Evaluation of Hemostaitc Parameters of Sudanese patients with liver Disease attending Khartoum Teaching Hospital

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ABSTRACT

Background: Various hemostatic abnormalities can occur in patients with liver disease, the severity of these abnormalities is dependent on the degree of hepatic dysfunction. Liver disease can cause both quantitative and qualitative abnormalities in coagulation factors, fibrinolytic system and platelets abnormalities, with consequent variable impairment of coagulation parameters.

Methods: In this case control study we examined the 60 liver diseases patients and 30 control healthy subjects, in Khartoum Teaching Hospital (Khartoum, Sudan) during the period 10/3/2012 to 12/6/2012. Prothrombin time (PT), Activated partial Thrmboplastine time (APTT) and fibrinogen level (FL) were determined and categorized by types of liver disease, age, and sex in all study subjects.

Results: The result revealed that there were significant increased in (PT) (P=0.00), APTT (P=0.00) and significant decreased in fibrinogen level (P=0.00) among patients of liver disease when compared with control group. There were no significant changes in coagulation parameters related to age and gender.

Conclusion: There were significant increased in PT and APTT associated with liver diseases and significant decreased in fibrinogen level among patients of liver disease when compared to normal control.

Keywords: Prothrombin time (PT), Activated partial Thrmboplastine time (APTT), Fibrinogen level (FL), von Willebrand Factor (vWF).

INTRODUCTION

The liver plays a major role in hemostasis, as most of the coagulation factors. anticoagulant proteins and components of the fibrinolytic system are synthesized by hepatic parenchymal Additionally, cells. the reticuloendothelial system of the liver helps to regulate coagulation and fibrinolysis by clearing these coagulation factors from the circulation. Finally, because the liver is a highly vascularized organ with vital venous systems draining through the parenchyma, liver diseases can affect abdominal blood flow and predispose significant patients to bleeding problem (Quick AJ., 1973). The etiology of impaired hemostasis resulting from abnormal liver function is often multifactorial. (Peltz S., 1991) And may

include impaired coagulation factor synthesis, synthesis of dysfunctional coagulation factors, increased consumption of coagulation factors, altered clearance of activated coagulation factors and quantitative and qualitative platelet disorders. (Mammen EF, 1994).

Various hemostatic abnormalities can occur in patients with liver diseases such as chronic liver disease (CLD), liver cirrhosis (LC), hepatitis B virus hepatitis C (HBV), virus (HCV), hepatocellula carcinoma (HCC) and obstructive jaundice (Czaja A., et al. severity ,2002). The of these abnormalities is dependent on the degree of hepatic dysfunction. (Mammen EF 1994). Liver disease can cause both gross abnormalities in coagulation factors. (Kramer L., et al. 2002) Commonly, the vitamin K-dependent factors decreased first, starting with factor VII and protein C owing to their short half-life of six hours, followed by reductions in factor II and X levels. Factor V level decreased in both acute and chronic liver disease. (Lee WM et al., 2004). Factor IX level is modestly reduced until advanced stages of liver disease occurs. In contrast, von Willebrand Factor (vWF) which synthesized by the endothelial cells and factor VIII levels may be normal even in the presence of advanced liver disease because there is an increased production VIII by the of factor sinusoidal endothelial cells when the liver is damaged, combined with decreased clearance of the vWF/VIII complex. Fibrinogen levels are rarely decreased and may even be elevated because of abnormal non-functional fibrinogen (dysfibrinogenaemia) related to defective polymerization. A decrease in fibrinogen levels may indicate the presence of disseminated intravascular coagulation (DIC) or progression to fulminant hepatitis with hepatic failure. (Pernambuco 1993) JR., et al. (HarmonDC., et al. 1979) In a study of patients with significant liver injury and associated coagulopathy, factors II, V, VII and X were reduced to a similar degree and were significantly lower than factors IX and XI. Factor VIII. (Pernambuco JR, et al. 1993).

