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Original Research Article

FREQUENCY OF THROMBOCYTOPENIA AMONG PATIENTS WITH CIRRHOSIS

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Abstract: *Thrombocytopenia is a frequently observed condition in individuals suffering from liver cirrhosis.* ***Objective:*** *To find out the frequency of thrombocytopenia in patients with cirrhosis.* ***Methodology****: This cross-sectional study was conducted in the Department of Medicine, Khyber Teaching Hospital, Peshawar, from January 2022 to January 2023. All patients with cirrhosis of duration > six months, with ages of 18-60 years, both genders, and any grade of cirrhosis severity were included in the study. Patients with diseases like malaria, dengue fever, ITP and haematological malignancy, SLE, leukaemia, aplastic anaemia, or on drugs like quinine, penicillin, and digoxin were excluded from the study. Platelet counts were done by sending blood to the hospital laboratory.* ***Result****: Mean age was 47.43 ± 6.22 years, mean BMI was 25.29 ± 4.06 kg/m2, and mean disease duration was 14.86 ± 5.36 years. Males were 75 (53.1%), and females were 67 (46.9%). Thrombocytopenia was present in 108 (75.5%) and not in 35 (24.5%) patients. There was no association of age, gender, or Child-Pugh score with the occurrence of thrombocytopenia. Still, the increased BMI and increased disease duration were significantly associated with thrombocytopenia (p-value <0.05).* ***Conclusion:*** *There is quite a high prevalence of thrombocytopenia in patients with liver cirrhosis. The duration of the disease and increased BMI are significantly associated with the occurrence of thrombocytopenia. Further studies are recommended to have further proof.*

Keywords: Keywords: Liver cirrhosis, Thrombocytopenia, Child-Pugh Score, Body Mass Index

Introduction

Cirrhosis is a common complication of acute and chronic liver injury that involves progressive destruction and regeneration of the liver parenchyma, leading to fibrosis. Hematologic abnormalities are widespread in cirrhosis (1). Pathogenesis of hematological changes is multifactorial and includes portal hypertension-induced sequestration, alteration in bone marrow stimulating factors, and viral and toxin-induced bone marrow suppression (2, 3). Previous studies show the prevalence of abnormal hematologic indices, i.e., Anemia, thrombocytopenia, and leucopenia (alone or in combination) in 6% and 77% of patients with cirrhosis (4). Thrombocytopenia is one of the most common hematological abnormalities in cirrhotics. About 76 % patient of cirrhosis have thrombocytopenia (5). Multiple factors, including splenic sequestration, reduced activity of the hematopoietic growth factor thrombopoietin, autoantibodies against platelet surface antigens, cirrhotic bone marrow suppression by chronic HCV infection and anti-cancer agents, and antiviral treatment with interferon-based therapy, can contribute to the development of thrombocytopenia in cirrhotic patients (4). Thrombocytopenia is caused by splanchnic and splenic sequestration of platelets secondary to portal hypertension (2, 6). Thrombopoietin is the dominant thrombopoietic hormone primarily produced by hepatocytes and helps regulate platelet production. The study by Koike et al. showed that the gradual decline in liver function in patients with cirrhosis causes a decline in thrombopoietin production, resulting in thrombocytopenia (7). In cirrhotic patients, autoantibodies against platelet surface antigens cause the removal of platelets by the splenic and hepatic reticuloendothelial system, leading to rapid platelet destruction and contributing to thrombocytopenia (8). Thrombocytopenia is also caused by bone marrow suppression due to various etiologies like viruses, alcohol abuse, iron overload, and medications. Thrombocytopenia can be caused by HCV suppressing platelet production in the bone marrow and other viral infections (9, 10). It has been suggested that flaviviridae, like HCV, have a direct myelo-suppressive effect in humans (10-12). Long-term alcohol abuse results in toxicity to the bone marrow and peripheral blood elements, causing depressed hematopoietic cell formation, increased destruction, and altered morphology and function of hematopoietic cells (13). Cirrhotic patients are exposed to drug-induced thrombocytopenia through multiple mechanisms that include both direct bone marrow suppression and immunological platelet destruction. Examples of medications commonly prescribed to the cirrhotic patient and associated with thrombocytopenia include interferon (14, 15), azathioprine (16), and antibiotics(17, 18).Thus, the study was designed to determine the frequency of thrombocytopenia in cirrhotic patients.

