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Original Research Article

A Cross Sectional Study of Coagulation Profile in Various Liver Diseases at Tertiary Care Centre

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Abstract:

Introduction: The liver is the cornerstone of the coagulation system. The physiology of blood coagulation is closely linked to liver function as it synthesizes most of the factors of coagulation cascade and fibrinolytic proteins. So it is responsible for regulation of haemostasis. Hepatic disorders are widely present in tropical countries and are responsible for morbidity and mortality.

Objectives of Study: The objective of this study was to evaluate coagulation abnormalities associated with various liver diseases.

Materials and Methods: The study was conducted in the Central Laboratory of Pathology department, during the period from May 2021 to April 2022. This study included 187 patients clinically diagnosed with liver disease. The coagulation tests PT and APTT were performed and the results were evaluated in groups.

Result: Out of 187 patients, 142(75.9%) were males and 45(24.1%) were females. It was found that Chronic liver disease and Acute viral hepatitis was the most commonly present in most of the participants; 73 (39%) and 46 (24.6%). Followed by Alcoholic Liver Disease, Hepatitis, Hepatocellular Jaundice, Liver Abscess, Acute Liver Failure and Portal Hypertension and Least number of participants had Obstructive Jaundice. In this study, 141 (75.4%) of the participants had Prothrombin time > 16 seconds and 46 (24.6%) of participants had 11 – 16 seconds. Mean PT was 21.9 ± 9.9 sec. PT time in this study ranged from 12.5 - 93.3 sec. 119 (63.6%) of the participants had INR > 1.3 and 68 (36.4%) of participants had 0.9 – 1.3. Mean INR was 1.65 ± 0.75. 125 (66.8%) of the participants had APTT 25 – 40 seconds and 62 (33.2%) of participants had >40seec. Mean APTT was 37.6 ± 5.1 sec. It was found that PT was maximum with acute liver failure followed by chronic liver disease, acute viral hepatitis and Alcoholic liver disease. INR was maximum raised in acute liver failure followed by chronic liver disease and Alcoholic Liver Disease. APTT was maximum in acute liver failure followed by obstructive jaundice.

Conclusion: In advancing liver diseases, damage to liver parenchyma resulting in reduced production of coagulation proteins so there is increase in PT and APTT which increase the risk of bleeding tendencies. Prolongation of PT and APTT in advancing liver cirrhosis indicates damage to the liver parenchyma resulting in decreased production of coagulation proteins with increased risk of bleeding tendencies, which can be detected before these ensue.

Keywords: Cirrhosis, Viral Hepatitis, Obstructive Jaundice, Coagulation.

Introduction

Liver is an important organ of the body having functions of synthesis of plasma proteins and a range of blood clotting factors being produced, some of them exclusively in the organ. [1] All of them are deranged in various liver disorders. Liver plays a predominant role in the regulation of haemostasis. Both cellular and plasmatic coagulation are defective, representing a hallmark of advanced liver disease. [2]

The coagulation cascade in blood is closely linked to liver function as the liver synthesizes most of the factors of the coagulation cascade and fibrinolytic proteins. In addition, the liver is also involved in facilitating the clearance of activated clotting and fibrinolytic factors. [3]

There is substantial increased risk of thrombosis and hemorrhage in patients with liver disease. Because of overlap in the hematological abnormalities observed in the patients with acute infectious or toxic hepatitis, chronic hepatitis, and cirrhosis, the severity of liver function derangement is typically more informative than the etiology.

Prothrombin time (PT) correlates well with the severity of hepatocellular damage as well as with the occurrence of abnormal bleeding and the overall prognosis. Studies have shown that significant prolongation of PT and activated partial thromboplastin time (APTT) in the absence of significant hypofibrinogenemia suggests their importance as a reliable marker of coagulopathies in chronic liver disease patients. [4]

Objectives of Study: The objective of this study was to evaluate coagulation abnormalities associated with various liver diseases.

Materials and Methods

This is a hospital based observational cross sectional study and a total 187 patients including all age groups and both sexes presenting with liver disease admitted in In Patient Department in our institute over a period of 1 year from May 2021 to April 2022 were included in our study.

Place of Study: Central Laboratory, Department of pathology, Jhalawar Medical College, Jhalawar.

Sample Size: 187 cases.

