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Coagulopathies in Patients with Liver Cirrhosis

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Abstract: This six months descriptive case series study was conducted in medical unit at Liaquat University Hospital Hyderabad and Jamshoro for the evaluation of the frequency of Coagulation abnormalities in patients with cirrhosis of liver. 118 patients presenting with cirrhosis of liver were selected through non probability consecutive sampling and were evaluate for coagulation profile. The data was collected via questionnaire form and analyzed by SPSS (Statistical Packages for Social Sciences) version 16. The frequencies and percentage were calculated for descriptive analysis. In the present study, out of 118, seventy (59.3%) were males and 48(40.7%) were females. According to Child's Pughs classification, 51(43.22%) cirrhotic patients were in class A, 18(15.25%) in class B and 49(41.53%) in class C. The PT was prolonged (mean + SD = 21.83 ± 4.82 sec) in 60 (50.85%) patients, while 58(49.15%) patients had normal PT which was less than 15 seconds (mean + SD = 12.51 ± 1.03sec). Activated partial thromboplastin time was prolonged in 61 (51.70%) patients, while 57 (48.30%) patients had normal APTT which was less than 40 seconds (mean + SD = 33.07 ± 3.21 sec). PT and APTT were significantly raised in cirrhotic patients.

Key words: Cirrhosis · Coagulation · Prothromobin · Clotting And Liver

INTRODUCTION

Hemostasis is defined as prevention of blood loss. Haemostasis can be disrupted by a variety of liver diseases; however in majority of patient's laboratory abnormalities reflecting impaired haemostasis are not apparent clinically [1]. Cirrhosis, which is a final stage of many liver diseases, is known to be associated with number of hematological complications, especially thrombocytopenia and coagulation disorders [2]. The chronic hepatitis constitutes a major health issue and can be caused by different etiological agents. Hepatitis B virus (HBV) and hepatitis C virus (HCV) infections account for a substantial proportion of liver diseases worldwide [3]. Asymptomatic infection occurred initially, but chronic hepatitis developed which lead to inflammation, signs and symptoms may appear that generally caused by either decreased liver function or increased pressure in the liver circulation [4]. In chronic liver diseases the levels of anticoagulative proteins like antithrombin III, proteins S, protein C and alpha-2 macroglobulin are reduced. At the same time, levels of plasminogen and heparin cofactor II are elevated. Precisely because of this specific reason the coagulopathy pattern in liver disease is not limited to being anticoagulation limited, rather this group of disorders (resulting from cirrhosed liver) encompasses pro-coagulant as well as anti-coagulation tendencies. In majority of cases both pro-coagulant as well as anti-coagulation are in equilibrium state, hence there are no bleeding or thrombotic tendencies [5]. Cirrhosis of liver is a common cause of mortality amongst Pakistani population and frequent cause of admission to our hospitals, however, in Pakistan and other developing countries where cost of health care has always been an issue, cirrhosis and its complications are a major health problem and pose a big challenge to the health economy [6]. The main clinical importance of these coagulation disorders lies in the fact that the ability of the fragile coagulation system to tolerate or recover from an insult is markedly impaired in cirrhotic, easily tipped into a state favoring either hemorrhage or less frequently thrombosis [7]. The objective of this study was to evaluate coagulation abnormalities in patients with liver cirrhosis.

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A heightened state of awareness for healthcare providers would ultimately result in a better standard of care for the patients.

MATERIALS AND METHODS

This six month descriptive case series study was conducted at Medical Unit IV (in door patients only) of Liaquat University Hospital Jamshoro and Hyderabad. Confirmed cases of cirrhosis (by clinical, biochemical, radiological and prior biopsy as described earlier) were selected, both sexes with age >14 years (to exclude pediatric age group). The exclusion criteria of the study were, patients of cirrhosis with a previous history of coagulation disorders and drug intake that causes changes in the coagulation parameters e.g. oral Contraceptive, aspirin, heparin, warfarin, etc, pregnant ladies and other liver disease patterns (non-cirrhotic liver disorders). All cirrhotic patients admitted (from OPD or casualty) in the Medical unit, Liaquat University Hospital Hyderabad, that meets the inclusion and exclusion criteria were enrolled in this study. Informed consent was taken from all patients (or next of kin in case patient is unconscious) and approval was sought from bio-ethics committee of Liaquat University of Medical and Health Sciences. At first an adequate history was taken regarding hematemesis, melena, hemoptysis and hematuria, the presence of petechial hemorrhages or bruises. A focused clinical examination was done regarding the presence of petechial hemorrhages, bruises, the presence of ascites (via shifting dullness and fluid thrill), the grade of hepatic encephalopathy (according to West Haven System) and per rectal examination was done to assess the presence of melena. The clinical examination was focus on bleeding tendencies and the clinical parameters of Child Pugh Class of severity of cirrhosis of liver. Secondly blood tests were done for platelet count, PT and APTT. All the data was collected on predesign proforma and statistical package for social sciences (SPSS) version 16 was used for data processing purpose. Frequencies and means ± Standard Deviation of data like age PT and APTT was calculated. All values considered significant when p value is ≤ 0.05.