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Methodology

This descriptive cross-sectional study was conducted at the Department of Medicine, Khyber Teaching Hospital, Peshawar, from January 2022 to January 2023. The sample size was determined to be 143, calculated using a proportion of 76% for thrombocytopenia in patients with cirrhosis, a 95% confidence interval, and a 7% margin of error utilizing the OpenEpi sample size calculator. Data collection was performed through non-probability consecutive sampling.Patients meeting the inclusion criteria, encompassing individuals with cirrhosis lasting more than six months, aged between 18 to 60 years, of both genders and presenting with any grade of liver cirrhosis severity (Child-Pugh A, B, C), were enrolled in the study. Exclusion criteria included concurrent illnesses capable of inducing thrombocytopenia, such as malaria, dengue fever, immune thrombocytopenic purpura (ITP), hematological malignancies, systemic lupus erythematosus (SLE), leukemia, and aplastic anemia. Patients using medications known to cause thrombocytopenia or those who had received platelet transfusions within the last seven days were also excluded.Following approval from the hospital's ethical and research committee, eligible patients were recruited from the outpatient (OPD) and emergency departments and subsequently admitted to the ward for further evaluation. Written informed consent was obtained from all participants, who were then subjected to a detailed medical history, clinical examination, and liver ultrasound to confirm cirrhosis. Blood samples were collected from each patient and sent to the hospital laboratory for platelet count assessment. Thrombocytopenia was defined as a platelet count below 150,000 per cubic millimeter. Data on demographics, liver cirrhosis severity, disease duration, and body mass index (BMI) were recorded in a predesigned proforma, adhering strictly to the exclusion criteria to minimize bias.Statistical analysis was performed using SPSS 22, computing means and standard deviations for quantitative variables and frequencies and percentages for qualitative variables. Thrombocytopenia rates were stratified based on age, gender, liver cirrhosis severity, disease duration, and BMI to explore potential effect modifications. Post-stratification chi-square tests were applied, with a significance level of $p \leq 0.05$. Results were presented using tables and graphs to facilitate interpretation and visualization.

Results

The age ranged from 32 to 60 years, with a mean of 47.43 years and a standard deviation of 6.222. weight varied from 47 to 105 kg, with a mean of 73.52 kg and a standard deviation of 9.309. heights ranged from 1.36 to 2.14 meters, with a mean of 1.7137 meters and a standard deviation of 0.12533. the BMI ranged from 15 to 40 kg/m^2, with a mean of 25.29 kg/m^2 and a standard deviation of 4.067. The duration of the disease ranged from 7 to 30 months, with a mean of 14.8671 months and a standard deviation of 5.36451.

Table 1 Demographic data of participants

	N	Minimum	Maximum	Mean	Std. Deviation
Age (years)	143	32	60	47.43	6.222
Weight (Kg)	143	47	105	73.52	9.309
Height (m)	143	1.36	2.14	1.7137	0.12533
BMI (kg/m^2)	143	15	40	25.29	4.067
Duration of disease (months)	143	7.00	30.00	14.8671	5.36451

Stratification of gender against thrombocytopenia showed that in 76 males, 60 (78.9%) were having thrombocytopenia, while the remaining 16 (21.1%) did not show thrombocytopenia. In 67 females, 48 (71.6%) showed thrombocytopenia, and the remaining 19 (28.4%) did not. This difference was not significant, as the p-value for this was 0.311. Stratification of age against thrombocytopenia showed that in 58 of ≤45 years, 39 (67.2%) had thrombocytopenia, while the remaining 19 (32.8%) did not show thrombocytopenia. In 85 of ≤45 years patients, 69 (81.2%) showed thrombocytopenia, and the remaining 16 (18.8%) did not show thrombocytopenia. This difference was not significant, as the p-value for this was 0.05

. **Table 2 Baseline data of participants**

Gender	**Frequency**	**Percent**
Male	76	53.1
Female	67	46.9
Total	143	100.0
Child-Pugh Score		
Child-Pugh A	39	27.3
Child-Pugh B	65	45.5
Child-Pugh C	39	27.3
Total	143	100.0
Thrombocytopenia		
Yes	108	75.5

No	35	24.5
Total	143	100.0
Age Groups		
≤45 years	58	40.6
>45 years	85	59.4
Total	143	100.0
BMI Groups		
≤27	97	67.8
>27	46	32.2
Total	143	100.0
Duration of disease groups		
≤12 months	49	34.3
>12 months	94	65.7
Total	143	100.0

Also, the duration of the disease was statistically associated with the occurrence of thrombocytopenia. Stratification of duration of disease against thrombocytopenia showed that in 49 of ≤12 months duration of disease, 32 (65.3%) were having thrombocytopenia while the remaining 17 (34.7%) did not show thrombocytopenia. In 94 patients of >12 months duration, 76 (80.9%) showed thrombocytopenia, and the remaining 18 (19.1%) did not show thrombocytopenia. This difference was significant as the p-value for this was 0.043.

