

Thrombocytopenia a Presenting Feature Of Hepatitis C

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Background: Hepatitis C is now a very common disease in our setup. A majority of patients suffering from this illness present with thrombocytopenia while being investigated for any other medical or surgical illness.

Objective: To determine the frequency of association of thrombocytopenia to hepatitis C in newly diagnosed cases.

To identify the risk factors for acquiring hepatitis C.

Study design and duration of study: It is a Descriptive study conducted at the Department of Hematology (Pathology), Benazir Bhutto Hospital, Rawalpindi from May 2009 to June 2010.

Materials and methods: Hundred consecutive patients who were diagnosed for the first time to be suffering from Hepatitis C in the Pathology Department were included in the study. A detailed history was taken to identify any risk factors for the disease causation of Hepatitis C. A peripheral blood sample was taken and complete blood picture analysis was performed to notify the presence of thrombocytopenia.

Results: Out of all the 100 patients who were diagnosed for the first time, 25% (n=25) had thrombocytopenia (Platelet count $<150 \times 10^3/\text{ul}$) as a presenting feature. Out of those 25 patients, 13 were females and 12 were males. 8 patients out of these had platelet count $<100 \times 10^3/\text{ul}$. The most common risk factor in 30% patients (n=30) was frequent management from local General Practitioner, followed by patients with significant history of surgical or invasive procedures in 27% (n=27) and history of dental procedures in 23% patients (n=23). The next in sequence are 17% of those having history of delivery by midwives and history of previous blood transfusion in 10% patients. In order of frequency the other risk factors are; patients with family history of Hepatitis C (10%), patients having multiple sex partners (5%) and finally intra venous drug abusers (2%). However none of the patients who presented to the department had history of dialysis or organ transplant. There was an overlap of risk factors amongst the patients.

Conclusion: There is a high frequency of presentation of thrombocytopenia in patients with hepatitis C, causing a considerable morbidity, as diagnosis is delayed and the patients are mismanaged due to lack of awareness and different beliefs regarding the diagnosis and management of this common disease.

Key words: Hepatitis C, Thrombocytopenia.

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Introduction

Thrombocytopenia is a common clinical problem that is discovered in daily laboratory testing and often leads to further investigations. Thrombocytopenia is the platelet count $<150 \times 10^3/\text{ul}$ and occurs in 64 - 76% of patients with liver cirrhosis and / or fibrosis, compared with 6% of non cirrhotic patients with chronic liver disease¹. The most well known causes of thrombocytopenia are infectious diseases such as HIV infection and HCV, cancer, toxic chemicals, medicines, pregnancy and autoimmune diseases. HCV infection is

strongly associated with thrombocytopenia, which is correlated with hepatocellular damage and hepatic fibrosis, and its prevalence and severity increases with increasing hepatocellular damage.² Advanced hepatic fibrosis, causing an altered production of thrombopoietin and portal hypertension plays the central role in the pathogenesis of thrombocytopenia in chronic viral hepatitis.³

The pathophysiology of thrombocytopenia in patients with chronic liver disease resulting from hepatitis C virus (HCV) infection is complex and involves several complementary mechanisms that likely act in

concert.⁴ In patients with untreated hepatitis C, both prevalence and severity of thrombocytopenia increase in parallel with the extent of disease, usually becoming clinically relevant when patients develop extensive fibrosis and / or cirrhosis. The pathogenetic mechanisms include hypersplenism secondary to portal hypertension, bone marrow suppression resulting from either HCV itself or interferon treatment, aberrations of the immune system resulting in the formation of anti-platelet antibodies and immune complexes that bind to platelets and facilitate their premature clearance.⁴ Relation between thrombocytopenia and hepatitis C led us to consider conducting a study to establish the frequency of thrombocytopenia in newly diagnosed patients of hepatitis C and also to identify the risk factors for its causation.

Materials and Methods

This is a descriptive study conducted over a period of one year in Benazir Bhutto Hospital, Rawalpindi. 100 consecutive patients who were diagnosed as cases of Hepatitis C for the first time from May 2009 to June 2010 were included.

