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THE PROSPECTIVE STUDY OF COAGULATION PROFILE IN CHRONIC LIVER DISEASES AT TERTIARY CARE CENTRE.

Pathology

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ABSTRACT

Background:- The liver is the body's largest and a vital organ and plays a major role in haemostasis, as most of the coagulation factors, anticoagulant proteins and components of the fibrinolysis system are synthesized here. Balance between these procoagulant and anticoagulant processes is essential to prevent unwanted thrombin generation under normal physiological conditions. **Objectives:-** To study coagulation defects in patients of chronic liver diseases and to assess the effect of chronic liver diseases on intrinsic and extrinsic pathway through various coagulation tests and its correlation with platelet count. **Materials and Methods :-** Total 100 cases suffering from liver cirrhosis, chronic hepatitis and hepatocellular carcinoma admitted in medical and surgical wards were studied. Venous blood was collected and coagulation tests like BT, PT, APTT, D-dimer were done. **Result :-** Out of 100 cases of chronic liver diseases, 58% were diagnosed as liver cirrhosis, 37% were chronic hepatitis and 4% were hepatocellular carcinoma. The commonest coagulation defect in chronic liver diseases was prolonged PT. BT,PT,APTT, D-dimer was significantly increased and platelet count decreased in hepatocellular carcinoma and liver cirrhosis but within normal range in chronic hepatitis. **Conclusion:-** Laboratory tests suggest the abnormality in coagulation system which if done routinely can be helpful in better management of patients with liver diseases.

KEYWORDS

Coagulation, cirrhosis, hepatitis, HCC

INTRODUCTION

Liver plays a major role in haemostasis, as most of the coagulation factors, anticoagulant proteins and components of the fibrinolysis system are synthesized here.[1,8] Impaired haemostasis resulting from abnormal liver function has multifactorial etiology like impaired coagulation factor synthesis, synthesis of coagulation factors with altered function, increased consumption of coagulation factors and altered clearance of coagulation factors. It regulates coagulation and fibrinolysis by removing these coagulation factors from the circulation.[2] These coagulation abnormalities can predispose patients from minor localized bleeding to massive life threatening haemorrhage or thrombosis formation.[3] Thrombocytopenia and thrombocytopathy usually complicate the clinical picture in primary haemostasis, which fundamentally involves the platelets and tissue factor, there is a near universal quantitative decrease in platelet numbers in cirrhosis patients. Clot formation is the second phase of haemostasis that is disrupted in chronic liver disease. It is well known that a quantitative deficit in standard procoagulant proteins is easily measured using traditional laboratory assessments, such as the activated partial thromboplastin time (APTT)and the prothrombin time (PT).[4] PT determines vitamin K dependent extrinsic factors VII, X, II, V and fibrinogen. The APTT measures the activities of intrinsic and common pathways of coagulation cascade most sensitive to factor VIII, IX, XI, XII and those of the contact system.[2]

MATERIALS AND METHODS

The prospective study was done at our tertiary care center at hematology section in the Dept. of Pathology.Primary criterion of inclusion was the presence of chronic diseases of liver, irrespective of etiology. Non co-operative patients, Pregnant women, intake of drugs leading to changes in coagulation parameters were excluded.Whole venous blood was collected in K_3 EDTA (Ethylenediaminetetraacetic acid) bulb and following tests were done on it.

1. Platelet count: Done on fully automated three part cell counter H-360 ERBA
2. Bleeding time- (Ivy's method)
3. Prothrombin time
4. Activated partial thromboplastin time
5. D-dimer

Tests 3,4,5 done on fully automatic coagulometer- STA satellite max(stago)

OBSERVATIONS AND RESULT

The prospective study of coagulation profile were done on 100 cases of chronic liver diseases which includes 58 (58%) liver cirrhosis, 38(38%) chronic hepatitis and 4(4%) hepatocellular carcinoma.

In present study, age ranges from 20 years to 79 years. Majority of patients with cirrhosis (LC) were between the age group of 40 and 49 years (34.48%). Patients with chronic hepatitis (CH) was more in the age group of 30-39 years (50%) and patients with hepatocellular carcinoma (HCC) was more in the age group of 70-79 years (50%). Mean age of the patients with liver cirrhosis was 47± 13, chronic hepatitis was 38±7.2 and hepatocellular carcinoma was 67±7.

74(74%) were males and 26(26%) were females. Male to female ratio was 2.84:1. Maximum number of patients were in the age group of 30-39 years of age (33%) followed by 40-49 years (32%), 50-59 years(14%), 60-69 years(10%) then 20-29 years(7%) and only 4 (4%) cases seen in age group of 70-79 years.