RESULTS

This six months study was carried out in Medical Unit IV (in patients only) of Liaquat University Hospital Jamshoro and Hyderabad. 118 patients presenting with cirrhosis of liver were selected for the analysis of coagulation profile. Frequencies in relation to age are shown in Table 1. In current study 70(59.3%) were males and 48(40.7%) were females. According to Child's Pughs classification, 51(43.22%) cirrhotic patients were in Grade A, 18 (15.25%) in grade B and 49 (41.53%) in grade C. PT was prolonged (mean+SD = 21.83±4.82 sec) in 60 (50.85%) patients, while 58(49.15%) patients had normal PT which was less than 15 seconds (mean+SD= 12.51± 1.03sec). Statistical analysis shows significant elevation of PT liver cirrhosis (p value is 0.001) as shown in Table 2. In this study, activated partial thromboplastin time was prolonged in 61 (51.70%) patients, while 57 (48.30%) patients had normal APTT which was less than 40 seconds (mean+SD=33.07±3.21 sec). Statistical analysis shows significant elevation of APTT in liver cirrhosis (p value is 0.001), shown in Table 3.

Table 1: Age distribution of patients

Age Groups (Years)	Frequency	%
30-39	4	3.39
40-49	20	16.95
50-59	48	40.68
60-69	32	27.11
70-79	14	11.87
Total	118	100

Table 2: cirrhotic patients in relation to prothrombin time

Prothrombin time (Normal range: 12-15 sec)	Frequency	%
Normal	58	49.16
Prolonged	60	50.85%
2-3	21	17.79
4-5	26	22.03
+6	13	11.02
Total	118	100

P-value: 0.001 (Significant)

Table 3: Cirrhotic patients in relation to activated partial thromboplastin time

Activated partial thromboplsatin time (Normal range: 30-40sec)	Frequency	%
Normal	57	48.30
Prolonged	61	51.70
Total	118	100

P-value = 0.001 (Significant)

DISCUSSION

Haemostasis is intimately related to liver functions, because most coagulation factors are synthesized in liver parenchymal cells and the liver's reticuloendothelial system serves an important role in the clearance of activation products. The extent of coagulation abnormalities depends upon the degree of disturbed liver

function [8]. Patients with cirrhosis suffer from a complex haemostatic disturbance, due to abnormalities in clotting and fibrinolytic system activation and in primary haemostasis [9].

In this study, the mean prothrombin time was 17.25 ± 5.8 seconds. In 60 (50.85%) patients, PT was prolonged (mean ± SD = 21.83 ± 4.82 sec). 58(49.15%) patients had normal PT which was less than 15 seconds (mean±SD = 12.51 ± 1.03sec). Our results are in agreement with the results of Saatea *et al*, according to which 72.5% cirrhotic patients had elevated prothrombin time [10]. Other studies also reported a prolonged prothrombin time in cirrhotic patients, one study conducted by Ahmed *et al* shows prolonged prothombin time in cirrhotic patients (mean + SD = 27.82 +15.9 sec) [11]. Our findings are also compatible with the other previous studies [12, 13].

In our study, a progressive delay in prothrombin time associated with altered APTT was significantly noted in the patients of liver cirrhosis. In our study, the mean activated partial thromboplastin time was 39.18 ± 7.18 seconds. In 61 (51.70%) patients, APTT was prolonged (mean + SD = 45.39 ± 4.49sec). 57 (48.30%) patients had normal PT which was less than 15 seconds (mean + SD = 33.07 ± 3.21 sec).Our results are in agreement with the results of Saatea *et al*, according to which 77.5% cirrhotic patients had elevated prothrombin time [10]. Other studies also reported a prolonged APTT in cirrhotic patients, one study conducted by Ahmed *et al* shows prolonged APTT in cirrhotic patients (mean + SD = 52.76 + 21.95sec) [11].

A prolongation of APTT in cirrhosis is the result of deficiencies or abnormalities of factors VII, IX, XI, XII, X, V, II (prothrombin) and I (fibrinogen). It is of great interest that the above mentioned work is in agreement with the work done by previous research workers [14, 15]. Prothrombin time is commonly increased in liver diseases because liver is unable to manufacture adequate amount of clotting factors including those involved in extrinsic pathway [16]. Out of factors II, V, VII and X, factor VII is the rate limiting factor in this pathway and thus has the greatest influence on the prothrombin time. Fall of factor VII which has shortest half life (6 hours) has bad prognosis. As the liver function worsens, the APTT may become abnormal, the reason being that factors IX, XI and XII and fibrin stabilizing factors are also produced by the liver. The prolongation of PT and APTT in our study suggests that abnormality may be a consequence of progressive liver damage in liver cirrhosis.

CONCLUSION

PT was significantly raised i.e. 50.85% patients have prolonged PT in cirrhotic patients. APTT was significantly raised i.e. 51.70% patients have prolonged APTT in cirrhotic patients. The etiology of impaired haemostasis due to liver disease is multifactorial and includes impaired synthesis of coagulation factors and altered clearance of activated coagulation factors. Further studies are needed in order to assess the relevance of these parameters in a larger population sample to identify additional risk factors.

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