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Original Article

Prevalence of thrombocytopenia in chronic hepatitis c patients arriving in out patient department

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ABSTRACT

Objective: To determine the prevalence of thrombocytopenia in chronic Hepatitis-C patients presenting at the outdoor patients department of Farooq Hospital, Lahore.

Methods: A Cross-sectional study was conducted in the medical outdoor patients department of Farooq Hospital, Lahore, from September 1st, 2023, to August 31st, 2024. Four hundred patients with hepatitis who were either newly diagnosed or taking treatment for the last 3 months and those who had relapse/failure to treatment were enrolled. After recording the baseline, their blood samples for serum platelet counts were withdrawn. Thrombocytopenia was labeled based on platelet counts of ≤150,000 uL. The prevalence of thrombocytopenia was presented as frequency and percentage.

Results: The mean age of patients was 41.18±6.51 years. There were 271 (67.7%) males. Diabetes, hypertension, and I.H.D. were found in 54 (13.5%), 69 (17.3%), and 29 (7.3%) patients. The mean duration since hepatitis C of the patients was 6.63±1.99 months. The mean platelet count of the patients was 160.77±62.46 ×(10^3/uL), and there were 151 (37.8%) patients had ≤150 platelet count. Thrombocytopenia was severe in 16 (10.6%) patients, moderate in 92 (60.9%) patients and mild in 43 (28.5%) patients. Since Hepatitis C was diagnosed, the mean duration was greater in severe thrombocytopenia than in mild and moderate thrombocytopenia ($p<0.001$).

Conclusion: Thrombocytopenia is a marker of severity in patients with hepatitis C, depicting its extrahepatic manifestation. The percentage of severe thrombocytopenia was higher in patients with longer durations, with features of cirrhosis.

Keywords: Chronic Hepatitis; Hepatitis; Hepatitis C; Liver disease; Platelets; Thrombocytopenia

1. INTRODUCTION

Thrombocytopenia is one of the extrahepatic manifestations of Hepatitis C.[1] Several mechanisms can lead to thrombocytopenia, including portal hypertension and hypersplenism in cirrhotic patients,2,3 an autoimmune reaction to platelets, direct infection of platelets and megakaryocytes with the hepatitis C virus, and cryoglobulinemia.[4,5] According to WHO, approximately 3% of the global population is chronically infected with hepatitis C. [6]

Hepatitis C is a clinically significant healthcare problem in Pakistan, with higher than global prevalence rates approaching 5%.[7] If hepatitis C is left untreated, there is a rise in severity and prevalence of thrombocytopenia and progression of liver fibrosis, leading to portal hypertension and esophageal varices. [8] Early evaluation of reduced platelet counts is valuable in planning further treatment strategies for chronic hepatitis C, thereby reducing the complication rate. In a study examining>1000 patients of Hepatitis C, the prevalence of thrombocytopenia (<150,000) was 36.49%.[4] Hepatitis C is a leading cause of mortality, especially in the developing world. The global mortality rate approaches 0.7 million deaths per annum.[9] Prevalence is higher in low socioeconomic countries.[7] The prevalence of extrahepatic manifestations is above 40%.[10]

Pakistan has one of the highest HCV prevalence rates; however, CHC thrombocytopenia data are scarce. Its prevalence affects treatment options, including antiviral treatments and bleeding risks during invasive procedures. Management is complicated by late presentation due to socioeconomic and healthcare constraints. This study seeks to close this gap, improve early detection, adapt therapies, and provide evidence-based guidelines for Pakistan's high-risk population. This study aims to detect thrombocytopenia early, characterize its severity, and inform chronic hepatitis C treatment. It will also identify patients with severe thrombocytopenia associated with a medication therapy for counseling and management.

2. METHODOLOGY

After the approval of IERB (M-23/112-Medicine; Dated 13-06-2023), a cross-sectional study was conducted at the medical ward of Farooq Hospital from August 1st, 2023, to February 1st, 2024. The minimum sample size was 356, calculated using the WHO calculator, based on a prevalence of thrombocytopenia of 36.49% [4] and a 5% margin of error. So, 400 patients, aged between 15-65 years, of both genders, those who had been diagnosed with chronic hepatitis C either by ELISA or PCR for more than 3 months, who were either undertreatment, non-responders to hepatitis C treatment (PCR positive after treatment) or patients of hepatitis C with cirrhosis on USG were included in the study using the non-probability consecutive sampling technique. Patients with a previous history of inflammatory disorders, i.e., rheumatoid arthritis, SLE, and vasculitis. Alpha-1 antitrypsin deficiency, alcohol intake, patients on any immunosuppressive therapy, i.e., Methotrexate, Azathioprine, HCQ, TMP/SMZ, Sulfasalazine. Acute febrile illness (fever less than 2 weeks ago) was excluded.