In cirrhosis, Number of males were 44 and females were14,male to female ratio were 3.14:1.In chronic hepatitis, Number of males were 27 and females were11,male to female ratio were 2.45:1. In HCC, Number of males were 3 and females were1,male to female ratio were 3:1.

Table No.1 :Frequency Of Abnormal Coagulation Parameters In Individual Liver Diseases.

Test	LC (n=58)	%	CH (n=38)	%	HCC (n=4)	%
BT	19	33%	1	3%	3	75%
PT	47	81%	16	42%	4	100%
APTT	26	45%	14	37%	3	75%
D-dimer	46	79%	1	3%	3	75%
PLC	36	62%	9	24%	3	75%

(n = number of cases, LC- Liver cirrhosis, CH- Chronic hepatitis,

HCC- Hepatocellular carcinoma, PLC – platelet count x10^3/mm^3).

In liver cirrhosis prolonged PT was the commonest coagulation defect (81%), followed by increased d-dimer (79%), decrease platelet count (62%), prolonged APTT (45%) and prolonged BT (33%).

In chronic hepatitis common defect was prolonged PT (42%) followed by prolonged APTT (37%), decrease platelet count (26%) with equally but not significantly prolonged BT and D-dimer that is only(3%).

In hepatocellular carcinoma increased PT (100%) was the commonest

coagulation defect and equally increased BT, APTT and D-dimer (75.00%) along with decrease platelet count (75%).

In present study increased plasma D-dimer level (>0.5ug/ml) seen in patients with cirrhosis (79%) followed by hepatocellular carcinoma (75%).

Table No. 2: Statistical Analysis Of Coagulation Parameters In Individual Liver Diseases .

Test	LC (n=58)	CH (n=38)	HCC (n=4)
	Mean ± SD	Mean ± SD	Mean ± SD
BT	7.26±1.92	6.18±0.636	10.8±2.88
PT	27±13	15.3±2.76	42.7±5.373
APTT	42.8±12.8	36.24±6.233	44.3±9.29
PLC	134.4±77.6	257.7±75.67	107±49.79
D-dimer	3.722±3.897	0.291±0.351	2.87±2.15

(n = number of cases)

In present study, PT, APTT and D-dimer was significantly increased in hepatocellular carcinoma and also increased in liver cirrhosis but within normal range in chronic hepatitis. Similarly, platelet count was decreased in hepatocellular carcinoma and liver cirrhosis but within normal range in chronic hepatitis.

Out of 100, 33 patients had bleeding history (haematemesis, melena, epistaxis and mucosal bleeding). History of bleeding is commonly seen in HCC (50.00%) and liver cirrhosis (48.27%). In present study we found that frequency of abnormal BT, PT, D-dimer, APTT and platelets counts were higher in bleeders compared to that of non-bleeders.

DISCUSSION

In present study, out of 100 cases, 74(74%) were males and 26(26%) were females. Male to female ratio was 2.84:1. Maximum were in the age group of 30-50 years of age. This finding is similar with findings of Prashant patel et al[2], Bhatia et al[5], shobhana et al[6] ,T. Kotadiya et al[7], Sura O Aldewachi et. Al[8]

Liver Cirrhosis

The most common coagulation abnormality in liver cirrhosis cases was prolonged PT (81%) followed by D-dimer(79%), APTT (45%) and thrombocytopenia (62%).

Similar to present study Hu et al[9] ,Gursoy et al[10] ,Siddiqui et al[3] ,Das RP et al[11],Bhatya et al(2017)[5], Kotadiya et al(2018)[7] , Shobhana et al(2020)[6] found prolonged PT as a commonest coagulation abnormality in their studies. In present study abnormal percentage of D-dimer is in comparison with Gursoy et al (2005)[10] ,abnormal percentage of APTT is in accordance with Blake JC et al (1990)[12] ,Hu et al[9] ,Bhatya et al(2017)[5] ,Shobhana et al(2020)[6] and similar findings of abnormal percentage of PLC were seen with Hu et al[6],Das RP et al[11],Bhatya et al(2017)[5]. Abnormal values of BT are similar with studies of Bhatya et al(2017)[5] ,Violi F et al (1994)[13] ,Blake JC et al (1990).[12]

plasma D-dimer level was increased in 46 (79 %) cases which is comparable with the study of Gursoy et al (2005)[10].