Inclusion Criteria

1. Primary criterion of inclusion was presence of liver disease including cirrhosis, hepatitis, acute or chronic liver failure, liver abscess, alcoholic liver disease and all other liver diseases.
2. All patients of both sexes, age ranging from 20 to 70 years and irrespective of socioeconomic status, were included.
3. Only clinically diagnosed and radiologically confirmed cases of liver pathology had done liver function test at time of admission were included in this study.

Exclusion Criteria

1. All those patients with incomplete history or not willing to participate in study.
2. Patients with primary coagulation disorder were not included.
3. Patients with previous history of coagulation disorders or who took any of the following drugs in the previous week were excluded: aspirin or non-steroidal anti-inflammatory drugs, antihistaminic, penicillin, thiazides, sulfonamides, and anticoagulants.
4. Rejected samples in pre-analytical phases– e.g. Sample not adequate, clotted samples, improper vacutainers collection etc.

Criteria of Liver Disease Patient:

1. Patients were labeled as liver disease patients on the basis of Liver Function Tests (LFT) done in the hospital at the time of admission.
2. Following parameters were included in Liver Function Test, serum bilirubin, SGOT, SGPT, ALP, Total Protein and serum albumin.

Sample Collection and Procedure: Blood sample was withdrawn by specially trained phlebotomists from antecubital vein in the forearm by means of vacutainer containing 3.2% sodium citrate as anticoagulant. While taking the sample, tourniquet was not tied, as it can change the hemo-concentration and results may vary. The ratio of volume of blood to anticoagulant was 9:1. When hematocrit is abnormal with either severe anemia or polycythemia the blood to citrate ration should be adjusted.

For 5 ml specimen the amount of citrate ration should be adjusted.

Hematocrit	Citrate (ml)
0.20	0.70
0.25	0.65
0.30	0.61
0.55	0.39
0.60	0.35
0.65	0.30
0.70	0.26

Sample of the patients were immediately transported to the laboratory and were centrifuged at 3000 to 4000 rpm for 20 minutes to obtain platelet poor plasma. The platelet count should be below 10x109/L. This is best achieved by double centrifugation. Bar code of specific reagent is scanned following which reagent is placed at appropriate site after removing cap (Red indicator will glow if reagent is placed properly). At the same time we add positive and negative controls as specific site for quality control measures. Subsequently, we add patient details with sample ID in system and put centrifuged blood sample at proper place after removing vacutainer cap. After pressing OK on monitor reading will be displayed on monitor after 10 minutes.

Note - STAGO Compact Max STA works on the principle of Viscosity based detection system.

Platelet poor plasma was used in all the coagulation studies. Samples were tested within 4 hours of collection of blood.

All these samples will be processed in central laboratory of the SRG hospital for estimation of different coagulation parameters like, Prothrombin Time and Activated Partial Thromboplastin Time (APTT) by Automated Coagulometer (STA Compact Max-Stago)/Semi Automated (STart Max-Stago) and for hematological parameters by 6-Part Automated Analyzer Sysmex XN-1000/5-Part

SFRI HEMIX5-60 Analyzer. The prothrombin time ratio was calculated and then used to calculate the international normalized ratio.

Statistical Analysis: All the data was collected on predesigned proforma and statistical package for social sciences (SPSS) version 26 was used for data processing purpose. Frequencies and means ± Standard Deviation of data like age, PT and APTT were calculated.

Results

Table-1: Distribution of patients according to Age group

Age Group (years)	Frequency	Percentage
21-30	46	24.6%
31-40	55	29.4%
41-50	37	19.8%
51-60	31	16.6%
61-70	18	9.6%

In this study, 29.4% of the study participants were in the age group of 31–40 years followed by 24.6 % of the participants were in the age group of 21–30 years, 19.8%, 16.5%, and 9.6% of the study participants were in the age group of 41-50 years, 51-60 years, and 61–70 years respectively. Mean age of the study participants in this study was 41.1 ± 13.4 years. 20 – 70 years of patients were included in this study.

Table 2: Distribution of patients according to Gender

Gender	Frequency	Percentage
Male	142	75.9%
Female	45	24.1%

Above table explains that, most of the participants in this study were males 75.9%. Female participants were 24.1%.

Table 3: Distribution of patients according to Clinical Diagnosis

Clinical Diagnosis	Frequency	Percentage
Acute Liver Failure	4	2.1%
Acute Viral Hepatitis	46	24.6%
Alcoholic Liver Disease	25	13.4%
Chronic Liver Disease	73	39.0%
Hepatitis	23	12.3%
Hepatocellular Jaundice	6	3.2%
Liver Abscess	5	2.7%
Obstructive Jaundice	2	1.1%
Portal Hypertension	3	1.6%

Above table explains distribution of study participants according to Clinical diagnosis. It was found Chronic liver disease and Acute viral hepatitis was the most commonly present in most of the participants; 73 (39%) and 46 (24.6%). Followed by Alcoholic Liver Disease, Hepatitis, Hepatocellular Jaundice, Liver Abscess, Acute Liver Failure and Portal Hypertension and Least number of participants had Obstructive Jaundice.

