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Thrombocytopenia as a Clinical Manifestation of Hepatitis C Among Patients With a Positive Anti-HCV Test

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Abstract

Background: The hepatitis C virus (HCV) has been recognized as the cause of thrombocytopenia (defined as a platelet count of < 150,000 platelets/uL) occurring in patients with chronic hepatitis *C*. Thrombocytopenia occurs in 64% - 76% of patients with cirrhosis and/or fibrosis, compared with 6% of non-cirrhotic patients with chronic liver disease.
Objectives: The aim was to study the prevalence of thrombocytopenia in HCV patients without cirrhosis and splenomegaly.
Patients and Methods: A cross-sectional study was carried out in the gastrointestinal out patient department (G.I. OPD) of the Sindh institute of urology and transplantation (SIUT) from September-November 2013. 30 patients aged between 18 - 60 years with a positive anti-HCV result were included. Patients with enlarged spleen, liver cirrhosis on an ultrasound of the abdomen, and thrombocytopenia related to other causes were excluded from the study.
Results: A total of 30 patients satisfying the inclusion criteria were selected for study. The mean age of the patients was 42.2 $\pm$ 11.4 (16 - 60), and they included 21 females and 7 males. The majority of patients had normal liver function tests with normal spleen size. On the CBC, 13 had platelets of less than 150,000/μL and 17 patients had a platelet count in the normal range, i.e., 150,000 - 400,000/μL. The prevalence of thrombocytopenia was found to be 43.3% among those with hepatitis C.
Conclusions: The conducted study showed moderate frequency of hepatitis C-induced thrombocytopenia in patients without hepatic fibrosis and splenomegaly among the Pakistani population.

Keywords: Hepatitis C, Pakistan, Thrombocytopenia

1. Background

Hepatitis C is an infectious disease primarily affecting the liver, caused by the hepatitis C virus (HCV). HCV is an important causative factor in the etiology of fibrosis, cirrhosis, and hepatocellular carcinoma (HCC) (1). The world health organization (WHO) has estimated that worldwide approximately 185 million people are infected with HCV, of which 3 - 4 million are new cases. Two-thirds of these newly infected patients develop chronic liver disease (2). In Pakistan, approximately 10 million people are documented as being infected with HCV, with infection rates as high as 2.2% - 14% (3, 4).

In chronic liver diseases such as HCV, thrombocytopenia is one of the commonest abnormalities that is reported (5). Briefly, thrombocytopenia is defined as a platelet count of < 150,000/μL. The main role of platelets is maintaining normal homeostasis and vessel wall repair. The most well-known causes of thrombocytopenia/low platelet count include failure of platelet production, increased destruction or consumption of platelets, sequestration of platelets, massive blood loss, and infectious diseases or viral infection.

Studies have documented that HCV infections are strongly associated with thrombocytopenia, showing that 64% - 76% of patients suffering from HCV, chronic infection, and cirrhosis/fibrosis exhibited manifestations of thrombocytopenia, as compared to 6% of non-cirrhotic patients (6, 7). This indicates that the prevalence and severity of thrombocytopenia increases with increased hepatocellular damage. The major clinical complication in such cases is the increased risk of variceal bleeding and death (8). The mechanism leading to thrombocytopenia in HCV is complex and involves various host and viral factors.

2. Objectives

Though thrombocytopenia is an important clinical manifestation with respect to patient management in HCV, a limited number of studies from Pakistan have documented data on this aspect (3). Therefore, the main aim of this study is to address the knowledge gap on the incidence of hepatitis C infection-induced thrombocytopenia, and comment on the dynamics of thrombocytopenia-related

complications and management in the HCV-infected Pakistani population.

3. Patients and Methods

3.1. Study Design and Setting

A cross-sectional study was carried out from September-November 2013 at the gastrointestinal out patient department (G.I. OPD) of the Sindh institute of urology and transplantation (SIUT), in Karachi, Pakistan. The study inclusion criteria were patients (18 - 60 years old) diagnosed with a chronic HCV infection through anti-HCV testing. All patients with enlarged spleen, liver cirrhosis on an abdomen ultrasound, and thrombocytopenia due to co-morbidities such as drug interaction, malaria, autoimmune, and other infectious diseases were excluded from the study. Informed verbal consent was taken from all enrolled patients.

3.2. Methods

The laboratory tests conducted for the study included: complete blood count (CBC), coagulation profile, liver function tests (LFT), and anti-HCV antibodies. Briefly, 10 cc of blood was collected to conduct the respective tests on automated analyzers, as per the manufacturers' instructions. A hematology analyzer BECKMAN COULTER LH 750, CA-1500, SYNCHRON CX-9 and ARCHITECT 1200sr were used for the CBC, coagulation profile, LFT, and Anti-HCV tests, respectively. Splenomegaly was tested via sonography. All abdomen ultrasounds were performed and reported by consultants.

3.3. Statistical Analysis

Data was recorded on Microsoft Excel and exported to statistical package for social sciences (SPSS) version 19.0 for analysis (SPSS, Chicago, IL, USA). Descriptive analyses, where applicable, were performed for the data set.