Chronic Hepatitis

In chronic hepatitis, we found that most common coagulation defect was prolonged PT (42%) followed by APTT (37%) and decrease platelets (24%). The BT and D-dimer were increased in only one patient i.e. only 3% patients with chronic hepatitis.

Bhatia et al[5], Patel et al[2], shobhana et al[6], Kotadia et al[7] also found increase PT followed by APTT in their studies similar to our study.

Similar to our study, Bhatia et al[5], Patel et al[2] also found thrombocytopenia in patients with chronic hepatitis in their study.

The mean values of PT and APTT were significantly prolonged. The mean BT and platelets count were within normal range.

In present study, mean values of PT and APTT are comparable with studies of Gursoy et al[10], Reza SSM et al[14], Saray et al[15], Elgary et al[16], koatdia et al[7] and mean value of platelets count is comparable with that of Saray et al[15].

- **Comparison Of Plasma D-dimer With Other Studies.**

The mean plasma D-dimer level in Gursoy et al[10] (400±300 ng/ml) and Saray et al[15] (100.63±29.16 ng/ml) not statistically significantly increased in cases of chronic hepatitis. In present study, D-dimer level was < 500 ng/ml i.e. <0.5ug/ml. The mean value of D-dimer was 0.291±0.351 in 38 patients with chronic hepatitis which is comparable with study of Saray et al[15] and Gursoy et al[10].

Hepatocellular Carcinoma

In hepatocellular carcinoma, increased PT (100%) was the commonest coagulation defect, followed by decreased platelets, increased BT and APTT were (75%).

Bleeding Time (BT)

In our study, mean value of BT (10.8±2.88) was significantly prolonged in patients with HCC. Chu CJ et al (1997)[17] studied mean BT (11.05±1.75) was statistically significantly prolonged in cases of HCC.

Prothrombin Time (PT) And Activated Partial Thromboplastin Time (APTT) In HCC:- In our study, mean value of PT (42.7±5.373) and APTT (44.3±9.29) are significantly prolonged in cases of HCC. Mean PT (15.4±2.3 sec) and APTT (57.2±9.4sec) were significantly prolonged in the study of Van der Walt et al (1977).[18] Wang et al noticed prolonged PT (14.16±1.46) and APTT (40.19±4.11) in preoperative patients with HCC as compared to reference value.[19] Elgari et al (2011) found that PT (28.2±10.1) and APTT (63±26.2) were significantly prolonged in patients with HCC.[16] Xuan et al found statistically significantly prolonged PT (13.56±1.87) and APTT (40.17± 7.41) in HCC patients.[20] Hessien et al (2013) found significantly prolonged PT (20.60±3.85) in HCC.[21] Saja et al (2013), observed significantly prolonged PT (151.7±41.4 %) and APTT (128.7±19.7 %) in HCC.[22]

Our findings are in accordance with Van der Walt et al[18] ,Saja et al[22] ,Wang et al[19] ,Hessien et al[21] and Elgari et al[16] for increased PT and APTT.

Platelet Count (PLC)

In present study, platelets counts (107±49.79) were significantly decreased.

Wang et al[19], Xuan et al[20] and Hessien et al[21] also showed significantly decreased mean value of platelet count in HCC patients.

The mean value of D-dimer was (2.87±2.15), which was significantly increased in 75% cases of HCC which is similar to Ibrahim et al study showing significantly increased D-dimer in all patients (100%) with HCC.[23]

Bleeding And Coagulation

In present study percentages of prolonged BT, PT, APTT, increased D-dimer and thrombocytopaenia were greater in bleeders than non-bleeders.

Violi F (1994) [13] Rastogi et al (1990) [24], Patel et al (2018) [2], Shobhana et al[6] ,Kotadia et al[7] also showed similar findings.

The mean value of BT, PT and APTT were significantly prolonged in bleeders than non bleeders and platelets significantly reduced in bleeders similar to the studies of Violi F et al[13], Kotadia et al[7].

CONCLUSION

Though clinical manifestations of deranged coagulation system are not seen commonly, laboratory tests suggest the abnormality in coagulation system which if done routinely can be helpful in better management of patients with liver diseases.

The study of coagulation profile in chronic liver diseases can help us in assessing the hepatic cellular function as well as in detecting the hepatic cell injury. Prolongation of coagulation tests like PT and APTT in advancing liver diseases indicate damage to liver parenchyma which results into decreased production of coagulation proteins and increased risk of bleeding tendencies. This can be detected before these appear by determining the level of PT and APTT. Therefore it is possible to prevent these life threatening bleeding complications in patients with chronic liver diseases.

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