Table 4: Distribution of patients according to Coagulation profile

		Frequency	Percentage
PT (in sec)	11 - 16 sec Normal range	46	24.6%
	> 16 sec Prolonged	141	75.4%
Mean ± S.D.	21.9 ± 9.9 sec		
INR	0.9 - 1.3 Normal	68	36.4%
	>1.3 Raised	119	63.6%
Mean ± S.D.	1.65 ± 0.75		
APTT (in sec)	25 - 40 sec Normal Range	125	66.8%
	> 40 sec Prolonged	62	33.2%
Mean ± S.D.	37.6 ± 5.1 sec		

In this study, 141 (75.4%) of the participants had Prothrombin time > 16 seconds and 46 (24.6%) of participants had 11 – 16 seconds. Mean PT was 21.9 ± 9.9 sec. PT time in this study ranged from 12.5 - 93.3 sec. 119 (63.6%) of the participants had INR > 1.3 and 68 (36.4%) of participants had 0.9 – 1.3. Mean INR was 1.65 ± 0.75. 125 (66.8%) of the participants had APTT 25 – 40 seconds and 62 (33.2%) of participants had >40seec. Mean APTT was 37.6 ± 5.1 sec.

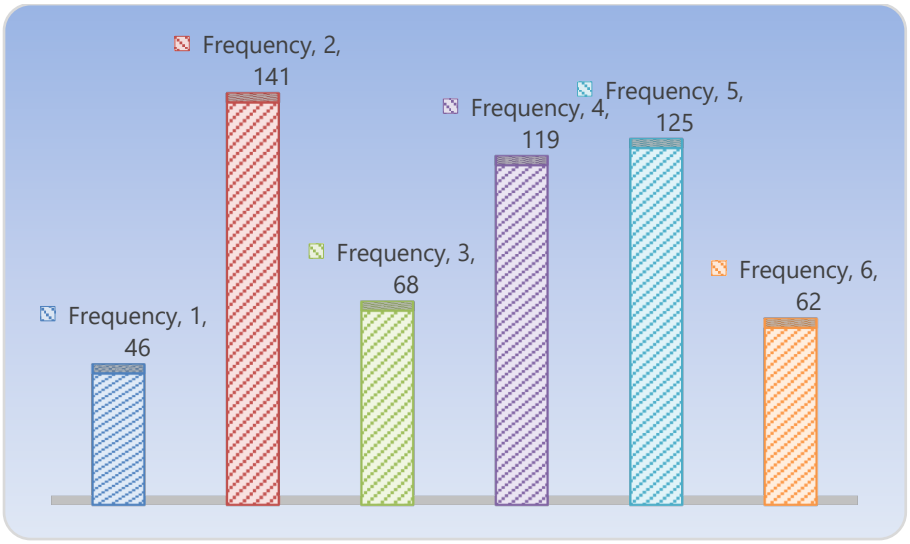

Table 5: Comparison of Mean (S.D) of coagulation factors with various clinical diagnosis

	Clinical Diagnosis								
	Acute Liver Failure	**Acute Viral Hepatitis**	**Alcoholic Liver Disease**	**Chronic Liver Disease**	**Hepatitis**	**Hepatocellular Jaundice**	**Liver Abscess**	**Obstructive Jaundice**	**Portal Hypertension**
PT (in sec)	54.8 (27.5)	21.3 (5.6)	21.3 (5.2)	23.2 (10.5)	17.5 (4.6)	17.6 (3.7)	14.7 (0.4)	18 (0.0)	19.3 (3.4)
INR	4.1 (2.)	1.6 0(.4)	1.6 (0.3)	1.7 (0.8)	1.3 (0.3)	1.3 (0.2)	1.1 (0.0)	1.3 (0.0)	1.4 (0.2)
APTT (in sec)	46.6 (3.1)	35.2 (3.6)	38.6 (4.6)	40.2 (4.5)	33.5 (4.2)	34.8 (4.9)	32.2 (1.1)	42 (0.)	34.7 (3.8)

