Original Article

FREQUENCY OF THROMBOCYTOPENIA AMONG DIFFERENT AGE GROUPS OF PATIENTS WITH LIVER CIRRHOSIS.

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ABSTRACT

Background: Patients with cirrhosis frequently exhibit thrombocytopenia, which might prompt an unnecessary referral for a bone marrow biopsy. The frequency of thrombocytopenia in liver cirrhosis is largely unknown in the study area. The main aim of our study is to evaluate the prevalence of thrombocytopenia in such patients in the study area.

Material and Methods: A retrospective cross-sectional study was conducted on 268 confirmed liver cirrhosis patients for thrombocytopenia in Khyber Teaching Hospital, Peshawar. Both, male and female subjects with established liver cirrhosis were included in the study while Patients had concurrent illnesses which can induce thrombocytopenia like malaria and dengue fever, ITP. This study takes a total of six months duration. Data analysis was done using SPSS software Version 20.

Results: Results showed that 74.8% of the studied subjects were diagnosed with thrombocytopenia while 25.2% were normal. Thrombocytopenic patients were also categorized into mild, moderate, and severe. Among different age groups, severe thrombocytopenia was found to be highest in all age groups having 113 (42.2%) subjects. Consequently, Severe thrombocytopenia in the age group 51-60 years was diagnosed in 99 (36.9%) cirrhosis patients which is statistically significant with a p-value =0.032. In addition, 56 (20.9%) of the age group 31–40 years age were diagnosed with severe thrombocytopenia.

Conclusion: Our study concluded that thrombocytopenia showed to be one of the diagnostic parameters while to check for complications, related to liver cirrhosis.

Keywords: Thrombocytopenia, Liver cirrhosis, Chronic Hepatitis, platelets

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INTRODUCTION

Thrombocytopenia, which is a common manifestation of liver cirrhosis, can be defined as a platelet count of <150,000 cells/μL.[1] Thrombocytopenia is further categorized as low (100 x 10^9), or moderate (<100 x 10^9). The severity of the liver disease is the main contributing factor despite its complex nature. In addition, a low platelet count is frequently a diagnostic indicator of cirrhosis and the existence of esophageal varices.[2]

The complication can adversely affect the treatment plan for liver cirrhosis by limiting the drug administration and delaying

surgical procedures.[3] As a result of cirrhosis, platelet sequestration in the spleen, bone marrow suppression, interferon-based treatments, and decreased thrombopoietin activity are all risk factors for developing thrombocytopenia (TPO).[4] TPO is mostly created in the liver, and thrombocytopenia can happen when platelets trapped in the congested spleen degrade more and more.[5] Autoantibodies against platelet surface antigens can encourage platelet sequestration and death by cells of the reticuloendothelial system in patients with liver dysfunction associated with hepatitis C.[6]

Cirrhosis is a histopathological diagnosis, although in patients with chronic liver disease (CLD), the presence of several clinical characteristics can point to cirrhosis, and liver biopsy is frequently unnecessary and dangerous.[7] Major indicators of underlying cirrhosis in clinical practice include a history of predisposing factors, the presence of stigmata of CLD, a palpable left lobe or a small liver span, splenomegaly, signs of liver decompensation, findings on abdominal imaging studies, laboratory data, and upper endoscopic findings.[8,9]

According to one study, cirrhosis can be accurately detected in 82–88% of CLD patients by using just a few ultrasonographic symptoms. However, the structural restrictions of this technique reduce the ultrasound's diagnostic efficacy.[10] In a sample of previously non-responders with chronic hepatitis C, a panel of serum fibrosis markers and regular laboratory tests were found to be useful in assessing the likelihood of histological cirrhosis.[11] Noninvasive testing has recently been proven to be effective at detecting severe fibrosis and cirrhosis.[12]

A fast-developing field is the pathogenesis of thrombocytopenia in chronic liver disease.[13] Previously, it was believed that thrombocytopenia was only brought on by portal hypertension-induced congestive splenomegaly, which sequestered the spleen. But now, there are numerous other hypothesized processes relating to platelet synthesis and destruction in cirrhosis.[14]

To date, the prevalence of thrombocytopenia in liver cirrhosis of different age groups is unknown in the study region. Routinely, we encounter several patients having severe thrombocytopenia in liver cirrhosis referred to us by a hematologist. The main aim of our study is to evaluate such prevalence in the study area.

MATERIALS AND METHODS

A retrospective cross-sectional study was conducted on 268 subjects from the Department of Medicine, Khyber Teaching Hospital, Peshawar on patients with liver cirrhosis. A written informed consent of the study was taken from patients included in the study. The study was approved by the Institutional Review Board of Khyber Teaching Hospital, Peshawar. All the samples were collected between 21 March 2021 to 21 Sept 2021 (six-month duration). The patients that were included in the study were identified for liver cirrhosis using the electronic medical record system of the hospital.

Both, male and female subjects with established liver cirrhosis were included in the study. The age margin used in the study was between 18-70 years. Patients having concurrent illnesses can induce thrombocytopenia like malaria, dengue fever, and ITP.

Detailed history and clinical examination were performed; an ultrasound abdomen showing serrated liver margins, dilated portal vein, and coarse liver was taken as cirrhosis. The clinical diagnosis of cirrhosis was made using combinations of several relevant clinical symptoms, such as ascites, splenomegaly, endoscopic evidence of esophageal varices, and/or radiologic evidence of cirrhosis.