Age and gender were noted. As a part of protocol a detailed history with special emphasis on the possible risk factors responsible for the disease causation of Hepatitis C were recorded. Anti HCV was detected using 3rd Generation ELISA in serial batches on Microplate reader, Dia 710, Diamate. Complete blood counts were performed on the automated Hematology analyzer. Peripheral films were stained with Giemsa's stain. Cases having thrombocytopenia were identified. Thrombocytopenia is defined as the platelet count < 150 x10³/ul.

Data was finally analyzed by SPSS version 15. The mean, standard deviations and percentages were calculated for statistical evaluation. Chi square test was applied to find the significance of **p value** < 0.05.

Results

A total of 100 patients were included in the study that were diagnosed for the first time as suffering from Hepatitis C. The patients' age ranged from 18 to 85 years. The mean age was 41.4 years. Out of these 100 patients 36% (n=36) were male and 64% (n=64) were female.

The frequency of patients presenting with thrombocytopenia suffering from Hepatitis C was 25% (n=25), which is found to be statistically significant (p < 0.05). Out of those 25 patients, 08 patients (8%) had platelet count <100x10³/ul with a range of 48x10³/ul - 95x10³/ul and the mean Platelet count was 75.7x10³/ul. However none of these patients had any clinical feature associated with thrombocytopenia. The breakup of

cases at different levels of platelets was that none of the patients had platelet count of <30 x10³/ul. Three patients had platelet count between 31 x10³/ul to 70 x10³/ul, five patients had platelet count between 71 x10³/ul to 100 x10³/ul, while the remaining 95 patients had platelet count between 101 x10³/ul to 150 x10³/ul.

The most common risk factor in 30% (n=30) was history of treatment for any illness by local General Practitioner. The second common risk factor in 27% (n=27) patients was history of surgical or invasive procedure, followed in sequence by history of dental procedure in 23% (n=23), history of delivery by midwives in 17% (n=17), history of blood transfusion in 13% (n=13), family history of Hepatitis C (10%), 5% patients having multiple sex partners and 2% with intravenous drug abuse. There was an overlap of risk factors in the patients as more than two factors were also identified in some patients. However 20% (n=20) of patients had no known risk factor.

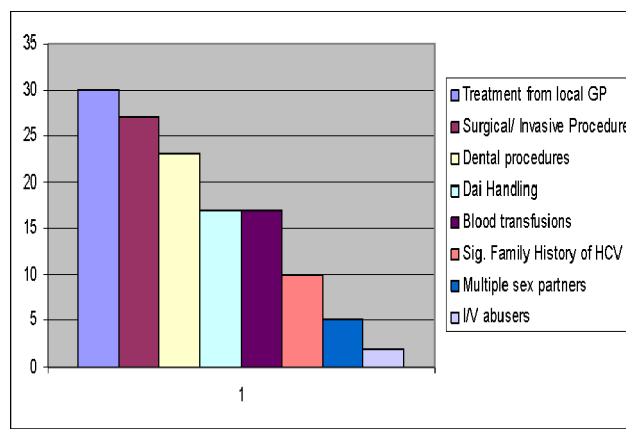


Figure I: Risk factors of Hepatitis C.

Thrombocytopenia is associated with the bleeding tendency and is a common laboratory finding. This important finding can complicate various diagnostic and therapeutic invasive procedures. Findings of low platelets on blood picture warrants further investigations to find out the etiology. Hepatitis C viremia is associated with thrombocytopenia and in the past, studies have been carried out to take it as a predictor of HCV viremia⁵.

