology: Subjects were eligible if they had a diagnosis of cirrhosis. Patient with advanced cirrhosis (Child-Pugh class C), human immunodeficiency virus (HIV) infection, hepatocellular carcinoma, portal vein thrombosis, parenteral drug addiction, current alcohol abuse and previous or current treatment with β-blockers, diuretics and other vasoactive drugs were excluded from the study. On the basis of platelet count patients were divided into four groups; Group I with platelets ≤ 20000/mm³, Group II with values of 21000-50000/mm³, Group III with count of 51000-99000/mm³ and Group IV with count of 100000-150000/mm³. Correlation of severity of thrombocytopenia with the grading of esophageal varices was assessed using Spearman's correlation with r-values of 0.01 considered significant.

RESULTS: One hundred and two patients with thrombocytopenia and esophageal varices were included in the study. There were 62 (60.8%) males and 40 (39.2%) females. The mean age of onset of the disease in these patients was 49.49±14.3 years with range of 11-85 years. Major causes of cirrhosis were hepatitis C (n=79, 77.5%), hepatitis B (n=12, 11.8%), mixed hepatitis B and C infection (n=8, 7.8%) and Wilson's disease (n=3, 2.9%). Seven patients had esophageal grade I, 24 had grade II, 35 had grade III, and 36 had grade IV. Gastric varices were detected in 2 patients. Portal hypertensive gastropathy were detected in 87 patients. There was an inverse correlation of platelet count with grading of esophageal varices (r=-0.321, p < 0.001).

CONCLUSION: The severity of thrombocytopenia increased as the grading of esophageal varices increased. Thrombocyte count was significantly and inversely correlated with the grade of esophageal varices.

Key words: Thrombocytopenia. Grading. Esophageal varices. Correlation. Chronic liver disease. Hepatitis C.

INTRODUCTION

Esophageal and para-esophageal varices are abnormally dilated collateral veins within the wall of the esophagus that project directly into the lumen and are prone to haemorrhage. These are a result of portal hypertension secondary to cirrhosis.1,2 Bleeding from gastro-esophageal varices is the most serious and life threatening complication of cirrhosis, accounts for 10% of all cases of bleeding from the upper gastrointestinal tract. Approximately two-third of patients with decompensated cirrhosis and one third of those with compensated cirrhosis have varices at the time of diagnosis.3 About 30% of these patients will experience an episode of variceal haemorrhage within one year of the diagnosis of varices.4-5 Patients with advanced cirrhosis have a complex haemostatic disturbance, and thrombo cytopenia (platelet count < 150,000/µl) is a common complication in patients of chronic liver disease (CLD).6-8 Thrombocytopenia is reported in as many as 76% of cirrhotic patients.9 In CLD patients, the pathogenesis of thrombocytopenia is multifactorial. Possible causes include splenic sequestration of platelets, suppression of platelet production in bone marrow, and decreased activity of the hematopoietic growth factor thrombo-poietin.10

The objective of the study was to determine the correlation of the thrombocytopenia with esophageal variceal grading, that may predict the large esophageal varices and help select patients for upper gastrointestinal endoscopy.

METHODOLOGY

This cross-sectional analytical study was conducted at Hepatology Unit of Ward-7, Jinnah Postgraduate Medical Centre, Karachi, from January to December 2008. Subjects were eligible if they had a diagnosis of cirrhosis based on history, physical examination, biochemical parameters and liver biopsy in some cases. All patients of cirrhosis with esophageal varices and concomitant thrombocytopenia were included in the study. Patient with advanced cirrhosis (Child-Pugh class C), antibodies
against human immunodeficiency virus (HIV), hepatocellular carcinoma and portal vein thrombosis evident on ultrasonography, parenteral drug addiction, current alcohol abuse, previous or current treatment with β-blockers, diuretics and other vasoactive drugs were excluded from the study. Demographic data such as age, gender and residence were recorded. At entry, a full medical history was taken. All patients underwent a complete physical examination.

Haematological and biochemical workup included complete blood picture, liver function tests, prothrombin time, albumin and total protein estimation. All patients were asked about alcohol intake and tested for hepatitis BsAg, anti-HCV antibody using ELISA method to determine the cause of liver cirrhosis. Tests for other causes of cirrhosis (serum ceruloplasmin and slit lamp examination for Wilson’s disease, tests for autoantibodies for autoimmune liver disease, iron studies for hemochromatosis) were carried out only if there was a suggestive clue.

A verbal and written consent for extended examination was taken from patients and/or their attendants after explaining the intention of procedure. All patients underwent upper gastrointestinal endoscopy after consent. All patients were kept fasting overnight prior to the procedure at our institution. All the endoscopies were performed by the first author. Endoscopic variceal band ligation was our first line management for patients with active variceal bleeding. They were evaluated for the presence and grade of esophageal varices (EV), the presence of gastric varices and portal hypertensive gastropathy. In the presence of esophageal varices size of thrombocytopenia with the grading of esophageal varices was assessed. Upper gastrointestinal endoscopy was done on Olympus EVIS 180 Series endoscopes.

Correlation of thrombocytopenia with grading of esophageal varices was analyzed by applying Spearman’s rank correlation test. A p-value of < 0.01 was considered as significant correlation. Descriptive statistics were obtained for the variables where applicable, using SPSS version 15.

