



Occurrence of Thrombocytopenia in Non-Cirrhotic Hepatitis C Positive Patients

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Abstract

Thrombocytopenia is commonly encountered hematological abnormality, which might be attributed to hepatitis C virus (HCV) in acute and chronic infection. This study aims to determine the prevalence of thrombocytopenia as a clinical manifestation of chronic HCV infection in non-cirrhotic patients having spleen of normal size. A cross sectional study was carried out in Ayub Teaching Hospital, Abbottabad, Khyber Pakhtunkhwa, Pakistan in Gastroenterology and Medical Outpatient Department from January to October 2017. The investigation was carried out on patients between age 20 to 60 years with anti-HCV antibody positive. All patients having liver cirrhosis, or fibrosis and splenomegaly, or having thrombocytopenia from other causes i.e. any drug use or other chronic infections were excluded from the study. A total of 67 patients fulfilling the criteria were selected. Thrombocytopenia was observed in 34.3% of the subjects, among them 17.9% exhibited mild thrombocytopenia (150000/ μ L to 400000/ μ L); 11.9% (51000/ μ L to 100000/ μ L) exhibited moderate thrombocytopenia while 4.5% (less than 50000/ μ L) showed severe thrombocytopenia. Thus, the study exhibited the presence of thrombocytopenia in chronic HCV patients without liver cirrhosis and splenomegaly that proves the contribution of HCV to induce thrombocytopenia.

Keywords: Thrombocytopenia, HCV, Cirrhosis

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1. INTRODUCTION

Hepatitis C virus (HCV) is considered as one of the major causes of morbidity and mortality during the last decade contributing more than 185 million infections all over the world¹. The situation is even worse in developing countries, as only in Pakistan approximately 10 million of HCV infection cases were reported exhibiting a higher infection rate from 2.2-14%^{2,4}. Recently, it was reported that 5% of the Pakistani

population was infected with HCV, and they were unaware of their HCV status. The major causes of disease spread among Pakistanis are unhygienic conditions, reuse of syringes and non-sterile surgical equipment. Due to this serious situation, Pakistani Government has established first National Hepatitis Strategic Framework (NHSF) that will strictly follow the strategies of world health organization while covering the duration of 2017-21⁵. Many factors are contributing in a constant rise in HCV infection that include deficit health care facilities, low socioeconomic conditions, bad governance, illiteracy and unawareness of HCV infections and its fetal consequences⁶. The major abnormalities caused by Hepatitis C virus includes chronic hepatitis, liver fibrosis/cirrhosis and hepatocellular carcinoma (HCC)⁷; however, thrombocytopenia is considered as the most commonly found hematological abnormality⁸. Thrombocytopenia (a platelet count of $< 150,000/\mu$)⁹ in chronic HCV infection is a major problem, particularly in patients with advanced liver disease. Some studies have documented that chronic HCV infections were strongly associated with thrombocytopenia. In previous studies, thrombocytopenia was reported in 64-76% of chronic HCV infected patients while they were also exhibiting the symptoms of cirrhosis/fibrosis; however, only 6% of non-cirrhotic patients developed thrombocytopenia^{10,11}. Various mechanisms are known to cause thrombocytopenia in chronic liver disease due to HCV i.e. decreased platelet production by bone marrow, increased destruction or consumption of platelets due to autoimmunity, sequestration of platelets in the enlarged spleen. In addition, several studies have suggested that HCV may have a direct pathogenic role in the process leading to thrombocytopenia^{12,14}.

A few studies already considered thrombocytopenia as one of the important manifestation of HCV infection; however, a limited number of studies were reported among Pakistani population. Specifically, khyber pakhtunkhwa (KPK) is considered as a neglected province of Pakistan in terms of medical research, and HCV data is not easily available for the population of this specific area. For this concern, this study deals with the relation between HCV infection and thrombocytopenia among population of very specific location of Pakistan i.e. Abbottabad, KPK. Moreover, those cases were excluded from the study where thrombocytopenia could be attributed to other factors i.e. splenomegaly, liver cirrhosis, ascites, drug use, co morbid condition or any chronic ailments, to impose a complete focus on the relation between thrombocytopenia and non-chronic HCV infection.

2. MATERIALS AND METHODS

This cross sectional study was carried out in Ayub Teaching Hospital, Abbottabad in Gastroenterology and Medical Departments from January 2017 to October 2017. A total of 67(including both male and female) patients fulfilling the criteria were included in the study. Informed consent was taken from all the patients. A pro-forma was designed to collect the information related to clinical laboratory tests like anti HCV antibody, complete blood count (CBC), liver function tests including bilirubin, alanine aminotransferase (ALT), alkaline phosphatase (ALP), coagulation profile like prothrombin time (PT) and international normalized ratio (INR). Abdominal ultrasound were performed and reported by consultants in radiology departments to rule out splenomegaly or ascites.

2.1 Inclusion Criteria

Patients with chronic HCV infection diagnosed on anti HCV testing were included in the study.

2.2 Exclusion Criteria

Patients with splenomegaly, liver cirrhosis, ascites and thrombocytopenia from other causes i.e. drug use, co morbid condition or any chronic ailments were excluded.