5ml of blood sample was taken from the patient for lab detection of thrombocytopenia. A platelet count was performed using a hematology analyzer (Sysmex XP-100). All the samples, having a platelet count lower or higher than the

normal range (i.e. from 150k to 450k per microliter of blood), were confirmed by manual microscopic method.

Data analysis was done using SPSS software for Windows (Version 20.0, SPSS Inc. Chicago). Descriptive statistics were used to calculate the mean, standard deviation, and percentages of data. Thrombocytopenia was stratified among age, gender, duration of disease, and platelet count to see effect modifications. Post-stratification chi square test was applied keeping the P value equal or less than 0.05.

RESULTS

During the six-month study period, data of 268 patients were collected of which 164 (61%) were male subjects and 104 (39%) were female subjects. The mean age of the patients was 45.9 years. The body mass index (BMI) of each patient was calculated with average results of 24.7 for all 268 subjects (Table 1).

Table 1: Baseline demographics of the patients included in the study.

Total	268
Age in years (mean ± SD)	45.9± 17.3
Gender	
➢ Male-N (%)	164 (61%)
➢ Female -N (%)	104 (39%)
Average BMI	24.7

All the study subjects were divided into five different age groups. Similarly, thrombocytopenic patients were also categorized into mild, moderate, and severe. Among different age groups, severe thrombocytopenia was found to be highest in all age groups having 113 (42.2%) subjects. Consequently, 65 individuals were found to be normal (no thrombocytopenia) in all age groups (Table 2).

Severe thrombocytopenia in the age group 51-60 years was diagnosed in 99 (36.9%) cirrhosis patients which is statistically significant with a p-value =0.032. In addition, 56 (20.9%) of the age group 31–40 years age were diagnosed with severe thrombocytopenia. Mild thrombocytopenia was diagnosed in 34 individuals of the age group 51 - 60 years while 11 in the age group 31 - 40 years.

Table 2: Frequency of Thrombocytopenia (mild, moderate, and severe) among different age groups**.**

Platelet count	**20-30 years**	**31-40 years**	**41-50 years**	**51-60 years**	**61-70 years**	**Total N (%)**
Normal (150,00-400,000 cells/µL)	13	19	4	18	11	65 (24.2%)
Mild (101,000-140,00 cells/µL)	4	11	3	34	0	52 (19.4%)
Moderate (51,000-100,00 cells/µL)	5	10	4	16	3	38 (14.2%)
Severe (21,000-51,000 cells/µL)	2	16	35	31	29	113 (42.2%)
Total N (%)	24 (9%)	56 (20.9%)	46 (17.2%)	99 (36.9%)	43 (16%)	268

DISCUSSION

The most frequent and the first aberrant hematologic indicator to show up in cirrhotic patients is thrombocytopenia, which is followed by leukopenia and anemia.[15] Therefore, thrombocytopenia should be given the utmost consideration when assessing individuals with chronic liver disease. However, mild thrombocytopenia is the most typical manifestation in individuals with cirrhosis-related hematological abnormalities. Severe thrombocytopenia (platelet count 50,000) is common in cirrhosis with age > 40 years. It is observed that having a platelet count of 88,000 or less is related to having gastroesophageal varices.[16] In our whole study group, the mean platelet count was 69.9 33 k/uL, while in research participants with cirrhosis, it was 70.1 28.4 k/uL.

Although leukemia is considered a leading cause of thrombocytopenia, liver cirrhosis is now considered to be the most common contributing factor in patients aged>50 years.[17] Our study demonstrates that 36.9% of patients aged 51-60 years have the highest cases of thrombocytopenia compared to the other age groups. This demonstrates the fact that liver disease is more likely to affect the production of platelets in old age as compared to recent liver cirrhosis.[18]

The study demonstrates that about 74.8% of the total patients develop thrombocytopenia during liver cirrhosis. In previous literature different factors contribute to thrombocytopenia in liver cirrhotic patients, some of them include decreased activity of the thrombopoietin and hematopoietic growth factor, antiviral therapy, chemotherapy, and chronic hepatitis C virus infection's suppression of the marrow interferon-based therapy, which can help with the thrombocytopenia developing in cirrhotic patients.[19] Platelet sequestration in the spleen and decreased thrombopoietin production in the liver are the two main factors causing thrombocytopenia in liver cirrhosis.[20]

Our study emphasizes the importance of cirrhosis clinical diagnosis. The diagnostic process outlined in the literature may be deceptive and underestimates cirrhosis as a significant contributor to thrombocytopenia. Like this, there are currently no suitable recommendations for primary care doctors to direct thrombocytopenic patients to suitable subspecialties.[21] The study thus emphasizes the need for training medical professionals in the noninvasive diagnosis of cirrhosis and the correlation of metabolic syndrome symptoms with chronic liver disease.[22] Without understanding the diagnostic relevance of thrombocytopenia in cirrhosis, healthcare professionals may be led astray, which could have an impact on patient care overall and put more strain on available resources. It is significant to note that mortality rates related to the liver and overall, among people with NASH are higher.[23]

CONCLUSION

In summary, this study signifies the high prevalence of thrombocytopenia (75%) among liver cirrhosis patients and highlights the varying severity of thrombocytopenia across different age groups. These findings emphasize the importance of age-specific monitoring and potential interventions for managing thrombocytopenia in cirrhosis patients.

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AUTHOR'S CONTRIBUTION

SK:Introduction/objectives formulation
MAK: Literature search
ZU: Discussion
AN: Result and Analysis
WA: Data Collection and analysis
SE: Data Collection and analysis

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