

## Original Article

### Thrombocytopenia in chronic liver disease due to hepatitis c virus

Noor-ul Iman,<sup>1</sup> Humera Khan<sup>2</sup>

From <sup>1</sup>Al-Ibrahimi Hospital and <sup>2</sup>Rehman Medical Institute, Peshawar, Pakistan.

Tel: 0333 9131322 E-Mail: druliman@yahoo.com

Correspondence: Dr Noor-ul Iman, Assoc. Prof. Khyber Medical University. 207/E-I, Street 9, Phase I, Hayatabad, Peshawar.

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#### ABSTRACT

**Objectives:** To evaluate the frequency of thrombocytopenia in chronic liver disease due to hepatitis C virus (HCV) infection.

**Patients and methods:** In this prospective study, patients with chronic liver disease (CLD) due to HCV were assessed using Child-Pugh class. All had full blood count, peripheral smear, Anti-HCV antibodies, abdominal ultrasound and esophago-gastro-duodenoscopy.

**Results:** Total number of patients were 155 [69 male (44.5%), 86 female (55.5%)]. Mean age was 43.58 years. Fifty patients (32.3%) had thrombocytopenia (platelet count  $<150,000/\text{mm}^3$ ). After excluding patients with esophageal varices (45 patients, 29.03% of the total), the frequency of thrombocytopenia was 4.76%. Gender had no effect, however, thrombocytopenia was more common (26.5%) in older age group ( $>40$  years) as compared to age  $<40$  years (5.8%).

**Conclusion:** Thrombocytopenia is a common and important finding in CLD due to HCV. Patients presenting with lone thrombocytopenia should be screened for HCV, especially in endemic areas or where blood and blood products are not properly screened (Rawal Med J 2009;34:72-74).

**Keywords:** Thrombocytopenia, chronic liver disease, HCV.

## **INTRODUCTION**

Hepatitis C virus (HCV) infection has become a global health and socio-economic problem<sup>1</sup> as 60%-85% of infected persons develop chronic liver disease (CLD).<sup>2</sup> Thrombocytopenia in HCV infection<sup>3</sup> has been known since 1993.<sup>4</sup> The association led to suggestion that patients with autoimmune thrombocytopenia should be screened for HCV infection.<sup>5</sup> Thrombocytopenia in CLD due to HCV is significant as it can predict prognostically important features of CLD. The aim of the study was to evaluate the frequency of thrombocytopenia in CLD due to HCV infection.

## **PATIENTS AND METHODS**

This prospective, cross-sectional study was carried out at Al-Ibrahimi Hospital, Khyber Teaching Hospital and Rehman Medical Institute, Peshawar, from October 2006 to December 2007. Patients with CLD due to HCV (Anti-HCV antibodies positive by ELISA) were assessed using Child-Pugh Class. All had abdominal ultrasound, full blood count by autoanalyzer (Cell Dyn 1700, Abbott, Beckman Coulter, USA), peripheral smear by a hematologist and upper gastrointestinal endoscopy. Thrombocytopenia was defined as a platelet count  $<150000/\text{mm}^3$ .<sup>3</sup> Patients with history of alcohol intake, upper gastrointestinal bleeding/sclerotherapy/band ligation, those receiving prophylactic

treatment for portal hypertension, diuretics, interferon (current or preceding six months), those with portal vein thrombosis/hepatoma on abdominal ultrasound, coinfection with hepatitis B and C, and acute febrile illness were excluded. Patient with age <40 years constituted Group A and those with age >40 were labeled as Group B. Data was analyzed using SPSS v 14.

## RESULTS

Out of 155 patients, 69 (44.5%), were male and 86 (55.5%) were female. Mean age was 43.58 years (range 15-80). More patients belonged to Child-Pugh Class A (Table 1). Mean Platelet count was 215154/mm<sup>3</sup> (range 30000/mm<sup>3</sup> - 484000/mm<sup>3</sup>).