3. RESULTS AND DISCUSSIONS

From all of the selected patients, 65.7% (44/67) were female, while 34.3% (23/67) were male (Table 1). The mean age of subjects was 46.07 ± 10.89 years. Majority of the subjects were exhibiting normal range of liver function test. The percentage of the subjects exhibiting normal range was 100% for bilirubin; 95.5% for ALT and 92.5% for ALP; 89.4% for PT and 94% for INR. Splenomegaly was not present in any of the subjects; moreover, there was no evidence of ascites on ultrasound. Thrombocytopenia was observed in 34.3% of the subjects, among them 17.9% exhibited mild thrombocytopenia ($150000/\mu\text{L}$ to $400000/\mu\text{L}$), 11.9%

(51000/ μ L to 100000/ μ L) exhibited moderate thrombocytopenia and 4.5% (less than 50000/ μ L) showed severe thrombocytopenia.

Table 1. Demographics characteristics of non-cirrhotic hepatitis C positive patients

| | |
|--|-------------------|
| No. of total patients | 67 |
| Mean age of patients with standard deviation | 46.07 \pm 10.89 |
| Male | 23 |
| Female | 44 |

The presence of thrombocytopenia in HCV infection is one of the major hematological abnormalities in blood. This study was conducted to determine the frequency of thrombocytopenia in HCV positive patient excluding patients with cirrhosis. A total of 67 patients fulfilling the criteria were selected. Thrombocytopenia was observed in 34.3% of the total subjects, which was much is higher than previous studies, in which the prevalence of HCV-induced thrombocytopenia was reported as 6, 10.2 and 13%^{15, 16}. The varying results of the studies might be attributed to the sample size, sample selection, co morbid conditions, laboratory to laboratory variations or certain drug usage or living conditions of the specific area of KPK.

In cirrhotic patients, thrombocytopenia might be attributed to sequestration of platelets in the enlarged spleen¹⁶; however, similar cases could be observed in chronic HCV infected patients without cirrhosis. Another mechanism reported the autoimmune reaction where auto antibodies were directed against surface antigens of platelets ultimately leading to thrombocytopenia caused by the destruction of platelets^{9, 11, 15, 18}. Similarly, some reports indicated a pathogenic mechanism where platelets destruction by reticulo-endothelial system was attributed to the expression of platelets-associated immunoglobulin G (PAIgG)^{19, 20}.

It has also been reported that inadequate production of platelets due to bone marrow suppression caused by HCV infection also played a crucial role in the development of thrombocytopenia²¹. The severity and the prevalence of thrombocytopenia were considered to have direct relations with the severity of the extent of fibrosis and other liver diseases; however, the development of thrombocytopenia in chirosis could also be attributed to the decreased thrombopoietin (TPO) production by liver²².

In addition, several studies suggested that HCV might have a direct pathogenic role in the process leading to thrombocytopenia²³. Previous studies reported that 30% of patients exhibiting no advanced liver disease were seropositive for hepatitis C virus, thus considering its direct association with immune mediated thrombocytopenia (ITP). The rate of ITP among HCV infected patient was reported as 30.2 per 100,000 person, which was noticeably higher in comparison to non HCV infected individuals exhibiting 18.5 cases per 100,000 persons²⁴. Although thrombocytopenia in chronic HCV infection is typically low grade and not life-threatening, it may impede the initiation and continuation of antiviral therapy, potentially decreasing the probability of successful HCV treatment²⁵.

Table 2. Complete blood count of of non-cirrhotic hepatitis C positive patients

| White blood cells / μ L | |
|-----------------------------|----|
| 4000 to 11000 | 57 |
| Less than 4000 | 4 |
| More than 1100 | 6 |
| 400000 to 6000000 | 63 |
| Less than 400000 | 4 |
| 150000 to 400000 | 43 |
| Less than 150000 | 23 |
| More than 400000 | 1 |

Table 3. Liver function tests.

| Prothrombin time (seconds) | |
|-----------------------------------|----|
| 11 to 15 seconds | 60 |
| More than 15 seconds | 7 |
| Equal to 1 | 63 |
| More than 1 | 4 |
| 10 to 40 | 64 |
| More than 40 | 3 |
| 40 to 100 | 62 |
| More than 100 | 5 |
| Less than 1.2 | 67 |

LFT give information about the state of a patient's liver. PT is measured in seconds. Results are provided in INR (international normalized ratio)

Table 4. Ultrasonographic findings of abdomen.

| Spleen size (in cms) | |
|-----------------------------|----|
| Less than 12cm | 67 |
| Ascites | 0 |

Normal (not splenomegaly) the largest dimension is approximately 12 cm

4. CONCLUSIONS

The study revealed that thrombocytopenia can be observed in chronic HCV patients without any clear evidence of liver cirrhosis and splenomegaly. Thus, it can be revealed from the study that thrombocytopenia was observed even in the absence of other abnormalities in the patient like liver cirrhosis and splenomegaly that proves its association with chronic HCV infection. Therefore, while dealing with chronic HCV infected patient, the associated thrombocytopenia should be kept in mind that can be one of the major cause of bleeding in these patients. The chronic HCV associated thrombocytopenia can also contribute in excessive visceral bleeding and ultimately can cause death of these patients. While treating such patients, major focus should be imposed on thrombocytopenia to mitigate its effect that will ultimately reduce the morbidity rate.

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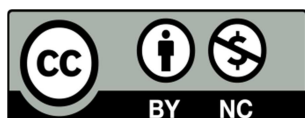
CONFLICT OF INTEREST

All authors declare no conflict of interest regarding this article.

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