### RESULTS

A total of 130 patients were reviewed, out of whom 102 patients with thrombocytopenia and esophageal varices were included in the study. There were 62 (60.8%) males and 40 (39.2%) females. The mean age of onset of the disease in those patients was 49.49±14.3 years with range of 11-85 years. Anti-HCV antibody was positive in 79 (77.5%), hepatitis BsAg in 12 (11.8%), mixed hepatitis B and C infection in 8 (7.8%) and Wilson’s disease in 3 (2.9%) patients. The presenting symptoms were haematemesis in 47 (45.07%), ascites in 17 (16.6%), malena in 6 (5.88%), and hepatic encephalopathy in 21 (20.6%). Seven patients had esophageal variceal grade I, 24 had grade II, 35 had grades III and 36 had grade IV. Gastric varices were detected in 2 patients. Portal hypertensive gastropathy were detected in 87 patients. Thrombocytopenia was found to have correlation with grading of esophageal varices presented in Table I. Spearman’s rank correlation test revealed an inverse relation between platelet count and grading of esophageal varices (r=-0.321). It was a significant correlation with p-value of < 0.001, suggested that, as platelet count decreased the grading of esophageal varices increased as shown in Table II.

#### Table I: Correlation of thrombocytopenia with grading of EV (n=102).

<table>
<thead>
<tr>
<th>Platelet count</th>
<th>Grade I</th>
<th>Grade II</th>
<th>Grade III</th>
<th>Grade IV</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>≤ 20000</td>
<td>00</td>
<td>00</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>21000-50000</td>
<td>00</td>
<td>04</td>
<td>11</td>
<td>15</td>
<td>30</td>
</tr>
<tr>
<td>50000-99000</td>
<td>05</td>
<td>15</td>
<td>19</td>
<td>17</td>
<td>56</td>
</tr>
<tr>
<td>100,000-150,000</td>
<td>02</td>
<td>05</td>
<td>04</td>
<td>02</td>
<td>13</td>
</tr>
</tbody>
</table>

#### Table II: Correlation of esophageal varices and other variables in patients of liver cirrhosis.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Mean±SD</th>
<th>r</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Platelets</td>
<td>66715.69±30481.41</td>
<td>-0.321*</td>
<td>0.001</td>
</tr>
<tr>
<td>Haemoglobin</td>
<td>8.955±2.374</td>
<td>-0.195</td>
<td>0.051</td>
</tr>
<tr>
<td>Bilirubin</td>
<td>3.319±5.463</td>
<td>-0.086</td>
<td>0.456</td>
</tr>
<tr>
<td>Albumin</td>
<td>2.747±0.064</td>
<td>-0.036</td>
<td>0.791</td>
</tr>
</tbody>
</table>

*Correlation is significant at the 0.01 level (2-tailed).

#### DISCUSSION

The main aim of the present study was to evaluate the correlation of thrombocytopenia with the grade of the esophageal varices. Variceal gastrointestinal bleeding is a life threatening complication of portal hypertension in patients with chronic liver disease, leading to significant morbidity and mortality as well as higher hospital care costs. Variceal haemorrhage occurs in 25-35% of patients with cirrhosis and accounts for 80-90% of bleeding episodes in these patients. The study showed that male gender had a greater frequency of chronic liver disease and its complications. The mean age of developing CLD in developing countries including Pakistan is much lower as compared to developed countries. In this study, hepatitis caused by C and B viruses was the leading cause of cirrhosis, but none of the patients had alcoholic liver disease as an underlying pathology. In Pakistan, it is estimated that at
Correlation of thrombocytopenia with grading of esophageal varices in chronic liver disease patients

least 9 million people harbor Hepatitis B virus, and over 14 million are chronically infected with Hepatitis C.14-17 Esophageal varices being an inclusion criterion were present in all patients in this study, but only 46.07% of the patients presented with haematemesis. Guidelines of the American Association for the Study of Liver Diseases (AASLD) suggest that patients with Child’s stage A liver cirrhosis and signs of portal hypertension, specifically a platelet count of less than 140,000/mm³ and/or enlarged portal vein diameter of greater than 13 mm or those classified as Child’s B or C at diagnosis should have screening endoscopy.18 AASLD guidelines recommend endoscopic screening of patients with cirrhosis for varices and treatment of patients with medium/large varices to prevent bleeding. Recommended endoscopic screening intervals are 1-3 years, depending on presence/absence of varices and whether patient has compensated/decompensated liver disease.19-20 However, this recommendation imposes a major burden on endoscopy units and incurred high costs on patients. Thrombocytopenia was previously suggested as an important and reliable predictor of varices in CLD patients studied in different studies.21-25 In this study, the severity of thrombocytopenia was evaluated as the non-endoscopic factor to predict the size and grade of esophageal varices. This study found significant correlation between severity of thrombocytopenia and EV in CLD patients. Severity of thrombocytopenia was found to be inversely related to the grading of EV. This study model helps the general practitioners and physicians working in the villages and peripheries of the country where the facilities of ultrasonography and endoscopy are not available to practice a prophylactic approach for esophageal varices without waiting for the above mentioned investigations. It also makes it easier to filter appropriate patients to refer to the tertiary care centres for endoscopy. Selecting patients for an upper GI endoscopy becomes cost effective and on the other hand, defines patients who need a critical management. The treatment can be planned on the basis of severity of thrombocytopenia and therefore, patient can be referred early, to tertiary care unit band ligation and primary prophylaxis of haematemesis.

**CONCLUSION**

The severity of thrombocytopenia increased with the increasing grade of esophageal varices. The platelet count was significantly and inversely correlated with grading of esophageal varices so that, as the grading of esophageal varices increased the count of platelets decreased.

**REFERENCES**


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