Hepatitis C was labeled and diagnosed via PCR over 3 months ago. Progressive scarring of the liver is visualized on Ultrasound as liver surface irregularity or nodularity, and coarse or heterogeneous parenchymal echotexture, presence of splenomegaly, portal vein diameter >13mm, and/or presence of ascites was labeled as cirrhotic liver disease. Thrombocytopenia was labeled if the platelet count was $\leq 150 \times 10\text{^}3/\text{uL}$. Mild thrombocytopenia if platelet count is 101-150x103/uL, moderate 51-100x103/uL, and severe when platelet count is $\leq 50 \times 10^3/\text{uL}$. Patients who received Hepatitis C

treatment but whose Hepatitis C PCR remained positive at the end of therapy were labeled as non-responders.[8]

Permission was asked from the Akhtar Saeed Medical and Dental College Institutional Review Board. Informed consent was taken from patients arriving at the Farooq Hospital dialysis center. Relevant history and a review of previous records, such as last treatment, non-responders, relapse of disease, USG report done within 15 days (if not available, then USG was done), and drugs for hepatitis C were taken to meet the inclusion and exclusion criteria. Blood samples were collected and sent to the central lab of Farooq Hospital for each individual's platelet count levels using a hematology analyzer. Findings were recorded on a pro forma, along with other demographic information and relevant medical history.

Data was entered and analyzed in SPSS v26. Quantitative variables, such as age, duration of hepatitis C treatment, and platelet count, were presented in mean and standard deviation. Categorical variables, such as gender, diabetes, hypertension, IHD, previous history of treatment, the outcome of prior therapy (non-responders/relapse), type of drugs taken, and USG findings, will be presented in frequency and percentage. The frequency and severity of thrombocytopenia were presented as frequency and percentage. All data will be stratified accordingly. A p-value of ≤0.05 was taken as significant.

3. RESULTS

The mean age of patients was 41.18±6.51 years, with most patients aged 50 years or younger, accounting for 360 (90.0%). There were 271 (67.7%) males and 129 (32.3%) females. There were 162 (40.5%) patients in urban areas and 238 (59.5%) in rural areas. Diabetes, hypertension, and I.H.D. were found in 54 (13.5%), 69 (17.3%), and 29 (7.3%) patients. The mean duration since the diagnosis of hepatitis C for the patients was 6.63±1.99 months. (Table. I).

According to USG findings, the liver surface was smooth in 67 (16.8%) patients and irregular in 333 (83.2%). Liver parenchymal echotexture was homogeneous in 50 (12.5%) patients and heterogeneous in 350 (87.5%) patients. Spleen was up to 12 cm in 268 (71.5%) patients and >12 cm in 114 (28.5%) patients. Portal vein diameter was up to 13 mm in 368 (92.0%) patients and >13 cm in 32 (8.0%) patients. Ascites was found in 39 (9.8%) patients. The mean platelet count of the patients was 160.77±62.46 $\times(10^3/uL)$, and there were 151 (37.8%) patients had ≤150 platelet count. (Table. II). Thrombocytopenia was severe in 16 (10.6%) patients, moderate in 92 (60.9%) patients and mild in 43 (28.5%) patients. (Figure. I). Since Hepatitis C was diagnosed, the mean duration was greater in severe thrombocytopenia than in mild and moderate thrombocytopenia ($p<0.001$). It was seen that ascites and spleen >12 cm were the significant effect modifier for thrombocytopenia ($p<0.001$). (Table. III).

Table-I: Demographics and baseline profile

Variable	Presence
Age (years)	41.18±6.51
Up to 50 years	360 (90.0)
More than 50 years	40 (10.0)
Gender	
Male	271 (67.7)
Female	129 (32.3)
Area of residence	
Urban	162 (40.5)
Rural	238 (59.5)
Comorbidities	
Diabetes	54 (13.5)
Hypertension	69 (17.3)
I.H.D	29 (7.3)
Duration Since Diagnosis (month)	6.63±1.99
Indication of treatment	
New onset	263 (65.8)
Relapse	107 (26.8)
Recurrence	30 (7.5)
Drugs received	
Interferon	30 (7.5)
Ribavirin	32 (8.0)
Direct acting agents Sofosbuvir	338 (84.5)

Mean±S.D, N (%)

Table-II: USG findings and platelets counts

Variable	Presence
Liver Surface	
Smooth	67 (16.8)
Irregular	333 (83.2)
Liver Parenchymal echotexture	
Homogenous	50 (12.5)
Heterogenous	350 (87.5)
Spleen	
Up to 12 cm	268 (71.5)
>12 cm	114 (28.5)
Portal Vein diameter	
Up to 13 mm	368 (92.0)
>13 mm	32 (8.0)
Ascites	
Yes	39 (9.8)
No	361 (90.2)
Platelet Count (10^3/uL)	160.77±62.46
Mean±S.D, N (%)	