In patients with liver cirrhosis, most coagulation factors and inhibitors of the coagulation and fibrinolytic systems are markedly reduced because of impaired protein synthesis, except for factor VIII and fibrinogen levels, which may be normal or increased. Possible explanations for the increased factor VIII levels increased are the hepatic biosynthesis of vWF and decreased expression of low-density lipoprotein receptor related protein, both of which modulate the level of factor VIII in plasma, rather than increase factor VIII synthesis. Because fibrinogen is an acutephase reactant, its synthesis tends to be preserved in patients with stable cirrhosis. (Sanjo A, et al., 2003). Patients with advanced hepatic failure may present with the entire spectrum of coagulation deficiencies. factor (Heathcoat E, 2000). The levels of coagulation activity markers in patients with chronic liver disease were significantly different in comparison to those in healthy (Sheikh Sajjadieh et al. 2008). Liver cirrhosis causes significant morbidity and mortality in our country, (Albornoz L., et al. 1999). However early diagnosis prevents complications and carries good prognosis. Estimation of fibrinogen level may be helpful in preventing bleeding tendencies. (Mackie IJ., et al. 2003) Plasma fibrinogen levels of confirmed liver cirrhosis in 18-60 years age admitted patients of Khyber Teaching Hospital were determined and compared with normal controls, to establish it as a marker for diagnosis in cirrhosis liver and prognosis. Significantly low levels in patients were recorded as compared to controls. 40% cases showed low fibrinogen level, while nearly 44% had normal levels. Fibrinogen level was low in early and terminal cirrhosis and high in advancing cirrhosis as compared to controls levels (Saatea A, et al., 1999). Many of these hepatic functions may be assessed by laboratory procedures to gain insight into the integrity of the liver. (Zimmerman H. 1999).

MATERIALS AND METHODS

This is a case control study conducted from 10 March 2012 to 12 June 2012 in Khartoum teaching hospital. Individuals affected with liver disease were selected for this study. 4.5 ml of venous blood was collected from 40 liver diseases' patients and 20 samples collected from healthy individuals as control under sterile condition and drained into container with 0.5 trisodium citrate anticoagulant (Lewis S.M, *et al.*, 2006). Platelet poor citrate plasma were obtained to be used for prothrombin time, activated partial time and fibrinogen level by using automated Coagulometer analyzer Sysmex (CA 500 base on Clauss method (Clauss A., *et al.* 2002)) . Data analyzed using statistical package for social science (SPSS) version 13 using independent t-test significant level set at (P value ≤ 0.05).

Ethical Considerations: All participants informed about the were study objectives; informed consent was obtained from all participants. It was consider that all data from such patients regarded as secret data and all personal published information will not or permute.

RESULTS

Table1 showed characteristics of the study population (patients and control group). The mean levels of PT in

Table1: Characteristics of the study population

patient's categorized liver disease were 18.5 ± 8.20 in CLD 40 ± 2.27 in liver cirrhosis, 43 ± 3.0 in hepatitis B virus, 39 ± 3.1 in hepatitis C virus, 28.2 ± 10.1 in hepatocellular carcinoma, 30 ± 2.6 in obstructive jaundice and 12.5 ± 6.0 in control subjects (Table 2).

The mean levels of APTT in patient's categorized liver diseases were 39.0 ± 11.2 in CLD 55 ± 17.3 in liver cirrhosis, 58 ± 27.8 in hepatitis B virus, 60 ± 24.8 in hepatitis C virus, 63 ± 26.2 in hepatocellular carcinoma, 48 ± 22.2 in obstructive jaundice (O. Jaundice) and 29.4 ± 2.3 in control subjects (Table 2). The mean levels of FL in patient's categorized liver diseases were 3.41 \pm 1.53 in CLD 1.92 ± 1.55 in liver cirrhosis, 3.7 ± 3.88 in hepatitis B virus, 1.97 ± 0.87 in hepatitis C virus, 3.3 ± 1.0 in hepatocellular carcinoma, 3.54 ± 2.21 in obstructive jaundice and 2.6 ± 0.4 in control subjects (Table 2).

| Characters | patients | Control | | |
|----------------------|--------------|--------------|--|--|
| Study group | 60 | 30 | | |
| Male & female | 40 & 20 | 21 & 9 | | |
| Age group | 35 ± 4.6 | 35 ± 4.5 | | |
| CLD | 15 | - | | |
| Cirrhosis | 15 | - | | |
| HBV | 15 | - | | |
| Obstructive jaundice | 14 | - | | |
| НСС | 4 | - | | |
| HCV | 2 | - | | |

Table shows the data of the patients and frequency of liver diseases among them.

| Table 2: Coagulation | parameters in | different types | s of liver diseases |
|----------------------|---------------|-----------------|---------------------|
| <u> </u> | 1 | 21 | |

| rable 2. Congulation parameters in anterent types of inver diseases | | | | | | | |
|---|------------|-------------|----------|------------|------------|-------------|----------|
| Parameter | CLD | L.cirrhosis | HBV | HCV | HCC | O. Jaundice | Control |
| PT / (sec) | 18.5±8.20* | 40±2.27* | 43±3.0* | 39±3.1* | 28.2±10.1* | 30±2.6* | 12.5±0.6 |
| Mean \pm SD | | | | | | | |
| APTT (sec) | 39±11.2* | 55±17.3* | 58±27.8* | 60±24.8* | 63±26.2* | 48±22.2* | 29.4±2.3 |
| Mean \pm SD | | | | | | | |
| FL (g/dl) | 3.41±1.53 | 1.92±1.55* | 3.7±3.88 | 1.97±0.87* | 3.3±1.0 | 3.54±2.21 | 2.6±0.4 |
| Mean \pm SD | | | | | | | |

The table shows the data as mean values \pm standard deviation.

