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RESEARCH ARTICLE

EVALUATION OF HAEMOSTATIC CHANGES AMONG CHRONIC LIVER DISEASE SUDANESE PATIENTS WITH HEPATITIS C INFECTION

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ABSTRACT

Hepatitis C virus (HCV) infection is a common global public health problem. HCV is considered as the main cause of chronic liver diseases. In patients with liver disease, substantial changes within the haemostatic system are frequently observed. This study aimed to evaluate haemostatic changes among chronic liver disease patients due to hepatitis C infection in Sudan. The study included 97 patients, their fibrinogen levels, PT, APTT, TT, platelets count and liver function tests were measured and compared with 50 healthy subjects as controls. Mean fibrinogen level (443.37±59.00 mg/dl), mean PT (24.22±9.09 seconds), mean APTT (43.60±4.48 seconds) and mean TT (23.09±6.11 seconds) were significantly higher among patients than the controls (p 0.000 for each parameter). Mean platelets count (100.89±29.26X10^9/L) was significantly low among patients, when compared with the controls (p value 0.000). The study showed a significant association between fibrinogen levels and ALP (p value 0.043). There was no significant association between fibrinogen level and the other liver function tests. In conclusion, our study observed haemostatic changes with higher fibrinogen level, lower platelets count and prolonged PT, APTT and TT among the study group than the controls.

INTRODUCTION

Hepatitis C virus (HCV) infection is a common global public health problem (Alavian and Fallahian, 2009; Alavian *et al.,* 2011). Approximately 200 million individuals are infected with HCV worldwide (Alavian *et al.,* 2009). The prevalence of HCV in Sudan is reported to be (2.2–3%) among the general population (Elhawary *et al.,* 2011; Mudawi, 2008), and it was found to be 23.7% in haemodialysis patients (Abou *et al.,* 2009). HCV is considered as the main cause of liver diseases in both developed and developing countries and contributes to the increasing risk of liver failure and hepatocellular carcinoma (HCC) (Alavian *et al.,* 2009; Alter, 2007; Alavian, 2010a; Alavian *et al.,* 2005). It is responsible for 20% of all acute hepatitis cases, 70% of all chronic hepatitis cases, 40% of all liver cirrhosis cases, 60% of HCCs, and 30% of infections in liver transplants in Europe (Ahmadipour *et al.,* 2005; Alavian *et al.,* 2010 b). In patients with liver disease, substantial changes within the haemostatic system are frequently found (Lisman *et al.,* 2002). These changes include thrombocytopenia and platelet function defects, decreased circulating levels of coagulation factors and inhibitors, and decreased levels of proteins involved in fibrinolysis (Lisman and Leebeek, 2007). Although routine haemostatic tests among chronic liver disease patients such as the platelet count, prothrombin time (PT) and activated partial thromboplastin time (APTT) may indicate a bleeding tendency, clinical and laboratory evidences indicate that the haemostatic system is in a 'rebalanced' status, since changes in prohaemostatic pathways are accompanied by changes in antihaemostatic pathways (Lisman *et al.,* 2006; Lisman and Leebeek, 2007; Caldwell *et al.,* 2006) For example, decreased levels of procoagulant proteins are accompanied by decreased levels of natural anticoagulant proteins (Tripodi *et al.,* 2009). The net effect of all haemostatic changes thus is often a rebalanced, yet functional system. However, the balance is far more precarious and potentially unstable compared to the haemostatic balance in healthy individuals, which explains the potential occurrence of both bleeding and thrombotic complications in patients with cirrhosis. This study aimed to evaluate the haemostatic changes among chronic liver disease patients due to hepatitis C infection in Sudan, by determining fibrinogen level, PT, APTT, TT and platelets count.

MATERIALS AND METHODS

This is a prospective case-control study which included 97 patients with established diagnosis of chronic liver disease due to hepatitis C infection (diagnosis based on liver biopsy or on obvious clinical, endoscopic, biochemical or imaging features;

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and positive anti-HCV) who were admitted to Khartoum Teaching Hospital; and fifty age and sex matched healthy individuals as controls. None of the patients were receiving anticoagulant therapy at the time of the study. Patients with other known causes of haemostatic changes such as pregnancy, smoking, diabetes, malignancy and hypertension were excluded. Informed consent was obtained from each subject before enrollment in the study. Five ml of venous blood was collected from each subject: 2 ml in 3.8% trisodium citrate (9:1 vol/vol), kept on ice until centrifugation at 2500g for 30 minutes at 4°C, plasma samples were immediately frozen and stored at - 80°C for subsequent coagulation analysis; 2 ml in heparin for chemical analysis; and one ml in EDTA for platelets count. Laboratory analysis was performed at the Department of Haematology, Faculty of Medical Laboratory Sciences, Alneelain University.