Table 3 Comparison of thrombocytopenia in stratified gender

Variables		Thrombocytopenia		Total	*P*-value
		Yes	No		
Gender	Male	60	16	76	0.311
		78.9%	21.1%	100.0%	
	Female	48	19	67	
		71.6%	28.4%	100.0%	
Total		108	35	143	
		75.5%	24.5%	100.0%	

Table 4 Comparison of thrombocytopenia in stratified Child-Pugh score

Variables		Thrombocytopenia		Total	*P*-value
		Yes	No		
Child-Pugh Score	Child-Pugh A	28	11	39	0.398
		71.8%	28.2%	100.0%	
	Child-Pugh B	50	15	65	
		76.9%	23.1%	100.0%	
	Child-Pugh C	30	9	39	
		76.9%	23.1%	100.0%	
Total		108	35	143	
		75.5%	24.5%	100.0%	

Stratification of Child-Pugh score against thrombocytopenia showed that in 39 child pug A patients, 28 (71.8%) had thrombocytopenia while the remaining 11 (28.2%) did not. In 65 patients of Child-Pugh B, 50 (76.9%) showed thrombocytopenia, and the remaining 15 (23.1%) did not. In 39 patients of Child-Pugh C, 30 (76.9%) showed thrombocytopenia, and the remaining 9 (23.1%) did not. This difference was not significant, as the p-value for this was 0.398

Discussion

Thrombocytopenia is one of the most common hematological abnormalities in cirrhosis. In our patients, we found that Thrombocytopenia was present in 75.5% and not in 24.5% of patients. This result is similar to that found by Afdhal et al., who showed that one of the most common hematological abnormalities in cirrhotics was thrombocytopenia, which was 76 % of cirrhosis patients have thrombocytopenia (5). Another author, Bashour et al., showed that in cirrhotic patients, thrombocytopenia occurs in up to 64% of patients and is independent of the cause of cirrhosis19, similar to our result.

Multiple factors, including splenic sequestration, reduced activity of the hematopoietic growth factor thrombopoietin, autoantibodies against platelet surface antigens, cirrhotic bone marrow suppression by chronic HCV infection and anti-cancer agents, and antiviral treatment with interferon-based therapy, can contribute to the development of thrombocytopenia in cirrhotic patients (4). The study by

Koike et al. showed that the gradual decline in liver function in patients with cirrhosis causes a decline in thrombopoietin production, which results in thrombocytopenia(7). Both the prevalence and severity of thrombocytopenia increase in parallel with the extent of the disease, usually becoming clinically relevant when patients develop extensive fibrosis and cirrhosis (19). So, in general, increased disease duration causes increased prevalence of these causes. In our study, we found that patients with an increased duration of disease of more than 12 months have an increased incidence of thrombocytopenia, which was 80.9% of these patients (p-value 0.043). Some studies have found an association between BMI and the incidence of liver cirrhosis. Per 1 kg/m^2, there is an increased incidence of liver cirrhosis in chronic liver disease patients (20). However, the association of BMI with the incidence of thrombocytopenia in cirrhotic patients is scanty, although we find a significant association between thrombocytopenia and increased BMI. In our study, in 97 patients of ≤27 kg/m^2, 73 (75.3%) had thrombocytopenia, and in 46 of ≤27 kg/m2 patients, 35 (76.1%) showed thrombocytopenia (p-value 0.012).

The gender, age, and Child-Pugh score did not show a significant association with the occurrence of thrombocytopenia. Although some studies have found the association of cirrhotic severity with the occurrence of thrombocytopenia (21, 22), the exact values are still lacking. The limitation of our study included the specific population of cirrhotic patients who visit our hospital for symptoms. It does not include patients who are cirrhotic but not present in the hospital so that it may affect the overall prevalence of thrombocytopenia in cirrhotic patients. Another limitation is the lack of cause of cirrhosis in our study and also the lack of other confounding variables like hypothyroidism and metabolic syndrome, which may have increased the BMI and resultant association between BMI and thrombocytopenia, as observed in the result.

Conclusion

There is quite a high prevalence of thrombocytopenia in patients with liver cirrhosis; the duration of the disease and increased BMI are significantly associated with the occurrence of thrombocytopenia. There is no significant relation between the occurrence of thrombocytopenia and gender, age, or Child-Pugh score. Further studies are recommended to have further proof.

Declarations

Data Availability statement
All data generated or analyzed during the study are included in the manuscript.

Ethics approval and consent to participate
Approved by the department concerned. (KTHP-IRB/2021-08-PSH-008)

Consent for publication
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Conflict of interest

The authors declared absence of conflict of interest.

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Coordination of collaborative efforts.
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Conception of Study, Development of Research Methodology Design, Study Design,, Review of manuscript, final approval of manuscript.
Conception of Study, Final approval of manuscript.
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Data entry and Data analysis, drafting article.