Figure-I: Severity of Thrombocytopenia

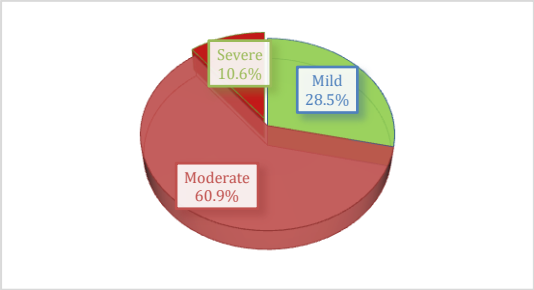

Table-III

Association of severity of thrombocytopenia with effect modifiers

Variables	Severity of thrombocytopenia			p-value
	Mild	Moderate	Severe	
Duration since Hep-C diagnosis (months)	6.23±2.09	6.61±2.05	8.94±1.48	F=7.64, p<0.001
Indication of treatment				
New onset	27 (62.8)	57 (62.0)	10 (62.5)	χ^2=0.250, d.f=4, p=0.993
Relapse	12 (27.9)	28 (30.4)	5 (31.3)	
Recurrence	4 (9.3)	7 (7.6)	1 (6.3)	
Drugs received				
Interferon	3 (7.0)	10 (10.9)	1 (6.3)	χ^2=2.04, d.f=4, p=0.727
Ribavirin	3 (7.0)	4 (4.3)	0 (0.0)	
Direct acting agents Sofosbuvir	37 (86.0)	78 (84.8)	15 (93.7)	
Liver surface				
Smooth	6 (14.0)	17 (18.5)	1 (6.3)	χ^2=1.69, d.f=2, p=0.429
Irregular	37 (86.0)	75 (81.5)	15 (93.7)	
Liver Parenchymal echotexture				
Homogenous	6 (14.0)	13 (14.1)	2 (12.5)	χ^2=0.030, d.f=2, p=0.985
Heterogenous	37 (86.0)	79 (85.9)	14 (87.5)	
Spleen				
Up to 12 cm	25 (58.1)	73 (79.3)	12 (75.0)	χ^2=6.71, d.f=2, p=0.035
>12 cm	18 (41.9)	19 (20.7)	4 (25.0)	
Portal Vein diameter				
Up to 13 mm	40 (93.0)	87 (94.6)	15 (93.8)	χ^2=0.127, d.f=2, p=0.938
>13 mm	3 (7.0)	5 (5.4)	1 (6.3)	
Ascites				
Yes	2 (4.7)	10 (10.9)	16 (100.0)	χ^2=33.47, d.f=2, p<0.001
No	41 (95.3)	82 (89.1)	0 (0.0)	
N (%)				

4. DISCUSSION

Hepatitis C infection is one of the most common diseases in Pakistan, resulting in a significant economic burden. Data published between 2003 and 2021, encompassing 765,426 individuals, revealed a mean prevalence of 16.47% [8]. In one study, the survey-adjusted HCV seroprevalence was 13.5%, and the survey-adjusted viraemic prevalence was 4.1%, with a viraemic ratio of 32% (95% confidence interval 24.3-40.5). One study found that 44% had previously received therapy for chronic hepatitis C [11]. Aside from other poor prognosis factors such as high viral load, recurrent infection, fibrosis, congenital prevalence, and decompensated liver disease, thrombocytopenia is also a poor prognostic indicator. [12,13]

In our study, the mean age of patients with hepatitis C infection was approximately 41 years, with the majority of patients aged 50 years or less, at 360 (90.0%). Additionally, most patients, 238 (59.5%), resided in rural areas. In the United States, the highest prevalence occurs among people aged 30-49, who account for two-thirds of all infections [14]. Similar age distributions were observed in investigations conducted in China, Italy, and Pakistan [15]. Patients aged 21-30 and at least 31 years at infection had a higher chance of developing cirrhosis over 30 years compared to those aged <20 years at infection (4.51 and 12.29, respectively) [16].

The mean platelet count of the patients was 160.77±62.46 ×(10^3/uL), and 151 (37.8%) patients had ≤150 platelet count. Consistent with our study, a 2009 study in Peshawar reported a prevalence of

thrombocytopenia in hepatitis C of 32%, [17], which decreased to 22% in a 2019 study. [18] Most of the patients receiving drug therapy for hepatitis C in our study were sofosbuvir (84%). One of the major benefits of this drug was the correction of thrombocytopenia, as evidenced by an increase from a mean of 100x10^3 to 122x10^3 after three months of treatment. [19] Another benefit of this drug, with daclatasvir, is achieving nearly 90% sustained viral response at 12 weeks [20]. In our study, thrombocytopenia was more prevalent with increased duration, irregular liver surface, splenomegaly, and ascites. These features have been adequately studied in numerous studies, as they are related to cirrhosis and fibrosis, which lead to portal hypertension, splenomegaly, and, in turn, platelet sequestration and thrombocytopenia [21-23].

A limitation of our study was that it was a single-center, descriptive study. More advanced surveys at the national level are recommended. More studies about thrombocytopenia with different drug therapies, duration, and treatment, thrombocytopenia in cirrhosis, and response to drug therapy in terms of cirrhosis improvement along with thrombocytopenia are expected.

5. CONCLUSION

It is concluded from our study that thrombocytopenia is prevalent in a significant population of hepatitis C presenting outdoors of Farooq Hospital Lahore, which can be more severe in patients with increased duration and more features of chronicity and fibrosis.

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