

FREQUENCY OF ACQUIRED DYSFIBRINOGENEMIA AMONG CHRONIC LIVER DISEASE PATIENTS PRESENTING AT TERTIARY CARE HOSPITAL

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Abstract: A cross-sectional study was conducted at the Department of Pathology, Sharif Medical and Dental College Lahore, Pakistan, from January 2023 to June 2023. The total no of patients was 120 presented with chronic liver disease. The frequency of acquired dysfibrinogenemia was determined. The Chi-Square test with a P value < 0.05 as significant was used for the association between categorical variables. Most of the patients presenting were male patients compared to female patients. The frequency of acquired dysfibrinogenemia was 45 (38.3%). We found a significant association between acquired dysfibrinogenemia and the severity of the disease on the Child-Pugh Score. Our study concluded that the frequency of acquired dysfibrinogenemia in chronic liver disease patients was 45 (38.3%).

Keywords: Hepatitis C Virus, Hepatitis B Virus, Chronic Liver Disease, Acquired Dysfibrinogenemia.

Introduction

The liver is a complex organ, and liver disease encompasses a vast spectrum of diseases with varying and sometimes mysterious causes. In 2017, cirrhosis was directly responsible for 1.32 million deaths globally, or 2-4% of all deaths (Sepanlou et al., 2020). Over more than six months, the liver's ability to produce clotting factors and other proteins, detoxify toxic metabolic products and excrete bile progressively declines, leading to chronic liver disease (CLD) (Cheemerla and Balakrishnan, 2021). Liver parenchyma is chronically inflamed, damaged, and regenerated due to CLD, resulting in fibrosis and cirrhosis. Toxins, long-term alcohol misuse, metabolic abnormalities, autoimmune disorders, infection, and genetics are only a few potential causes of chronic liver disease (Marik and Liggett, 2019; Merli et al., 2019).

Different sorts of structural problems in the fibrinogen molecule can lead to dysfibrinogenemia, a clotting condition that is subjective in character. It can be either inherited or acquired (Shapiro, 2018), and both varieties exist. In acquired dysfibrinogenemia, a rise in the sialic acid content of the carbohydrate side chain of fibrinogen molecules is the most common event, explaining this functional anomaly's etiology (Li et al., 2022; Yan et al., 2022). Ultimately, fibrin clot abnormalities are the end outcome of dysfibrinogenemia. Functional defects of fibrinogen limit fibrinogen's normal clot-forming capabilities when activated by thrombin (Francis and Armstrong, 1982).

The fibrinogen clotting activity-antigen ratio is the gold standard for diagnosing dysfibrinogenemia (Francis and Armstrong, 1982). Laboratory abnormalities in other family members are used to confirm a diagnosis of the hereditary

type, and the patient's fibrinogen proteins or fibrinogen genes may be analyzed if further confirmation is needed. In most cases, liver or biliary tract illness is blamed for acquired dysfibrinogenemia (Acar et al., 2017; Sirhindi et al., 2020). Cirrhosis, chronic active liver disease, acute liver failure, acetaminophen overdose, choledochal cyst of the bile duct, and other etiologies of obstructive jaundice are all linked diseases (Casini et al., 2018; Sirhindi et al., 2020). Increased sialylation of fibrinogen's carbohydrate side chains is thought to have a role in the development of acquired dysfibrinogenemia (Nagler et al., 2016).

Due to the high prevalence of hepatitis in our country, this research will aid in the early detection and evaluation of patients to prevent disease progression. Hematologists and gastroenterologists will benefit greatly from this information as they better manage and treat patients with chronic liver disease with coagulation abnormalities and consequences such as bleeding and thrombosis.

