A study of coagulation profile in diseases of liver: At tertiary care center hospital

Tarun P. Kotadiya[1], Varsha Khant[2,*], Bhavesh Prajapati[3]

[1]Associate Professor, [2]Tutor, [3]Resident, Dept. of Pathology, [1,2]GMERS Medical College Himmatnagar, Gujarat, [3]Shri M P Shah Government Medical College, Jamnagar, Gujarat, India

***Corresponding Author: Varsha Khant**
Email: varshaskhant@gmail.com

Received: 9th April, 2018 **Accepted:** 20th August, 2018

Abstract

Introduction: The liver is the main site of organ for coagulation system. Liver plays a predominant role in regulation of hemostasis. Hepatic disorders are widely prevalent in tropical countries are responsible for morbidity and mortality.

Aims and Objective: The diagnosis of liver diseases by assisting in differential diagnosis with various coagulation tests. In assessment of prognosis of patients of various liver disease.

Materials and Methods: The study was conducted in the laboratory of Guru Gobind Singh Hospital, Jamnagar. This study included 100 patients clinically diagnosed with liver disease who were divided into three categories – cirrhosis, viral hepatitis, and obstructive jaundice. The coagulation tests PT, APTT, BT, CT, and platelet count were performed and the results were evaluated in groups.

Result: Out of the 100 patients, 40 were diagnosed with cirrhosis, 40 were of viral hepatitis, and 20 were of obstructive jaundice. About 75% (75/100) had prolonged PT. About 39% (39/100) had prolonged APTT. Thrombocytopenia was seen in 58% (138/300) patients.17 cases out of 100 patients (17%) show result of Hypofibrinogenemia.

Conclusion: The conclusion of this study reveals various coagulation abnormalities vary with different liver diseases, duration and severity of disorders. In advancing liver cirrhosis, raised level of PT and APTT indicates damage to liver parenchyma resulting in reduced production of coagulation proteins with increased risk of bleeding tendencies which can be detected before these ensue.

Keywords: Coagulation, Cirrhosis, Viral hepatitis, Obstructive jaundice.

Introduction

Liver is an important organ of the body having functions of synthesis of plasma proteins and a range of blood clotting factors being produced, some of them exclusively in the organ. All of them are deranged in various liver disorders.[1]

Liver plays a predominant role in the regulation of haemostasis. Both cellular and plasmatic coagulation are defective, representing a hallmark of advanced liver disease.[2]

Laboratory tests, coagulation tests and liver function tests are useful in the evaluation, management and assessment of prognosis. They provide a sensitive, non-invasive method of screening for the presence of liver dysfunction.[3]

Along with function of synthesis of protease inhibitors, liver also clears activated clotting factors from blood. Intravascular coagulation has been reported as frequently occurring in patients with acute liver failure. The resultant consumption coagulopathy complicates a pre-existing coagulation defect due to further depletion of fibrinogen, factor V and factor IX and X.[5]

Considering above mentioned factors and importance of coagulation tests which is helpful in evaluation of various hepatic disorders, the present study is undertaken.

Aims and Objectives

1. The diagnosis of liver diseases by assisting in differential diagnosis with various coagulation tests.
2. In assessment of prognosis of patients of various liver disease.
3. In the prediction of response to treatment for liver disease.

Materials and Methods

The present study was conducted on 100 patients having liver disease attending Medicine and Paediatric clinics at tertiary care hospital. They were divided into following three groups: 40 cases of cirrhosis (Bleeders, Non bleeders), 40 cases of viral hepatitis and 20 cases of Obstructive jaundice.

Blood samples from the patients were collected and following coagulation tests were performed.

1. Bleeding time- Ivy's Method
2. Clotting time- Lee an White Method
3. Platelet count- By automated haematology analyzer. (Cell Dyn 3700).
4. Prothrombin time- By reagent kit Lyoplastin – manufactured by Tulip diagnostic ltd.
5. Activated Partial Thromboplastin time- By diagnostic kit manufactured by Diagnostica Stago S.A.S.
6. Plasma fibrinogen estimation-- By diagnostic kit manufactured by Diagnostica Stago S.A.S.

The clinical history and data of patients liver disease were correlated and results were recorded.

Inclusion Criteria: Criterion of inclusion was presence of liver disease including cirrhosis, viral hepatitis, obstructive jaundice. All patients of both sexes, age ranging from 20 to 70 years and irrespective of socioeconomic status, were included.

Exclusion Criteria: Patients with previous history of coagulation disorders or who took any of the following drugs in the previous week were excluded: aspirin or nonsteroidal anti-infl ammatory drugs, antihistaminics, penicillin, sulfonamides, beta blockers, and anticoagulants.

Result

A study of 100 cases in various liver diseases was carried out for various coagulation tests like, bleeding time(BT), Cotting time(CT), Prothromin time(PT), Activated partial Thromboplastin time, Plasma fibrinogen and platelet count at Department of pathology during period of June 2005 to October 2006.

Various observations and results were taken and studies in table form.

Table 1 shows bleeding time, clotting time, prothrombin time, activated partial thromboplastin time, fibrinogen level in patients with various liver diseases.

Table 1: Test results in various liver diseases

Test name		Normal Cases	Cirrhosis 40 cases		Viral Hepatitis	Obstructive Jaundice
			Bleeders	Non bleeders		
Total cases		25	20	20	40	20
Bleeding time	Normal Range-120-420 sec	25	20	20	20	40
		120-420 270	160-300 230	120-240 210	120-170 145	120-150 135
Clotting time		25	20	20	40	20
		240-600 420	240-450 345	240-350 295	230-340 285	240-310 275
Prothrombin Time	Control 12-16 sec	-	1	10	10	04
	PT-17-35sec high	-	19	10	30	16
aPTT	Normal 30-40 sec	-	4	17	11	9
	40-55 sec high	-	16	3	9	11
Fibrinogen Level (mg%)	150-200 Low fibrinogen level		11	8	1	0
	200-250 Control range		9	14	31	16
	250-450 Upper limit control value		0	1	7	4

Discussion

One hundred patients of various liver diseases with various clinical manifestations studied for coagulation abnormalities by doing coagulation tests like bleeding time, platelet count, fibrinogen estimation and prothrombin time and activated partial prothrombin time. With this other normal 25 persons also studied for control.

The results obtained are tabulated and compared with those of previously published studies in various years and similar work of well-known workers in this field.

Table 2 shows, in cirrhosis, the bleeding time in both bleeders and non bleeders is within normal range, as shown by present study and other worker's study. But the mean value for bleeders is quite higher than non bleeders as shown by Poonam Rastogi[9] et al in 18 cases and present study in 20 cases. So this values are quite comparable in present study with study of Poonam Rastogi et al.[9]

In viral hepatitis, 40 cases show range of 140± 25 sec which is normal range and similar observations was made by Ratnoff et al[7] and Donaldson et al and Singh et al.[8]

In obstructive jaundice, bleeding time is comparable with those of other studies.

Table 3 shows in cirrhosis, the Clotting time in both bleeders and non bleeders is within normal range, as shown by present study and other worker's study. But the mean value for bleeders is quite higher than non bleeders as shown by Poonam Rastogi et al[9] in 18 cases and present study in 20 cases. So this values are quite comparable in present study with study of Poonam Rastogi et al.[9] Similar observations are made by other Authors. Thus it is clear that Clotting time is not much significant test for cirrotic patients.

In viral hepatitis, present study show range for clotting time 285±55 sec. Similar observations was made by other studies and present study is comparable with other studies and indicate that clotting time is not much significant test for hepatitis. