



## Original Research Article

## Coagulopathy associated with Hepato-renal disorders and its significance in critically ill patients

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## ABSTRACT

**Introduction:** Coagulopathy has a high prevalence among critically ill patients and is the result of the derangement of both procoagulant and anticoagulant components of the coagulation system. Liver and renal function tests are some of the most commonly performed blood tests which assess the liver and kidney injury and these are one of the commonest causes of deranged coagulation parameters in these patients.

**Materials and Methods:** This prospective observational study was conducted for two years in Department of Pathology in a tertiary care hospital in university medical college in western India. 219 cases with underlying liver and renal disorders were included in this study. Complete blood counts and coagulation studies including Prothrombin time (PT), Activated Partial Thromboplastin time (APTT), Fibrinogen were done. Statistical analysis was done to evaluate the correlation between various parameters.

**Results :** In our study, hepatic encephalopathy was the commonest cause followed by alcoholic liver disease and liver cirrhosis. Chronic kidney disease was common cause in patients with renal disorders. Deranged Bilirubin levels had a significant statistical association with PT while APTT had a significant association with blood urea levels. Advanced diagnostic and laboratory methods, early recognition of the signs and symptoms of coagulopathy and the complicating factors in liver and renal disorders in these patients is possible today.

**Conclusion :** Liver and renal disorders are one of the important underlying causes for development of coagulopathies in critically ill patients. Prompt and correct identification of these disorders and associated coagulopathy is important for proper management and improving outcome in these patients.

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### 1. Introduction

Coagulopathy has a high prevalence among critically ill patients and is the result of the derangement of both procoagulant and anticoagulant components of the coagulation system. The procoagulant elements include the endothelium, thrombocytes, individual coagulation factors and fibrinogen. The anticoagulant system includes proteins C and S and antithrombin. The third component of coagulation is the fibrinolytic system.<sup>1</sup>

Critically ill patients can be prone to bleeding for a wide variety of reasons including hereditary or acquired

bleeding disorders (platelet function abnormalities, factor deficiencies and factor inhibitors), underlying medical conditions such as hepatic or renal disease and concomitant anticoagulation medications. Besides, certain connective tissue disorders can impact on the integrity of blood vessels, which make them more prone to bruising/bleeding.<sup>2</sup>

Assessment of coagulopathy in critically ill patients is a highly relevant clinical need; however, it is characterized by multiple limitations. The most commonly used tests, including platelet count and PT, APTT, fibrinogen only reflect a limited part of the haemostatic process and thus cannot reliably predict potential bleeding risk.<sup>3</sup>

A critically ill patient with an established coagulopathy may not be able to provide any history, and the diagnosis

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may only be questioned in the light of an abnormal coagulation profile. Coagulopathies are associated with poor patient outcome. It is imperative to appreciate that a significant coagulopathy may exist even in the presence of a 'normal' coagulation profile. Liver and renal function tests are some of the most commonly performed blood tests which assess the liver and kidney injury and is one of the commonest causes of deranged coagulation parameters in these patients.<sup>4</sup>

The liver manufactures thrombopoietin and the majority of haemostatic proteins, both procoagulant and inhibitory. The prothrombin time (PT) is a useful surrogate of liver synthetic function, as liver disease disrupts haemostasis. There is concomitant dysfibrinogenemia due to the failure to remove sialic acid from fibrinogen, and increased fibrinolysis due to impaired tPA clearance from the circulation.<sup>5</sup>

Renal impairment also attenuates haemostasis. The normal platelet response to vessel wall injury is platelet activation, recruitment, adhesion and aggregation and this is defective in advanced renal failure. Uraemia causes dysfunction of vWF with decreased adhesion to platelets and also decreased release of platelet granules and their procoagulant contents, which impairs formation of the primary haemostatic plug. Uraemic bleeding classically presents with signs of impaired microvascular haemostasis such as purpura, epistaxis and bleeding at puncture sites. Renal replacement therapy improves platelet function in end-stage renal failure through control of uraemia.<sup>6</sup>

The key basic management principle of all coagulopathies is that the decision to transfuse blood products should not be based on the results of coagulation tests alone, rather an individualized approach is warranted.

Prompt identification of underlying cause of coagulation abnormalities is required as each coagulation disorder necessitates very different therapeutic management strategies.

## 2. Materials and Methods

This prospective observational study was conducted for two years from 1<sup>st</sup> August 2018 to 31<sup>st</sup> July 2020 in Department of Pathology in a tertiary care hospital of university medical college in western India. 219 cases with underlying liver and renal disorders were included in this study. Complete blood counts (CBC), Prothrombin time (PT), Activated Partial Thromboplastin time (APTT), Fibrinogen were done. For CBC samples were collected in EDTA vacutainer and for PT, APTT, Fibrinogen and 3.2% Trisodium citrate vacutainers were used. Relevant liver and renal function tests were done from the samples taken in plain vacutainer. Institutional ethical committee approval was taken for this study.