* Significant compared to control group

Coagulation parameters show significant different between patients and control (P value < 0.05).

Significant prolonged PT and APTT in patients with liver diseases compared to normal control.

Significant lower levels of fibrinogen in patients with liver cirrhosis and HCV compared to normal control.

DISCUSSION

The liver plays a crucial role in hemostasis as it is responsible for the synthesis of most of the clotting and fibrinolytic proteins and the clearance of these coagulation factors from the circulation. Acute and chronic liver diseases are associated with a spectrum of hemostatic defects, and their severity tends to parallel the degree of hepatic injury. (Dufoui DR., et al. 2002) The etiology of impaired hemostasis due to liver disease is multifactorial and impaired includes synthesis of coagulation factors. vitamin K deficiency, and altered clearance of activated coagulation factors, excessive fibrinolysis, DIC and quantitative and qualitative platelet disorders. (Mammen EF, 1994). This study involved a total of sixty liver disease patient and thirty healthy persons as control. In case the males were 40 (66.7%), females were 20 (33.3%), according to age group less than 35 were 19 (31.7%) and more than 35 were 41 (68.3%). According to control male were 21(66.3%) and female were 9, less than 35 were 13 (43.3%) and more than 35 were 17(66.7%).

The study reveal that the PT and APTT of Sudanese patients with liver disease were significantly increase in comparison to normal control group, the finding is consistent with study in Ukraine (Sheikh Sajjadieh et al. 2008). And study reported in Krashi by (sohail A., 200). We observed that the mean of fibrinogen levels were significantly lower than the mean of control group (3.61 ± 0.67) P.value < 0.05 particularly in liver cirrhosis and hepatitis C virus infections the findings consistent with study in Pakistan reported that liver cirrhosis cases showed low fibrinogen level, while some portion patients had normal fibrinogen levels; the study concluded that fibrinogen level was low in early and terminal cirrhosis and high in advancing cirrhosis. (Saatea A et al. 1999).

Conclusion: We observed decreased mean fibrinogen levels and prolonged PT, APTT in patients with liver diseases except we found decreased mean fibrinogen levels in patients with liver cirrhosis compared to normal control either due to a mild damage to hepatic cells or due to inflammation.

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ARABIC SUMMARY

تقييم دلالات سيولة الدم في المرضى السودانيين الذين يعانون من أمراض الكبد في مستشفي الخيم دلالات سيولة الدم في المرضى الخرطوم التعليمي

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المقدمة:

هذه دراسة وصفيه تحليليه (حالة وحالة ضابطه) أجريت بمستشفي الخرطوم التعليمي في الفترة من2012/3/10 الى 2012/6/12 وتهدف هذه الدراسة لقياس زمن سيولة الدم الجزئي والجزئي المنشط ومعدل الفبرينوجين لمرضى الكبد في السودان.

طرق القياس:

حيث تم جمع ستين عينة دم مأخوذة من الوريد في حاويات سترات الصوديوم من مرضي الفشل الكبدي وكذلك تم جمع ثلاثين عينه دم من أفراد أصحاء كعينه ضابطه تم فصل البلازما وأجريت اختبارات السيولة الآتية : زمن البروثرومبين، معدل السيولة العالمي ، زمن البروثرومبين المنشط الجزئي وتم قياس معدل الفبرينوجين باستخدام جهاز _ Sysmex CA500 Coagulometer.

وتم تحليل النتائج باستخدام برنامج الحزم الإحصائية للمجتمع الإصدار (11.5) . وأوضحت الدراسة أن هنالك زيادة بدرجه معنوية في مرضي الكبد بكل من زمن البروثرومبين وزمن البروثرومبين المنشط الجزئي عند مقارنتها مع المجموعة الضابطة.

كما أوضحت انخفاض معدل الفبرينوجين للمصابين بمرض الكبد بدرجه معنوية عند المقارنة مع المجموعة الضابطة. بينما هنالك زيادة بدلالة معنوية في معدل الفبرينوجين للمرضى المصابين بتليف الكبد.