Methodology

A cross-sectional study was conducted at the Department of Pathology, Sharif Medical and Dental College Lahore, Pakistan, from January 2023 to June 2023 after obtaining an ethical certificate from the hospital's ethical committee. Patients were selected using non-probability consecutive sampling. We recruited 120 patients between 20 and 60 of the age of either gender presenting with chronic liver disease confirmed by serologic screening and liver function tests. Basic demographics of the patients were recorded, and every patient was subjected to screening for acquired dysfibrinogenemia. Fisher Diagnostics' Pacific Hemostasis Thromboplastin -DS kit was used to measure the

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Prothrombin Time (PT). The Pacific Hemostasis Activated Partial Thromboplastin Time reagents from Fisher Diagnostics were used to measure the Activated Partial Thromboplastin Time (APTT). The reference range for PT and APTT was between 12 and 15 seconds. Utilizing the Thrombin Time kit made available by Weiner Laboratory, the Thrombin Time was measured. The produced bovine thrombin was added to centrifuged plasma samples. The thrombin time began when clot formation began. 13–17 seconds was the typical reference range for this. Tolidine blue, a reagent supplied by British Drug House Ltd., was used to correct the thrombin time in cases where it was discovered to be prolonged. This adjustment aids the diagnosis of acquired dysfibrinogenemia. In cases of dysfibrinogenemia, toluidine blue, acting as a charged reagent, interacts with too much sialic acid linked to the fibrinogen molecule to normalize the thrombin time. To accomplish the correction, the centrifuged plasma sample and the toluidine blue reagent were mixed in a clear glass tube. The introduction of the bovine thrombin reagent was timed along with the start of the clot. All the data was analyzed using IBM SPSS 24. We used the Chi-Square test for associations between categorical data, keeping the P value at 0.05 as significant.

Results

We conducted this study on 120 patients presenting with chronic liver disease. The mean age of the patients was 40.52±11.49 years. The frequency of male patients was 66 (55%), while female patients were 54 (45%). Most patients had hepatitis C virus, 94 (78.3%), while hepatitis B virus was found in 26 (21.7%) patients. The frequency of acquired dysfibrinogenemia was 45 (38.3%). Among the presented patients, 27 (22.5%) had Child-Pugh Score A, Child-Pugh Score B was present in 48 (40%) patients, and Child-Pugh Score C was present in 45 (37.5%) patients. We

observed a significant association between acquired dysfibrinogenemia and Child-Pugh Score; patients with Child-Pugh Score B and C had higher frequencies of acquired dysfibrinogenemia (P = 0.0001). We found a significant association between fibrinogen levels and the severity of the disease, and we observed that the severity of liver disease was increasing with decreasing fibrinogen levels (P = 0.0001).

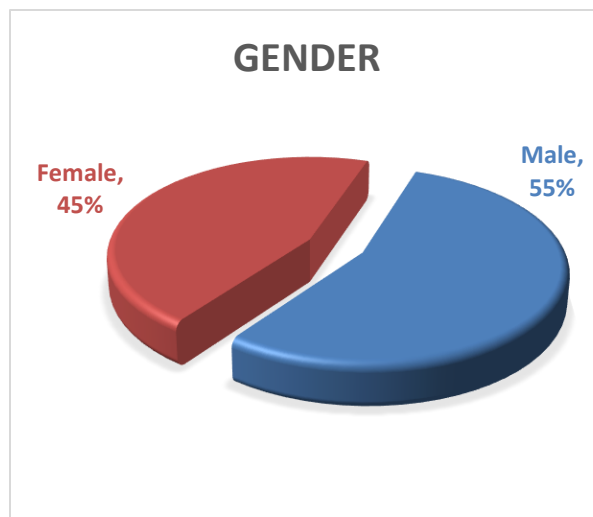


Figure 1 Gender distribution

Table 1 Frequency of acquired dysfibrinogenemia

Acquired dysfibrinogenemia	Frequency	Percent
Yes	46	38.3
No	74	61.7
Total	120	100.0

Table 2 Association of acquired dysfibrinogenemia with Child-Pugh Score

		Child-Pugh Score			Total	P-value
		A	B	C		
Dysfibrinogenemia	Yes	4	15	27	46	0.0001)
		8.7%	32.6%	58.7%	100.0%	
No	23	33	18	74	100.0%	
		31.1%	44.6%	24.3%	100.0%	
Total	27	48	45	120	100.0%	
		22.5%	40.0%	37.5%	100.0%	