### 2.1. Statistical analysis

The collected data was coded and entered in Microsoft Excel sheet. The data was analyzed using SPSS (Statistical Package for social sciences) version 20.0 software. The results were presented in tabular and graphical format. For Qualitative data various rates, ratios and percentage (%) was calculated. For Quantitative data Mean, Standard Deviation (SD), Median etc. were calculated. Pearson chi-square test was applied. A two tailed test with P-value <0.05 was considered as significant.

## 3. Results

Total 219 adult cases of liver and renal disorders were included in this study who presented with coagulopathy. Out of these, 119 patients were males and 100 were females. Out of these 173 were having underlying liver disease and 46 cases were of renal disorders. (Tables 1 and 2).

In liver disorder patients, Hepatic encephalopathy was the commonest cause followed by alcoholic liver disease and liver cirrhosis. Chronic kidney disease was common cause in patients with renal disorders.

**Table 1:** Liver disorders (n= 173)

S.No	Diagnosis	No of cases
1	Alcoholic liver disease	35
2	Chronic liver disease	22
3	Acute liver failure	5
4	Liver cirrhosis	22
5	Hepatic encephalopathy	54
6	Liver carcinoma	1
7	Liver parenchymal disease	11
8	Liver abscess	7
9	Viral hepatitis	13
10	Hepatic AVM	1
11	Fatty liver	2

**Table 2:** Renal disorders (n= 46)

S.No	Diagnosis	No of cases
1	AKI	3
2	CKD	43

The mean PT was 20.0 secs in patients with liver disorders and 21.3 secs in those with underlying renal disorders. The mean APTT was 39.4 in patients with liver disorder and 62.5 secs in patients with kidney disorders. Highest deranged PT was seen in patients with liver disease. The highest deranged APTT was observed in patients with renal disorders.

The mean (SD) fibrinogen was 303.15 mg/dl (203.40) in patients with liver disorders and 520.6 mg/dl in patients with renal disorders. The mean (SD) Serum Glutamic Oxaloacetic Transaminase (SGOT) was 47.69 U/L (37.85) and the mean (SD) Serum Glutamic Pyruvic Transaminase

(SGPT) was 256.40 U/L (779.75) in patients with liver disorders. The mean (SD) Blood urea was 126.28 mg/dl (51.58) and creatinine was 3.31 mg/dl (1.24) in patients with renal disorders.

### 3.1. Co-relation

**Table 3:** Liver: SGOT, SGPT, Bilirubinvs PT, APTT, Fibrinogen

Parameter	PT (p value)	APTT(p value)	Fibrinogen(p value)
SGOT	0.373	0.097	0.459
SGPT	0.083	0.203	0.156
Bilirubin	0.000	0.167	0.532

The values for Bilirubin showed a statistically significant association with Prothrombin time. However, the liver enzymes did not show any significant association with deranged PT, APTT and Fibrinogen levels.

**Table 4:** Renal: Urea,creatinine,vs PT, APTT, Fibrinogen

Parameter	PT (p value)	APTT (p value)	Fibrinogen(p value)
Urea	0.284	0.005	0.418
Creatinine	0.360	0.016	0.489

Deranged levels of Urea had a statistically significant association with APTT. Serum creatinine levels did not show any such association.

## 4. Discussion

Disorders of hemostasis and thrombosis are frequently encountered in critically ill patients. Abnormal blood coagulation often occurs in critically ill patients, which seriously affects their prognosis. In critically ill patients, coagulopathy is a potential problem placing them at greater risk for bleeding disorders. Critically ill patients have activation of both hemostasis and the inflammatory-immune system, leading to both physiological and potentially dangerous pathophysiological responses.<sup>3</sup>

Understanding the relevance of laboratory findings is essential in providing appropriate therapy. Various blood products and haemostatic agents are available to assist in the control of bleeding, and several different classes of anticoagulants are now available for thrombosis. Appropriate use of these agents maximizes therapeutic effect while minimizing complications.<sup>3</sup>

This study investigated the implications of changes in blood coagulation in patients with liver and renal diseases. Coagulopathy, one of the cardinal features of advanced liver disease, is related to multiple factors including impaired synthetic function, thrombocytopenia, excessive fibrinolysis, platelet dysfunction, and disseminated intravascular coagulation.<sup>7,8</sup>

Endothelial dysfunction, increased procoagulant activity especially Factor VIII activity is observed in patients with CKD. The abnormal haemostasis in these patients poses increased risk of thrombosis in these patients.<sup>9</sup>

CKD with high creatinine, urea is associated with hemostatic abnormalities. This was in concordance with study done by Wouter J Kikkert (Aug 2015), also study done by Diana I Jalal (2010).<sup>10</sup>

Due to availability of advanced diagnostic and laboratory methods, early recognition of the signs and symptoms of coagulopathy and the complicating factors is possible today. By use of appropriate interventions and treatment modalities in early stage, the progression of coagulopathy can be halted, and the morbidity and mortality can be reduced.

## 5. Conclusion

Liver and renal disorders are one of the important underlying causes for development of coagulopathies in ICU. Prompt and correct identification of these disorders and associated coagulopathy is important for proper management and improving outcome in critically ill patients.

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## 7. Conflicts of Interest

There are no conflicts of interest.

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