MEDICAL CHANNEL

Original Article

THE IMPORTANCE OF ABNORMAL COAGULATION TESTS AND MANAGEMENT OF BLEEDING IN CHRONIC LIVER DISEASE

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ABSTRACT

Objectives: This Study was basically conducted to high light the importance of plasma prothrombine time (PT), Activated Partial Thromboplastine Time (APTT), fibrinogen levels and platelet count /cumm in patients with liver disease such as chronic hepatitis and cirrhosis. To give recommendations for the management of bleeding in these patients.
Study Design: Descriptive and Experimental Study.
Place And Duration Of Study: Medical Unit-II Peoples Medical College Hospital and Pathology Department, Peoples Medical College, District Shaheed Benazirabad from Feb: 2008 to Feb: 2009.
Subjects And Methods: Total 100 subjects were selected among them 50 were patients while 50 were healthy controls which were age, sex and socio economically matched with patients. All the 50 patients were divided in to two groups A and B. Group A composed of 25 patients with chronic hepatitis. Group B composed of 25 patients with cirrhosis of liver, the diagnosis of chronic hepatitis and cirrhosis of liver was confirmed on the basis of clinical as well as laboratory findings.
Results: The mean ages and males to females ratios of patients with chronic hepatitis and cirrhosis of liver were 37.5±12.5, 40±15, 2.6:1 and 1.5:1 respectively. The statistically significant difference was found in gender of these patients $p<0.05$ The Plasma levels of PT, fibrinogen and platelet count /cumm in patients with chronic hepatitis were not significantly different from the healthy controls, while Plasma APTT level was significantly different from the controls. Both Plasma APTT and PT levels were significantly different from controls in patients with cirrhosis. while plasma fibrinogen level and platelet count were not significantly different from control.
Conclusions: From the above study, it was concluded that determination of plasma PT, APTT, fibrinogen levels and platelet count /cumm are important for clinician to control bleeding in patients with liver disease by fresh frozen plasma (FFP) and vitamin k administration.

Keywords: Activated partial thromboplastine time (APTT), Prothrombine time (PT), Fibrinogen level, Platelet count, Chronic hepatitis, Cirrhosis.

INTRODUCTION

The physiology of homeostasis depends upon coagulation and anticoagulation systems, the former one prevent blood loss at the site of vascular injury with formation of a platelet plug by their aggregation and fibrin clot after vasospasm.[1]The latter one prevent in appropriate intravascular clot formation with anticoagulant such as antithrombin, therefore balance between these two systems of homeostasis is essential to prevent bleeding and dangerous intravascular clots.[2] The liver plays a important part in homeostasis because synthesis of coagulation, anticoagulation factors, clearance of activated clotting factors and storage of vitamin k that activate factor ii, vii, ix, and x take place in liver.[3] The haemostatic abnormalities such as bleeding and thrombosis in patients with chronic liver disease due to hepatic dysfunction can results from impaired synthesis of coagulation

factors, disseminated intravascular coagulation (DIC) due to the failure of clearance of activated clotting factors and synthesis of anticoagulants, vitamin K deficiency and thrombocytopenia secondary to splenomegly.[4] The patients with bleeding and chronic liver disease should be assessed by plasma PT, APTT, Fibrinogen levels and platelet count /cumm determination.[5] Administration of vitamin K and fresh frozen plasma are required for management of bleeding in patients with chronic liver disease.[6] Hence our purpose of study is to high light important Association between laboratory coagulation tests such as plasma PT, APTT, Fibrinogen levels and platelet count /cumm determination and bleeding in patients with chronic hepatitis and cirrhosis of liver. We give strong suggestion and recommendation to the physician for management of bleeding in these patients but risk of DIC should be kept in mind in cirrhotic patients.

SUBJECTS AND METHODS

This study was a descriptive and experimental, performed at pathology and medicine departments of people's medical college from February 2008 to 2009. Total 100 subjects were selected and 50 were patients while 50 were healthy controls which were age, sex and socio economically matched with patients. All the 50 patients were divided in to two groups A and B. Group A composed of 25 patients with chronic hepatitis and their ages ranged between

TABLE: I

AGE AND SEX DISTRIBUTIOIN IN PATIENTS WITH CHRONIC HEPATITIS AND CIRRHOSIS (GROUP A" AND B")

N = 50

SEX	GROUP A N = 25	GROUP B N =25	AGE IN YEAR MEAN + SD
MALE	18(72%)	15(60%)	37.5±12.5
FEMALE	7(28%)	10(40%)	40±15
P-VALUE	P<0.05	P<0.05	P> 0.5 non significant

KEYS:

- P – VALUE OF 0.05 OR LESS ARE CONSIDERED STATITICALY

SIGNIFICANT.

- VALUES CAN EXPRESSED AS A MEAN STANDRED DEVIATION(±SD).
- N=NUMBER OF PATIENTS.