Table 3 Association of acquired dysfibrinogenemia with fibrinogen levels

		Fibrinogen levels			Total	P-value
		Normal	Increased	Decreased		
Child-Pugh Score	A	23	1	3	27	0.0001
		85.2%	3.7%	11.1%	100.0%	
	B	14	17	17	48	
		29.2%	35.4%	35.4%	100.0%	
	C	8	9	28	45	
		17.8%	20.0%	62.2%	100.0%	
Total	45	27	48	120		
	37.5%	22.5%	40.0%	100.0%		

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Discussion

Among patients with chronic liver disease (CLD), acquired dysfibrinogenemia—a hemostatic illness characterized by defective fibrinogen molecules—has become a significant worry. Because CLD appearances and patient demographics are so varied, there is a wide range in the prevalence of this disorder across research. The prevalence of acquired dysfibrinogenemia generally tends to rise with the development of CLD, with estimates ranging from 10% to 80% (Cunningham et al., 2002) An increased incidence of advanced liver disease, such as cirrhosis, is most likely caused by the combined impact of impaired hepatic synthesis function and altered coagulation mechanisms. The variable prevalence highlights the complex interaction between liver dysfunction and coagulation problems in CLD, calling for a thorough comprehension of the underlying mechanisms (Noor et al., 2018).

Hepatic dysfunction, coagulation mechanisms, and fibrinogen metabolism combine intricately to cause acquired dysfibrinogenemia in CLD. As CLD advances, the liver, a crucial component in the manufacture of coagulation components, including fibrinogen, loses the capacity to create functioning proteins. Due to compromised clearance systems, dysfunctional fibrinogen molecules build up and influence clot formation and stability (Arif et al., 2002). These abnormal fibrinogen structures complicate the clinical picture of CLD by contributing to both thrombotic and bleeding tendencies. The complex interplay of fibrinogen metabolism, coagulation cascade abnormalities, and hepatic dysfunction emphasizes the multifaceted nature of acquired dysfibrinogenemia in CLD patients (Arif et al., 2002).

Due to the complicated coagulation profile frequently associated with liver illness, diagnosing acquired dysfibrinogenemia in CLD patients presents significant hurdles. Specialized assays are required to appropriately measure the functionality of fibrinogen since conventional coagulation tests may not fully reflect the underlying fibrinogen malfunction. Additionally, the interpretation of diagnostic data may be hampered by additional coagulation disorders such as thrombocytopenia and low coagulation factor levels. This diagnostic complexity highlights the need for a thorough strategy that considers the unique coagulation abnormalities in the setting of CLD, allowing medical professionals to accurately diagnose and treat acquired dysfibrinogenemia and any associated adverse effects (Arif et al., 2002).

We carried out this study on 120 patients presenting with chronic liver disease. The mean age of the patients in our study was 40.52 ± 11.49 years. Male patients were 66 (55%), while female patients were 54 (45%). The majority of the patients were presented with hepatitis C virus. A study also reported similar demographics about their patients presented with chronic liver disease (Sirhindi et al., 2020). The frequency of acquired dysfibrinogenemia was 45 (38.3%) in our study. We observed a significant association between the increasing severity of chronic liver disease according to the Child-Pugh Score and acquired dysfibrinogenemia ($P = 0.0001$). The study, as mentioned earlier, has reported similar findings:

We also observed that the decreasing levels of fibrinogen were significantly associated with increasing severity of

chronic liver disease on Child-Pugh Score ($P = 0.0001$). Similar reports were shown by a study which reported the same findings (Noor et al., 2018).

Conclusion

Our study concluded that the frequency of acquired dysfibrinogenemia in chronic liver disease patients was 45 (38.3%). We observed a significant association between acquired dysfibrinogenemia and increasing severity of chronic liver disease on the Child-Pugh Score.

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.

Consent for publication

Approved

Funding

Not applicable

Conflict of interest

The authors declared absence of conflict of interest.

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