Several studies have shown that thrombocytopenia is frequently observed in chronic Hepatitis C, and has a strong association with HCV infection^{6,7}. It appears to be a distinct clinical entity and in the current study it was found that 25% of patients had thrombocytopenia when they were diagnosed to be suffering from Hepatitis C. In a study conducted in Iran it was found that the prevalence of thrombocytopenia was 17.7%.⁸ Hepatitis C has a global health impact, and infects people worldwide. The HCV infection is becoming hyperendemic.² The development of thrombocytopenia

in patients with chronic liver disease is complex and multifactorial. It involves several complementary mechanisms that act in concert. Pathogenetic mechanisms include hypersplenism secondary to portal hypertension, bone marrow suppression resulting from either HCV itself or interferon therapy, aberrations of the immune system resulting in the formation of anti-platelet antibodies and/ or immune complexes that bind to platelets and facilitate their premature clearance, development of immunologically mediated extra hepatic manifestations including mixed cryoglobulinemia with or without associated joint, renal or cutaneous involvement, and thrombopoietic deficiency secondary to liver dysfunction. In chronic liver disease the natural inverse relationship between thrombopoietin and platelet level is not maintained.⁴

In a study conducted by Almeida et al, it was indicated that autoimmune mechanisms play a role in the pathogenesis of HCV associated thrombocytopenia by detecting specific antibodies against platelet glycoproteins, GP II b/IIIa, GP Ia/IIa and GP Ib/Ix.⁹

In a study conducted by Adinolfi et al, it was found out that advanced hepatic fibrosis causes an altered production of thrombopoietin and portal hypertension plays a central role in the pathogenesis of thrombocytopenia in the chronic viral hepatitis.³

HCV is strongly associated with thrombocytopenia, which is correlated with hepatocellular damage and hepatic fibrosis. The prevalence of thrombocytopenia among anti-HCV positive subjects increases as the severity and progression of disease. Thrombocytopenia is highly associated with older age, elevated ALT levels, and abnormal sonography showing the severity of liver disease. The study conducted by Chong Shan Wong suggested that older persons (>65 years of age) are four times more likely than persons in other age groups to have thrombocytopenia.²

The pathogenesis of HCV associated thrombocytopenia is still unclear. The interferon based therapy is contraindicated in patients of HCV infection having low platelets count (<70 x 10³/ul) till their recovery^{10,16}. The improvement in platelet count that follows successful treatment of HCV clearly demonstrate the cause effect relationship between the two.^{11,12}

This study also indicates that people who are visiting local GP's, dental surgeons and midwives are especially at risk. Various studies have also suggested that all patients with thrombocytopenia with risk factors for HCV (history of multiple blood transfusions, haemodialysis, unexplained abnormal aminotransferase levels, needle stick injury, mucosal exposure to HCV positive blood, intravenous blood abusers, recipients of organ transplant, children born to HCV infected mothers, current sexual partners of HCV, infected persons or persons having multiple sexual partners) have to be

screened for the virus, especially in regions with higher prevalence of HCV infection.^{8,13}

The traditional therapy for thrombocytopenia consists of platelet transfusion, but now, newer approaches have opened the wide arena for its management directly by stimulating thrombopoiesis. Cytokines, growth factors (IL-11), thrombopoietic hormone, non peptide agonists (Eltrombopag and AKK-501) are good stimulants of thrombopoiesis. This approach may be proven safe and non effective in the treatment of thrombocytopenia in patients with HCV infection or chronic liver disease.¹⁴ Thus timely initiation of therapeutic management of thrombocytopenia in HCV infection could be life saving.

Conclusion

The results of the current study show that there is high frequency of association between thrombocytopenia and Hepatitis C. HCV infection is quite a common disease in our setup with a high morbidity. Moreover unsafe methods of sterilization are contributing a lot to its spread.

A significant number of patients present with thrombocytopenia. Increased awareness regarding early diagnosis is required to prevent the considerable morbidity associated with this disease. The ultimate aim of treating thrombocytopenia in anti-HCV positive case is not to normalize the platelet count¹⁵, but to attain and maintain a safe haemostatic level that avoids haemorrhage on one hand and thrombosis on the other. Further studies are recommended to establish the relative frequency of thrombocytopenia in Hepatitis C patients in Pakistan.

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