Author, year	**Mean age**
Garg RP et al, 2020 [7]	40.07 ± 15.21 years
Pahwa et al., 2019 [8]	42.78
Present study	41.1 ± 13.4

Author	**Mean PT value**
Chikkalingaiah K et al 2014 [11]	24.328±8.54
Ahmed et al, 2006 [10]	27.82 ±15.9 sec
Present study	21.9 ± 9.9

Above table explains comparison of Mean (S.D) of coagulation factors with various clinical diagnosis. It was found that PT was maximum with acute liver failure followed by chronic liver disease, acute viral hepatitis and Alcoholic liver disease. INR was maximum raised in acute liver failure followed by chronic liver disease and Alcoholic Liver Disease. APTT was maximum in acute liver failure followed by obstructive jaundice.

Discussion

Because the majority of coagulation factors are produced by parenchymal liver cells, and because the liver's reticuloendothelial system plays a crucial role in the removal of activation products, hemostasis is strongly related to liver activities. [5] The degree of liver function disturbance determines how severe the coagulation problems are. Cirrhosis patients experience a complex hemostatic disruption because anomalies in the activation of the fibrinolytic system, clotting, and primary hemostatic mechanisms. [6]

In this study Age 20 – 70 years of patients were included. Mean age of the study participants in this study was 41.1 ± 13.4 years. In our study male predominance was found. This was similar to other studies. [7], [8] Alcohol intake is predominant in our society irrespective of socioeconomic strata and female are not open to disclose it. Among 187 liver disease patients, the most common presenting complaints in descending order of frequency were

jaundice in 87.7% cases, ascites in 43.3%, abdominal pain in 39.5% and fever in 21.9%.

The PT is widely accepted test to monitor patients having disorders of specific coagulation factors in the extrinsic and common pathway of coagulation. In our study we found that mean PT was 21.9 ± 9.9 sec. Prolonged PT was found in 141 liver disease patient (75.4%).Further with the results of Saatea et al [9], according to which 72.5% studies are needed in order to assess the relevance of cirrhotic patients had elevated prothrombin time. These parameters in a larger population sample to identify other studies also reported a prolonged prothrombin time additional risk factors. In cirrhotic patients, one study conducted by Ahmed et al [10] shows prolonged prothrombin time in cirrhotic patients (Mean ± SD = 27.82 ±15.9 sec). Our findings are also compatible with the other previous studies.

In our study, a progressive delay in prothrombin time associated with altered APTT was significantly noted in the patients of liver disease. The APTT test is done for detection of defects in intrinsic coagulation pathway. It is done for factors XII, IX, XI, XIII, and platelet factor 3 adequacies. In our study, the mean activated partial thromboplastin time was 37.6 ± 5.1 sec. In 62 (33.2%) patients, APTT was prolonged .The present study findings agree with other study. [12] Mean INR was 1.65 ± 0.75 and 63.6% of patient with liver disease had elevated INR.

Thrombocytopenia can occur due to sequestration of platelets in enlarged spleen, in cirrhosis with portal hypertension due to congestive splenomegaly. In cases of hepatitis, there is decreased platelet count due to premature removal of platelets from circulation, formation of antiplatelet antibodies, and disseminated intravascular coagulation Reduced thrombopoietin level also contributes to thrombocytopenia in liver disease.

It was found that PT was maximum with Acute liver failure 54.8(27.5) followed by chronic liver disease 23.2(10.5), Acute viral hepatitis21.3 (5.6) and Alcoholic liver disease21.3 (5.2). INR was maximum raised in acute liver failure 4.1(2.0) followed by chronic liver disease 1.7(0.8) and Alcoholic Liver Disease 1.6(0.3). APTT was maximum in Acute liver failure 46.6(3.1) followed by obstructive jaundice 42(0.0).

Conclusion

We could find that various abnormalities of coagulation tests vary greatly with different liver disorders, duration of the disorders, and their severity. In this study, there was significant prolongation of PT (75.4%) and APTT (33.2%) in patients with liver disease. Study of coagulation profile can help in evaluating hepatic cell function and distinguishing cellular injury. The etiology of impaired prolonged hemostasis due to liver disease is multifactorial and patients include impaired synthesis of coagulation factors. Prolongation of PT and APTT in advancing liver disease shows a damage of liver parenchyma resulting in decreased production of coagulation proteins with increased risk of bleeding tendencies, which can be detected before these ensue, by the determining PT and APTT levels. Thus, preventing patients from landing in life-threatening bleeding complications is possible.

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