TABLE : II

CILINICAL FINDINGS IN PATIENTS WITH CHRONIC HEPATITIS AND CIRRHOSIS OF LIVER (Group A AND B) (N=50)

GROUP A (N=25)			GROUP B (N=25)		
Serial no:	**CILINICAL FINDINGS**		**Serial no:**	**CILINICAL FINDINGS**	
i	Fatigue ness	80%	I	Weakness	75%
ii	Loss of weight and Appetite	75%	Ii	Loss of weight and appetite	70%
iii	Spiderangioma	65%	Iii	Fatigue ness	72%
iv	Palmer erythemia	60%	Iv	Splenomegally	68%
v	Mild hepatomegaly 5% with tenderness		V	Loss of libido	30%
vi	Epistaxis	25%	Vi	Palmer erythemia, Spiderangioma	45%
vii	Purpuric spots	20%	Vii	Mild jaundice	15%
Viii	Menorrehgia	15%	Viii	Epistaxis	42%
Ix	Joint pain	30%	Ix	Purpuric spots	40%
X	Low grade fever	30%	X	Menorrhegia in Female	38%
Xi	Cushinoid face with acne	15%	xi	Haematemesis due 45% to esophageal varices	
Xii	Hirsutism	10%	xii	Ascitis	37%
Xiii	Pink cutaneous striae on abdomen and thigh	5%	xiii	Hepatic Encephalopathy	20%

KEYS

- P-VALUE OF 0.05 OR LESS ARE CONSIDERED STATITICALLY SIGNIFICANT.
- N= NUMBER OF PATIENTS.

20-45 years, out of 25 patients, 18 were male and 7 were female. Group B composed of 25 patients with cirrhosis of liver and their ages ranged between 25-55 years, out of 25 patients 15 were male and 10 were female. All the patients were admitted in medical unit II Peoples medical college hospital at shaheed benazir abad. The inclusion criteria were patients suffering from chronic hepatitis & cirrhosis of liver due to viral infection. The exclusion criteria were patients with obstructive jaundice, having malabsorption, acute or chronic DIC, vitamin K deficiency, malignancy, & patients taking anticoagulant therapy,

The diagnosis of chronic hepatitis and cirrhosis of liver was made on the basis of clinical and laboratory findings. All the samples were taken from patients and controls and sent to the pathology department of peoples medical college. Data were expressed as means ± standard deviation (SD). Students' t- test was used to compare statistical significant difference between patients and controls. P-values <0.05 were considered significant.

RESULTS

Group A composed of 25 patients with chronic hepatitis, out of 25, 18 were male (72%) and 7 were female (28%) with ratio of male to female 2.6: 1. The mean age of patients was 37.5±12.5 ranged between 20 and 45 years.

Group B composed of 25 patients with cirrhosis of liver, out of 25, 15 were male (60%) and 10 were female (40%) with ratio of male to female 1.5:1. The ages of patients were ranged between 25and 55 years with mean age of patients was 40±15. The statistically significant difference was found in gender of the patients in group A and B $p<0.05$ (Table I).

TABLE : III

LABORATORY FINDINGS IN PATIENTS WITH CHRONIC HEPATITIS AND CIRRHOSIS OF LIVER

(GROUP "A" AND "B")

N=50

Group "A" N=25		GROUP "B" N=25	
LABORATORY FINDINGS	**MEAN VALUES**	**LABORA-TORY FINDINGS**	**MEAN VALUES**
Serum bilirubin	5.0±2.5 mg/100ml	Serum bilirubib	1.2±0.4mg/ 100ml
SGPT	255±355 u/l	SGPT	170±20 u/l
S. alkaline phosphatase	590±115 u/l,	S. alkaline phosphtase	310±40 u/l
Serum albumin	1.5±0.8 g/l	Serum albumin	1.8±0.2 g/l
Serum globulin	6.5±1.5 g/l	Serum globulin	5.8±1.4 g/l

KEYS

- P-VALUE OF 0.05 OR LESS ARE CONSIDERED STATITICALLY

SIGNIFICANT.

- N= NUMBER OF PATIENTS.

TABLE:IV

PARCENTAGE OF HBsAG, HBeAG, HCV ANTIBODY POSITIVE AND BIOPSY FINDINGS IN PATIENTS WITH CHRONIC HEPATITIS AND CIRRHOSIS OF LIVER (GROUP "A" AND "B")

N=50

S no:	Group "A"		S no:	GROUP B N=25	
I	HBS Ag (+VE)	40%	I	HBS Ag (+VE)	25%
Ii	HBS eAg (+VE)	20%	Ii	HBS eAg (+VE)	15%
Iii	HCV antibody	15% (+VE)	Iii	HCV antibody (+VE)	10%
Iv	Biopsy Findings such as Hepatic necrosis with infiltration of mononuclear inflammatory cells seen.		Iv	Biopsy findings such as variable degree of hepatic fibrosis seen	

KEY

- P-Value <0.05 considered highly significant
- N= Number of patients

The clinical presentations and laboratory findings such as mean levels of serum bilirubin, SGPT, Alkaline phosphatase, Albumin and Globulin were observed statistically significant in groups A and B patients (Table: II and III).