4. Results

A total of 30 patients satisfying the inclusion criteria were enrolled in the study. Baseline demographics showed that the female to male ratio was 21:7. The mean age of patients was 42.2 $\pm$ 11.4. The majority of patients had liver function test results within the normal ranges. In the coagulation profiles, 22/30 patients (73.3%) had a prothrombin time within range, i.e., 10.5 - 13.5 sec. For the activated partial prothrombin time, 20/30 patients (66.7%) had abnormal values, i.e., < 25.7 seconds. Splenomegaly was not observed in any of the enrolled patients. Out of the 30 HCV-infected patients, it was found that 13 had platelet counts less than normal, i.e., < 150,000/μL, while the remaining patients had platelet counts within the normal range, i.e., 150,000 - 400,000/μL. Thrombocytopenia was observed in 43.3% of the participants (Table 1).

5. Discussion

This study was conducted to determine the frequency of hepatitis-induced thrombocytopenia in the Pakistani population, and to comment on the clinical implications of thrombocytopenia in HCV management. The study results showed that 43.3% of the study participants were suffering from HCV-induced thrombocytopenia. This result is higher than previous studies, in which the prevalence of HCV-induced thrombocytopenia was reported as 10.2% and 13%, respectively (9, 10). The varying incidences in different studies may be due to sample selection, therapy, or various other factors.

Though the pathophysiology of HCV-induced thrombocytopenia is not completely understood, several host and viral factors have been associated with this manifestation. It has been reported that auto antibodies directed against platelet surface antigens can promote platelet (11-13). In a study, 64% of patients with chronic liver disease with diverse etiologies were found to have platelet-associated antiglycoprotein (GP) antibodies, primarily against the GPIb-IX complex, either alone or in combination with anti-GPIIb-IIIa antibodies (13). It has been suggested that the binding of HCV to platelets may induce the development of neoantigens on the platelet surface, or alter the conformation of platelet membrane GPs, thereby contributing to autoantibody formation against target platelet GPs (14).

Immune complex-associated platelet clearance and reticuloendothelial destruction have also been proposed to contribute to thrombocytopenia in patients with chronic HCV (12). Studies have reported that idiopathic thrombocytopenic purpura (ITP) develops more frequently in patients with HCV infection than in healthy

Table 1. Frequency of HCV-Induced Thrombocytopenia

No. of Platelets, μL	No. (%)
< 50	2 (6.7)
51 - 100	4 (13.3)
101 - 150	7 (23.3)
151 - 400	15 (50.0)
> 401	2 (6.7)
Total	30 (100)

persons (15-17). HCV may contribute to or trigger the development of ITP, mediated in particular by circulating immune complexes (15). Therefore, coexistent ITP may contribute to thrombocytopenia in patients with HCV-associated liver disease. Furthermore, platelet sequestration and destruction in the spleen probably contribute significantly to thrombocytopenia in HCV infected patients. Higher platelet-associated immunoglobulin (PAIgG) levels have been detected in HCV-infected thrombocytopenic patients (11, 18). The current treatment of choice for HCV is Peg-Interferon with ribavirin. Studies have shown that hepatitis C-induced thrombocytopenia is as high as 37% during treatment with IFN-α2b (19). This is due to bone marrow suppression, including inhibition of megakaryocytopoiesis, which leads to thrombocytopenia.

HCV-induced thrombocytopenia has thus been documented as a major risk of bleeding in patients. Studies have documented that moderate thrombocytopenia (platelet counts of 50,000 -75,000/μL) in HCV-infected patients poses an increased risk of bleeding during invasive diagnostic procedures, such as liver biopsies. This bleeding can be exacerbated, especially in patients with coexistent coagulopathy (20), thus limiting diagnostic and treatment options for clinicians (21). Furthermore, in HCV-associated cirrhosis, severe thrombocytopenia has been identified as an independent risk factor for developing complications of variceal bleeding and death (8). In our study, abnormal activated partial prothrombin time values (< 25.7 seconds) were observed in 66.7% of patients. This may be due to host or viral factors. Therefore, HCV-induced thrombocytopenia should be considered during patient management to decrease morbidity rates.

This study provides baseline knowledge on the incidence of HCV-induced thrombocytopenia in Pakistani population. However, we would like to address the limitations of our study. The main limitation is the small sample size, which was due to the strict exclusion criteria maintained in the study. Furthermore, the study budget was for three months, and therefore sampling was stopped once the timelines were reached. Secondly, we acknowledge that the most appropriate test for an HCV diagnosis is PCR. However, due to budget constraints, the samples could not be tested by PCR and therefore the patients were screened on the basis of anti-HCV only, which is a relatively cheaper test but a sufficiently valid tool for screening patients suffering from an HCV infection. However, even with the small size and budgetary constraints we were able to determine the frequency of HCV-induced thrombocytopenia in anti-HCV positive patients. It is suggested that larger studies in different regions of Pakistan need to be done in order to determine the importance of this aspect. This would not only help to provide baseline data from Pakistan on this trend, but also serve as awareness guide for the interns, residents, and consultants working in both private and public sector hospitals of Pakistan.

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Footnote

Authors' Contribution: Khalid Zafar Hashmi designed and planned the study and approved the final manuscript. Safia Bano performed the tests, collected and analyzed data, and wrote the manuscript. Javeria Qureshi analyzed the data and provided input on the project. Afsheen Raza reviewed the manuscript and made revisions to the final manuscript.

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