References

1. Ashraf S, Naeem S. Frequency of hypersplenism in chronic liver disease patients presenting with pancytopenia. Annals of King Edward Medical University. 2010;16(1 SI).
2. Peck-Radosavljevic M. Thrombocytopenia in liver disease. Canadian Journal of Gastroenterology and Hepatology. 2000;14:60D-6D.
3. Bucsics T, Lampichler K, Vierziger C, Schoder M, Wolf F, Bauer D, et al. Covered transjugular intrahepatic portosystemic shunt improves hypersplenism-associated cytopenia in cirrhosis. Digestive Diseases and Sciences. 2022;67(12):5693-703.
4. Qamar AA, Grace ND, Groszmann RJ, Garcia–Tsao G, Bosch J, Burroughs AK, et al. Incidence, prevalence, and clinical significance of abnormal hematologic indices in compensated cirrhosis. Clinical gastroenterology and hepatology. 2009;7(6):689-95.
5. Afdhal N, McHutchison J, Brown R, Jacobson I, Manns M, Poordad F, et al. Thrombocytopenia associated with chronic liver disease. Journal of hepatology. 2008;48(6):1000-7.
6. Aster R. Pooling of platelets in the spleen: role in the pathogenesis of. The Journal of clinical investigation. 1966;45(5):645-57.
7. Koike Y, Yoneyama A, Shirai J, Ishida T, Shoda E, Miyazaki K, et al. Evaluation of thrombopoiesis in thrombocytopenic disorders by simultaneous measurement of reticulated platelets of whole blood and serum thrombopoietin concentrations. Thrombosis and haemostasis. 1998;79(06):1106-10.
8. Kajihara M, Kato S, Okazaki Y, Kawakami Y, Ishii H, Ikeda Y, et al. A Role of Autoantibody–Mediated Platelet Destruction in Thrombocytopenia in Patients With Cirrhosis. Hepatology. 2003;37(6):1267-76.
9. Hasan S, Jamdar SF, Alalowi M, Al Beaiji SMAA. Dengue virus: A global human threat: Review of literature. Journal of international society of preventive and community dentistry. 2016;6(1):1-6.
10. Young NS. Flaviviruses and bone marrow failure. Jama. 1990;263(22):3065-8.
11. García-Suárez J, Burgaleta C, Hernanz N, Albarran F, Tobaruela P, Alvarez-Mon M. HCV-associated thrombocytopenia: clinical characteristics and platelet

response after recombinant α2b-interferon therapy. British journal of haematology. 2000;110(1):98-103.
12. Wang C-S, Yao W-J, Wang S-T, Chang T-T, Chou P. Strong association of hepatitis C virus (HCV) infection and thrombocytopenia: implications from a survey of a community with hyperendemic HCV infection. Clinical infectious diseases. 2004;39(6):790-6.
13. Ballard HS. Hematological complications of alcoholism. Alcoholism, clinical and experimental research. 1989;13(5):706-20.
14. Sata M, Yano Y, Yoshiyama Y, Ide T, Kumashiro R, Suzuki H, et al. Mechanisms of thrombocytopenia induced by interferon therapy for chronic hepatitis B. Journal of gastroenterology. 1997;32:206-10.
15. Aizawa N, Enomoto H, Takashima T, Sakai Y, Iwata K, Ikeda N, et al. Thrombocytopenia in pegylated interferon and ribavirin combination therapy for chronic hepatitis C. Journal of gastroenterology. 2014;49:1253-63.
16. Connell W, Kamm M, Ritchie J, Lennard-Jones J. Bone marrow toxicity caused by azathioprine in inflammatory bowel disease: 27 years of experience. Gut. 1993;34(8):1081-5.
17. Dutta TK, Badhe BA. Ciprofloxacin-induced bone marrow depression. Postgraduate medical journal. 1999;75(887):571-3.
18. Shaik S, Kazi HA, Ender PT. Rapid-onset piperacillin-tazobactam induced thrombocytopenia. Journal of Pharmacy Practice. 2015;28(2):204-6.
19. Chen TS, Chen PS. The accomplishments of Sir James Cantlie. Journal of Medical Biography. 1999;7(4):197-9.
20. Angulo P. Nonalcoholic fatty liver disease. New England Journal of Medicine. 2002;346(16):1221-31.
21. Vuppalanchi R, Chalasani N. Nonalcoholic fatty liver disease and nonalcoholic steatohepatitis: Selected practical issues in their evaluation and management. Hepatology. 2009;49(1):306-17.
22. D'ALESSANDRO AM, Kalayoglu M, Sollinger HW, Hoffmann RM, Reed A, Knechtle SJ, et al. The predictive value of donor liver biopsies for the development of primary nonfunction after orthotopic liver transplantation. Transplantation. 1991;51(1):157-63.

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