FREQUENCY OF THROMBOCYTOPENIA IN CHRONIC ACTIVE HEPATITIS C PATIENTS – A HINDRANCE IN TREATMENT

AZIZ M. AND KHAN S.
Department of Haematology, Shaikh Zayed Hospital, Lahore – Pakistan

ABSTRACT
Background: Hepatitis C virus (HCV) is considered to be the main etiological factor for chronic liver disease. Thrombocytopenia is a common complication in patients with chronic liver disease which has been observed in 76% of cases. This occurs due to splenic platelet sequestration, bone marrow suppression by chronic hepatitis C and antiviral therapy.
Objective: The present study was designed to determine the frequency of Thrombocytopenia in Chronic Active Hepatitis (CAH) caused by Hepatitis C virus (HCV).
Study design: It was a Cross Sectional study.
Place and duration of study: This study was conducted in Department of Hematology, Shaikh Zayed Hospital Lahore from June to December 2010.
Results: In the present study the frequency of thrombocytopenia was 22.6%.
Conclusion: Patients who develop hematological abnormalities during treatment need hematological growth factor support so that treatment should be continued with no hindrance.
Key Words: Hepatitis C, Thrombocytopenia.

INTRODUCTION
Hepatitis C virus (HCV) is considered to be the main etiological factor for chronic liver disease and accounts for about 70 – 75% cases of chronic hepatitis and 15 – 20% cases of cirrhosis and hepatocellular carcinoma. Viral hepatitis is highly endemic in Pakistan. Pakistan carries one of the world’s highest burdens of chronic hepatitis and mortality due to liver failure and hepatocellular carcinomas. Although, prevalence of and risk factors for hepatitis B and hepatitis C are not exactly available, a weighted average of hepatitis C prevalence was 3.0% (range 0.3 – 31.9%). Rates in the high-risk subgroups were far higher. The seroprevalence of hepatitis C ranges from 0.27% –6.8% among healthy blood donors in different parts of the country.
CAH is associated with hematological side effects. These side effects are due to the disease itself, therapy related and also occur as a result of its complications.
Thrombocytopenia, (platelet count less than 150×10^9/l) is a common complication in patients with chronic liver disease, that has been observed in 76% of the patients. The severity of thrombocytopenia can be variable either from being transient and isolated, to a severe, life threatening condition.
The cause is multifactorial due to increased sequestration in the spleen, bone marrow suppression by HCV infection and by interferon treatment, and reduced production of thrombopoietin (a cytokine that regulates megakaryocyte maturation and platelet production). Prolonged bleeding time, and impaired aggregation, reduced adhesiveness and abnormal ultra structure of platelets reflect abnormal platelet function; these abnormalities have been attributed to an intrinsic platelet defect.
Liver is the main site for the production of thrombopoietin (TPO). Thrombopoietin is a glycoprotein, and a major regulator of megakaryopoiesis and platelet production in the body. Thrombopoietin levels and platelet counts are highly correlated with liver function impairment and severity of hepatic fibrosis in chronic HCV infection. Serum cryoglobulin and cardiolipin antibodies are also frequently seen in HCV related thrombocytopenia.
In addition, other mechanisms are also involved in the development of thrombocytopenia such as autoimmune and direct viral effects on megakaryocytes, HCV binding to platelet membrane with consequent binding of anti HCV antibody and phagocytosis of platelets and derangement of host immune system triggering the production of auto antibodies against platelet glycoprotein are the two most frequently postulated immune mechanisms explaining increase peripheral platelet destruction in HCV infected cases.
Hepatitis C in the absence of overt hepatic disease

Corresponding Author: Sofia Khan, Department of Haematology, Shaikh Zayed Hospital, Lahore – Pakistan. E-mail: drsofia.khan@hotmail.com

is also a well-established cause of chronic ITP (CITP). Different studies have reported positive HCV serology in almost 20% of patients with the clinical diagnosis of CITP. The treatment of HCV related thrombocytopenia is different from CITP.

Interferon therapy is also known to cause a 10 – 50% fall in platelet counts. It is more severe with PEG interferon and RBV therapy and worst with PEG interferon monotherapy. In patients treated with PEG alpha 2a and RBV, dose reduction is necessary in 3 to 4% of those treated with PEG and RBV versus 1% in those treated with standard IFN and RBV. Severe thrombocytopenia is usually seen only in those with established cirrhosis or in rare patients in whom IFN induces autoimmune thrombocytopenia.

Thrombocytopenia can impact routine care of patients with CAH, potentially postponing or interfering with diagnostic and therapeutic procedures including liver biopsy, anti-viral therapy, and medically indicated or elective surgeries.

The objective of this study is to determine the frequency of thrombocytopenia in patients with chronic active hepatitis (CAH) caused by Hepatitis C virus (HCV).

MATERIALS AND METHODS
This study was conducted in Department of Hepatology, Shaikh Zayed Medical Complex, Lahore. One hundred and fifty cases of chronic active hepatitis C on treatment that were diagnosed by HCV – RNA were included in the study. Patients of Hepatitis C with cirrhosis, Hepatitis B surface antigen positive cases and Chronic active hepatitis C patients with coexisting hepatocellular carcinoma or other malignancies, autoimmune disorders, alcoholism, Wilson’s disease, alpha antitrypsin deficiency were excluded. Informed consent was taken and socio-demographic data like name, age, and address were collected. Patients were investigated for complete blood count (CBC) including platelet count (Plt). These all were performed on Sysmex XT 1800i. All collected information was entered into SPSS version 10.0 and was analyzed through its statistical package. Age was presented in terms of mean and standard deviation, sex and Platelet counts were expressed as frequency and percentages.