Fibrinogen level was measured by Clauss modified method using a test kit produced by (TECHNOCLONE GMBH, AUSTRIA). The method uses a functional assay based upon the time for fibrin clot formation, in brief, Diluted plasma is clotted with a high concentration of thrombin, and the concentration of fibrinogen is determined by comparing the plasma clotting time to a calibration curve of a reference plasma with a series of dilutions (1:5 –1:40). PT, APTT and thrombin time (TT) were measured using coagulometer (Sysmex CA 50) which rely on scattered light detection method. Platelets cell count was performed by automated cell counter (Sysmex KX-21N).

Liver function tests, included total bilirubin, direct bilirubin, total protein, albumin, alkaline phosphatase (ALP), glutamic oxaloacetic transaminase GOT and glutamic pyruvic transaminase (GPT), were performed by automated chemical analyzer (Biosystem). Statistical analysis was performed using statistical package for social science (SPSS) software. Evaluation of patient's data was performed using the t-test and Pearson correlation test. Results with p value < 0.05 were considered statistically significant.

RESULTS

Patients included 93 male and 4 female, there median age was 33 year, with minimum age of 19 and maximum of 50 years. Table 1 showed the results of the fibrinogen level, PT, APTT, TT, platelets count and liver function tests. Mean fibrinogen level of the patients was 443.37±59.00 mg/dl, the levels were elevated (>400 mg/dl) in 76.3% (75/97) and were always normal among the control group with a mean level of 213.65±103.57 mg/dl. Fibrinogen level was significantly higher among patients than the controls (p value 0.000). PT, APTT and TT were prolonged among patients when compared to the controls (p 0.000 for each parameter). Thrombocytopenia was observed in 93.8% (91/97) of patients. Mean platelets count was significantly lower among patients than the controls (p value 0.000). The study showed a significant association between fibrinogen levels and ALP (p value 0.043). There was no significant association between fibrinogen level and total bilirubin (p value 0.844), direct bilirubin (p value 0.695), total protein (p value 0.859), albumin (p value 0.522), GOT (p value 0.853) and GPT (p value 0.126).

Table 1. Results of the coagulation and liver function tests

	Patients	Controls	P value
Number	97	50	
Fibrinogen mean±SD (mg/dl)	443.37±59.00	272.98±53.70	0.000
PT mean±SD (seconds)	24.22±9.09	14.98±0.82	0.000
APTT mean±SD (seconds)	43.60±4.48	34.10±2.72	0.000
TT mean±SD (seconds)	23.09±6.11	14.38±1.24	0.000
Platelets count	100.89±29.26	325.04±62.66	0.000
GPT	108.01±21.31	33.48±2.72	0.000
GOT	66.26±4.32	33.34±3.65	0.000
ALP	141.37±10.66	91.14±6.76	0.000
Albumin	3.27±0.75	3.60±0.61	0.009
Total Protein	5.63±0.61	6.26±0.41	0.000
Total bilirubin	4.20±0.93	0.74±0.62	0.000
Direct bilirubin	2.51±0.70	0.23±0.01	0.000

DISCUSSION

Hepatitis C virus (HCV) infection is a common global public health problem. It has emerged as a major cause of chronic liver disease worldwide. In this study we evaluated the haemostatic property among Sudanese patients with chronic liver disease due to hepatitis C infection by determining fibrinogen level, PT, APTT, TT and platelets counts. The study included 97 patients, their fibrinogen levels, PT, APTT, TT, platelets count and liver function tests were measured and compared with 50 age and sex match healthy subjects as controls. We observed higher fibrinogen levels among patients, when compared with the normal healthy controls. Similar finding, with higher fibrinogen level, had previously been reported (Alyan *et al.,* 2008; Amin *et al.,* 2014). The means PT, APTT and TT were also higher among patients than the controls; this observation suggests a contribution of insufficient coagulation factor activity in the aetiology of bleeding complications in this population. However, It was shown that routine coagulation tests (PTs, APTTs) often overestimate coagulopathy, and the prolongation in these tests does not necessarily have an increased bleeding tendency in liver disease (Lisman *et al.,* 2006; Tripodi and Mannucci, 2007), we observed lower platelets count among the study group than the controls, this is a common observation among liver disease patients (Lisman and Leebeek, 2007). The interpretation of these haemostatic abnormalities is much less straightforward as The haemostasis system of liver disease patients is "rebalanced" since changes along one pathway generate compensatory changes in the other pathway (Lisman and Leebeek, 2007; Tripodi & Mannucci, 2007). Although there was a significant association between the fibrinogen level and the ALP, the results of the other liver function tests did not reveals an association between the haemostatic changes and the extent of liver dysfunction among the study group..

Conclusion

In conclusion, we evaluated the haemostatic property among chronic liver disease patients due to hepatitis C infection in Sudan by determining fibrinogen level, PT, APTT, TT and platelets count. Our study observed haemostatic changes with higher fibrinogen level, lower platelets count and prolonged PT, APTT and TT among the study group than the controls.

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Authors Contribution

Marwa S. H. Saeed and Mahdi.H.A. Abdalla conceived the idea of the study, collected and analyzed samples and data and wrote the manuscript.

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