**Table 1. Child Pugh Class.**

Child Pugh Class	No; of patients	%
A	103	66.5
B	44	28.4
C	8	5.2
Total	155	100.0

Fifty patients (32.3%) had thrombocytopenia. Forty-five (29.03%) had esophageal varices and thrombocytopenia. Thrombocytopenia was present in five patients (4.76%) when patients with esophageal varices were excluded. There was no difference in thrombocytopenia in men and women [25 male (16.1%) and 25 female (16.1%)].

**Table 2. Platelet Count and age.**

Platelet Count	Group A	Group B
	<=40 years (% of total)	>40 years (% of total)
<150000/mm <sup>3</sup>	9 (5.8%)	41 (26.4%)
>=150000/mm <sup>3</sup>	61 (39.4%)	44 (28.4%)
Total	70 (45.2%)	85 (54.8%)

Group A had 70 patients (45.2%) with nine patients (5.8%) having thrombocytopenia. Group B had 85 patients (85.8%) with 41 patients (26.4%) having thrombocytopenia (Table 2).

## **DISCUSSION**

The major mechanism of thrombocytopenia in CLD is pooling and destruction<sup>6</sup> of platelets in the spleen which may be immune-mediated.<sup>7</sup> The observation that thrombocytopenia is more severe in cirrhotic patients than non-cirrhotics<sup>8</sup> indicates additional factors to its pathogenesis. Liver produces thrombopoietin (TPO) required for thrombopoiesis<sup>9</sup> and its levels are observed to rise in thrombocytopenic conditions<sup>10</sup>. TPO levels are significantly lower<sup>10</sup> in cirrhotic patients as compared to chronic hepatitis patients<sup>11</sup> indicating impaired production<sup>12</sup> or rapid degradation of thrombopoietin.<sup>13</sup> Rios et al showed that TPO levels were related to the splenic size with its levels rising after partial splenic embolization.<sup>14</sup> The incremental effect of Eltrombopag (thrombopoietin-receptor agonist) on platelet count in patients with thrombocytopenia due to HCV-related cirrhosis reaffirms the role of TPO.<sup>15</sup> A direct viral effect has also been proposed as mechanism for HCV-related thrombocytopenia.<sup>16</sup>

We found frequency of thrombocytopenia to be 32.2% in patients with CLD due to HCV. A study from Taiwan showed 10.2% had platelet count of  $<100,000/\text{mm}^3$  in patients with positive anti HCV antibody.<sup>17</sup> The low frequency of thrombocytopenia in their study could be due to their definition of thrombocytopenia used. The frequency of thrombocytopenia of 4.76% in our study, after exclusion of patients with esophageal

varices, suggests that fibrosis and portal hypertension have a major contribution but a direct viral effect and TPO production are also important. The high frequency of thrombocytopenia (26.4%) in patients >40 years age as compared to younger age group (5.8%) indicates that likelihood of liver injury, subsequent inflammation and consequent fibrosis increases as patients grow older.

Thrombocytopenia is common in malaria, viral/bacterial infections, and megaloblastic anemia<sup>18</sup> and is even suggested as a predictor of falciparum malaria in febrile patients.<sup>19</sup>

Hence, by exclusion of patients with acute febrile illness and reporting of peripheral smear by a hematologist, false thrombocytopenia were excluded.<sup>20</sup> Prospective nature of the study, exclusion of patients with acute febrile illness and eliminating the chances of false thrombocytopenia were probably the main reasons for better results in our study.

Thrombocytopenia in CLD due to HCV is important, not merely as an association but because it has been proposed as a significant predictive indicator of esophageal varices in these patients.<sup>21-23</sup> In conclusion, thrombocytopenia is a common and important hematological finding in CLD due to HCV. We recommend that patients presenting with lone thrombocytopenia should be screened for HCV, especially in endemic areas or where blood and blood products are not properly screened.

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