RESULTS
There were 99 (66%) female patients and 51 (34%) male patients in the cohort. Age ranged from 18 to 78 years. Mean age was 41.9 ± 12.8 years. Most of the patients were in the 4th decade of life.

Mean platelet count was 198.8 ± 77.3 x 10^9/l (range 150 – 400 x 10^9/l). Thrombocytopenia was present in 34 (22.6%) patients in the total cohort (Table 1). Sixteen of 51 (31.4%) were male patients, 18 of 99 (18.2%) were female patients. Thrombocytopenia was slightly more common in female patients as compared to males but this difference was not statistically significant (p = 0.104). Mean platelet count in thrombocytopenic male patients was 98.75 ± 28.73 x 10^9/l, mean platelet count in thrombocytopenic female patients was 95.88 ± 42.72 x 10^9/l, the difference was not significant (Table 2).

Patients were divided into two groups according to their age. Patient’s ≥ 40 years were included in group A and those who were less than 40 years were included in group B. In this total cohort 87 of 150 (58%) patients were in group A and 63 of 150 (42%) patients were in group B.

Thrombocytopenia was more common in group A i.e. 26.4% as compared to group B where only 17.4% of patients had thrombocytopenia. Mean platelet count was also lower in group A as compared to group B. The greater frequency and degree of thrombocytopenia in group A did not appear statistically significant when values were analyzed using chi square and t-test respectively (Table 3).

DISCUSSION
In our study thrombocytopenia was seen in 22.6% of patients. It

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Gender</th>
<th>Thrombocytopenic Patients n = 34</th>
<th>Mean</th>
<th>SD</th>
<th>p* value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>M</td>
<td>16 (31.4%)</td>
<td>98.75</td>
<td>28.73</td>
<td>0.823</td>
</tr>
<tr>
<td>2.</td>
<td>F</td>
<td>18 (18.2%)</td>
<td>95.88</td>
<td>42.72</td>
<td></td>
</tr>
</tbody>
</table>

Table 1: Platelet counts in 150 patients.

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>No. of Patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>34</td>
<td>22.6%</td>
</tr>
<tr>
<td>2.</td>
<td>116</td>
<td>77.3%</td>
</tr>
</tbody>
</table>

Table 2: Comparison of mean platelet counts in thrombocytopenic patients of two genders.

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Group</th>
<th>Total Patients</th>
<th>Patients with Thrombocytopenia</th>
<th>Patients without Thrombocytopenia</th>
<th>p* value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>A (≥ 40 years)</td>
<td>87</td>
<td>64 (73.6%)</td>
<td>23 (26.4%)</td>
<td>0.272</td>
</tr>
<tr>
<td>2.</td>
<td>B (&lt; 40 years)</td>
<td>63</td>
<td>52 (82.5%)</td>
<td>11 (17.5%)</td>
<td></td>
</tr>
</tbody>
</table>

* Statistically significant p value ≤ 0.05
was more common in males than in females (31.4% vs. 18.2%) and in group A than group B (26.4% vs. 17.5%) but the difference are not statistically significant.

In a community based study by Wang CS et al\(^8\) in Taiwan frequency of thrombocytopenia in HCV positive was 10.2 %. Our study showed a higher percentage of patients with thrombocytopenia (22.6%). The platelet count to define thrombocytopenia was lower i.e. 100\(\times\)10\(^9\)/l in their study than used in our study i.e. 150\(\times\)10\(^9\)/l. In their study mean platelet count in HCV positive was 180\(\times\)10\(^9\)/l which was close to mean platelet count of 198.8\(\times\)10\(^9\)/l in present study. They also reported that mean platelet count in HCV positive patients was lower than HCV negative persons (234\(\times\)10\(^9\)/l, \(p < 0.001\)).

Wang CS et al\(^8\) also reported that among HCV positive older people (> 65 years) were 3 times more likely than the persons in younger age group to have thrombocytopenia. Our study also reveal higher frequency of thrombocytopenia, in patients >40 years than the younger ones (26.4% vs. 17.5%) the milder difference may be due to the division of age groups at an earlier age of 40 yrs in our study as compared to 65 years in Wang CS study.\(^8\)

A study by Streiff et al,\(^9\) among HCV positive patients 4% had thrombocytopenia (platelets < 100,000) this showed a much lower frequency than our study. This study was a population based study where no HCV positive patients were on treatment and they had lower cut off platelet count to define as thrombocytopenia i.e. 100\(\times\)10\(^9\)/l instead of actual reference range of 150\(\times\)10\(^9\)/l. In the study of Streiff et al the severity of hematological findings were under estimated due to the fact that many patients with advanced hepatitis were likely to be hospitalized and thus not available for population based study.

It is **concluded** that treatment of HCV – related thrombocytopenia is based on the principle that eradication of HCV infection should result in remission of thrombocytopenia. Thus the usual protocol to treat HCV – related thrombocytopenia is to continue with IFN therapy but reduce its dose if platelet count falls. If thrombocytopenia persists even with reducing the dose alternative treatments like thrombopoietic growth factors should be considered, but in our population a study is needed to see the effect of these thrombopoietic agents so treatment should be continued with no hindrance.

**AKNOWLEDGEMENT**

We are grateful to the Dean of Sheikh Zayed Hospital, staff of Gastroenterology and staff of Hematology Department for allowing and helping us to complete this work.

**REFERENCES**

1. Mohammad N, Jan M.A. Frequency of hepatitis C in


