Coagulation Profile in Liver Diseases: A Study of 300 Cases in a Tertiary Care Hospital in Uttarakhand, India

Gautam Bhatia, Sanjay Kaushik, Rajnish Kumar, Sanjeev Kishore, Umesh Bhatia

ABSTRACT

Background: The liver is the cornerstone of the coagulation system. The physiology of blood coagulation is closely linked to liver function as the liver synthesizes most of the factors of the coagulation cascade and fibrinolytic proteins.

Objective: The objective of this study was to evaluate coagulation abnormalities associated with chronic liver diseases and determine the coagulation abnormalities using various coagulation studies [prothrombin time (PT), activated partial thromboplastin time (APTT), bleeding time (BT), clotting time (CT), and platelet count].

Materials and methods: This study included 300 patients clinically diagnosed with liver disease and who were divided into three categories – cirrhosis, hepatitis, and other liver diseases. The coagulation tests PT, APTT, BT, CT, and platelet count were performed and the results were evaluated in groups.

Results: Out of the 300 patients, 156 were diagnosed with cirrhosis, 75 were of viral hepatitis, and 69 were of other liver diseases. About 62% (186/300) had prolonged PT. About 39.3% (118/300) had prolonged APTT. The BT was prolonged in 34% (102/300), while CT was prolonged in 10.6% (32/300). Thrombocytopenia was seen in 46% (138/300) patients.

Conclusion: We concluded that various abnormalities of coagulation tests vary greatly with different liver disorders, duration of the disorders, and their severity. 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, Coagulation, Hepatitis.


Source of support: Nil

Conflict of interest: None

INTRODUCTION

The physiology of blood coagulation 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.

Patients with liver disease are at a substantially increased risk of thrombosis and hemorrhage. Owing to the substantial overlap in the hemostatic abnormalities observed in the patients with acute infectious or toxic hepatitis, chronic hepatitis, and cirrhosis, the severity of hepatocellular dysfunction 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.

Cirrhosis, which is an end stage of many liver diseases, is known to be associated with a number of hematological complications, especially thrombocytopenia and coagulation disorders. Chronic hepatitis, especially viral, constitutes a major health problem and can be caused by different etiological agents. In chronic liver diseases, the levels of anticoagulant proteins like antithrombin III, protein S, protein C, and alpha-2 macroglobulin are reduced. Therefore, the coagulopathy pattern in liver disease is not limited to being anticoagulation. Rather, this group of disorders (resulting from cirrhosis of liver) encompasses procoagulant as well as anticoagulation tendencies.

The objective of this study was to evaluate coagulation abnormalities with chronic liver diseases. A heightened state of awareness for health care providers would ultimately result in a better standard of care to the patients.

MATERIALS AND METHODS

This study included 300 patients clinically diagnosed with liver disease attending medicine clinics in a tertiary care hospital in Uttarakhand. The study was approved by the Institutional Ethical Committee.

The patients were divided into three categories as:
1. Cirrhosis
2. Hepatitis

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3. Other liver diseases (liver parenchymal disease, hepatic encephalopathy, cholestasis, fatty liver, liver abscess, chronic liver disease, hydatid cyst).

Inclusion Criteria
Primary criterion of inclusion was presence of liver disease including cirrhosis, hepatitis, pseudocyst, liver abscess, and all other liver diseases. All patients of both sexes, age ranging from 20 to 70 years and irrespective of socioeconomic status, were included.

Exclusion Criteria
Patients with previous history of coagulation disorders or who took any of the following drugs in the previous week were excluded: aspirin or nonsteroidal anti-inflammatory drugs, antihistaminics, penicillin, thiazides, sulfonamides, beta blockers, and anticoagulants.

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 hemoconcentration and results may vary. The ratio of volume of blood to anticoagulant was 9:1. Plasma was obtained following centrifugation of the anticoagulated blood at 3000 rpm for 20 minutes. Complete blood count of the patients was also done (by Automated analyzer Sysmex XP-100), which includes hemoglobin, total leukocyte count, differential leukocyte count, platelet count, and red blood cell count. Biochemical liver function test including serum glutamic oxaloacetic transaminase and serum glutamic pyruvic transaminase were also noted from the investigation chart of the patients.

Coagulation tests, PT – by reagent kit Dade® Innovin® – Siemens and APTT – by reagent kit Dade® Actin® FS activated PTT reagent – Siemens were performed using Transasia CA-50 coagulation analyzer. International normalized ratio by international sensitivity index chart was provided by the reagent manufacturer. Platelet count was done by automated hematology analyzer (Sysmex XP 100) and further confirmed by manual microscopic method. The bleeding time (BT) was done by Duke’s method and clotting time (CT) was calculated using capillary tube method.

OBSERVATIONS AND RESULTS
This is a prospective study of coagulation profile in 300 patients clinically diagnosed with liver diseases at a tertiary hospital in Uttarakhand, India. Cases included were cirrhosis, viral hepatitis, and other liver diseases.

The patients studied were from 20 to 70 years of age. Out of 300 patients, 219 (73%) were males and 81 (27%) were females. A total of 156 (52%) patients were of cirrhosis, 75 (25%) were of viral hepatitis, and 69 (23%) were of other liver diseases. Out of 75 patients of viral hepatitis, 21 (28%) were hepatitis B virus (HBV) positive. Out of 156 patients of cirrhosis, 131 (83.9%) were of alcoholic cirrhosis and 25 (16.1%) were of nonalcoholic cirrhosis. A total of 18 (72%) patients among nonalcoholic cirrhosis were HBV positive. Standard laboratory tests like PT, APTT, platelets, BT, and CT were carried out in all the cases. The following observations were noted. About 62% (186/300) had prolonged PT. About 39.3% (118/300) had prolonged APTT. Bleeding time was prolonged in 34% (102/300), while CT was prolonged in 10.6% (32/300). Thrombocytopenia was seen in 46% (138/300) patients.