The percentages of Hepatitis B surface antigen (HBsAg), hepatitis B envelope antigen (HBeAg), hepatitis C virus antibodies and biopsy findings in patients of group A and B were showed in (Table: IV)

In group A, the mean value of plasma PT was not significantly prolonged as well as mean plasma fibrinogen level and platelet count /cumm were not reduced significantly while mean plasma APTT level was significantly prolonged when compared with healthy controls in the patients with chronic hepatitis.

In group B, both plasma PT and APTT levels were significantly prolonged. While mean plasma fibrinogen level was not significantly reduced but platelet count /cumm was reduced significantly in the

TABLE : V

MEAN VALUE OF COAGULATION TESTS SUCH AS PLASMA PT, APTT, FIBRINOGEN LEVELS AND PLATELET COUNT /cumm IN PATIENTS WITH CHRONIC HEPATITIS AND CIRRHOSIS OF LIVER (Group "A" AND "B")

Coagulation tests	Group "A" N=25	Group "B" N=25	Controls
PT	22.5±1.5 sec P-Value <0.5	60.5±2.1 sec P-Value <0.05	13.5±0.5 sec
APTT	65.5±2.5 sec P-Value <0.05	95.5±2.8 P-Value <0.05	38.5±0.8 sec
Fibrinogen	0.8±0.1 g/l P-Value<0.5	0.5±0.1 P-Value<0.5	1.5±0.2 g/l
Platelet count /cumm	1,10,000± 12,000 /cumm P-Value<0.5	90,000± 10,000 /cumm P-Value<0.5	2,75,000± 50,000 / cumm

KEYS

P-Value <0.05 considered highly significant

N=Number of patients

patients with cirrhosis as compared to controls (Table: v).

DISCUSSION

Patients with advanced liver disease are at a substantially increased risk of both thrombosis and bleeding. The chronic liver disease is a cause of abnormal coagulation tests such as prolonged plasma PT, APTT, low Fibrinogen levels or low plasma clotting factors levels and thrombocytopenia or platelet dysfunction as stated by Thachil J et al[7] and MannucciPM.[8] These laboratory workers were found out that fibrinolytic activity was enhanced in these patients leading to increase fibrin degradation products in plasma with bleeding tendency, however bleeding pattern was not like those of patients who have coagulation factors deficiencies. Mehta AB[9] concluded that patients with liver disease were at greater risk of bleeding and thrombosis particularly those who were undergoing surgery or biopsy or superimposed by infection. The studies by M.Reza SS[10], Lisman et al[11] and Tripodi et al[12] reported that plasma PT, APTT, TT levels were prolonged while plasma fibrinogen and antithrombin iii levels were reduced in patients with liver disease and abnormalities in these clotting tests were associated with bleeding which could be exacerbated due to haemostatic defects such as DIC in cirrhosis and thrombocytopenia, therefore bleeding from esophageal varices or from gastritis with peptic ulceration of GIT or from biopsy site increased in cirrhotic patients . The current study confirms the results of various international studies[5, 8,9,10]. In our study, plasma PT level was not significantly different from healthy controls and APTT was prolonged significantly from the healthy controls in patients with chronic hepatitis. Both PT and APTT were prolonged significantly as compared to the healthy controls in patients with cirrhosis of liver .However plasma fibrinogen level and platelet count /cumm were not significantly reduced in patients with chronic hepatitis when compared with healthy controls, while in patients with cirrhosis of liver, plasma fibrinogen level and platelet count /cumm were significantly reduced to those of healthy controls.

CONCLUSIONS

In the light of above discussion in our study, following conclusion has been made

1) We high light the importance of plasma levels of PT, APTT, fibrinogen and platelet count /cumm determination in patient with chronic hepatitis and cirrhosis because there is good association between the degree of prolonged PT, APTT, low or normal fibrinogen levels and mild to moderate thrombocytopenia and risk of bleeding.
2) So for management of bleeding in patients with liver disease is concerned, the vitamin K deficiency is so common that it is a advisable for physician to administer vitamin K at a dose of 10mg I/V for 3 days in these patients but this may only partially correct the coagulation abnormalities. The fresh frozen plasma is required for these patients because it supplies all known coagulation factors. However draw backs of this form of therapy should be kept in mind such as large quantity of plasma aggravates hepatic encephalopathy and causes fluid and sodium over load.
3) The presence of sever thrombocytopenia and low fibrinogen level suggest the additional complication of disseminated intravascular coagulation (DIC) in cirrhosis, that may needed further investigations and treatments to control thrombosis and bleeding which are common in DIC.

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NOTE: ***2nd author contributed data analysis, reference collection and write a manuscript***