Out of 156 patients of cirrhosis, 66% (103/156) had prolonged PT and APTT in 47.4% (74/156). Thus, PT and APTT values were deranged in patients with cirrhosis. Approximately 55.7% (87/156) of patients of cirrhosis had thrombocytopenia; 31.4% (49/156) patients had increased PT and 10.8% (17/156) had prolonged CT.

In hepatitis, 60% (45/75) patients had prolonged PT and APTT was prolonged in 34.6% (26/75) patients. Approximately 40% (30/75) patients had thrombocytopenia. The BT was significantly prolonged in 44% (33/75) patients and CT was prolonged in 9.3% (7/75) patients of hepatitis. Thus, PT and APTT values were significantly raised in patients of viral hepatitis.

There were 69 (23%) patients of other liver diseases. The PT was prolonged in 55% (38/69) patients and APTT was prolonged in 26% (18/69) patients. Thrombocytopenia was seen in 30.4% (20/69) patients. The BT was prolonged in 28.9% (20/69) and CT was increased in 11.5% (8/69) patients of other liver diseases. Thus, PT was significantly raised in patients of other liver diseases as well.

DISCUSSION
The findings for age and sex distribution are compatible with previous studies. The patients’ age ranged from 20 to 70 years. The maximum patients were in the age group ranging from 40 to 50 years. Thus, all the patients were above 20 years. The present study age group is similar to that of Shah and Jansari2 in which all the cases are above the age of 20 years. In the present study, sex distribution is similar to other studies, such as by Devrajani et al3 and Ahmadhameed et al4 where male preponderance is seen in cases of liver diseases.

The patients presented with complaints, such as jaundice, fever, anorexia, fatigue, weight loss, edema of limbs, abdominal pain, and ascites. Among 156 cirrhotic patients, the most common presenting complaints in descending order of frequency were jaundice in 78 (50%) cases, ascites in 72 (46%), abdominal pain in 69 (44%),
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Pedal edema in 62 (40%), fatigue in 61 (39%), anorexia in 31 (20%), fever in 17 (11%), and weight loss in 13 (8%). Jaundice was the most common presenting complaint in hepatitis and cirrhosis. The patients with other liver diseases had fatigue as the commonest complaint.

The PT is the test widely accepted as a means to monitor patients having disorders of specific coagulation factors in the extrinsic and common pathway of coagulation. In the present study, 62% (186/300) patients had prolonged PT in liver diseases (Table 1). The present study findings agree with the study of Malik et al5 (66%; Table 2).

The APTT is the test for intrinsic coagulation pathway. It is especially sensitive for factors XII, IX, XI, XIII, and platelet factor 3 adequacies. There were 39.3% (118/300) patients of liver diseases having prolonged APTT (Table 1). The present study findings agree with Spector and Corn6 study (Table 3).

The BT reflects reduced platelet count.8 Thrombocytopenia is common in patients with liver diseases causing abnormal BT. In the present study, BT is prolonged in 34% (102/300) patients, which agrees with the study of Hedenberg and Korsan-Bengtsen.9

The CT can remain normal even in the presence of severe individual factor deficiency.10 In the present study, abnormal prolongation of CT was observed in only 32 (10.6%) out of 300 patients. The findings of increased CT agree with Mandel and Lazerson study (10%).11

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 cirrhosis. In the present study, 138 (46%) patients out of 300 were having thrombocytopenia in liver diseases. The findings agree with those of Shah and Jansari2 (48%).

Out of 75 patients of viral hepatitis, a total of 45 (60%) had prolonged PT and 26 (35%) patients showed prolonged APTT. There were 30 (40%) patients showing thrombocytopenia. The BT was prolonged in 33 (44%) patients and 7 (9%) were having increased CT. Thus, there is significant thrombocytopenia and prolonged PT in viral hepatitis. The present study findings of PT in patients of viral hepatitis are similar with the findings of Sapna et al.10 In the present study, 40% patients showed thrombocytopenia, which is consistent with the findings of Jain et al11 (50%).

Out of 156 patients of cirrhosis, a total of 103 (66%) had prolonged PT and 74 (47%) patients had prolonged APTT. A total of 87 (56%) showed thrombocytopenia. The BT was prolonged in 49 (31%) patients and 17 (11%) were having increased CT. The present study findings of patients with cirrhosis of liver with thrombocytopenia (56%) agree with the findings of Goulis et al12 (62.7%).

There were 69 (23%) cases of other liver diseases. Out of which, 38 (55%) patients showed prolonged PT. The APTT was prolonged in 18 (26%) patients, while thrombocytopenia was seen in 21 (30%) patients. The BT was increased in 20 (29%) patients and 8 (12%) patients had increased CT.

**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 (62%) and APTT (39.3%) in patients with liver disease. There is significant

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<td>PT</td>
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<td>1967</td>
<td>Spector and Corn</td>
<td>70</td>
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<td>1999</td>
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<tr>
<td>2014</td>
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<tr>
<td>2016</td>
<td>Present study</td>
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thrombocytopenia in 46% patients with liver disease. Study of coagulation profile can help in assessing hepatic cell function and detecting cellular injury. Prolongation of PT and APTT in advancing liver cirrhosis indicates 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 determination of PT and APTT levels. Thus, preventing patients from landing in life-threatening bleeding complications is possible.

REFERENCES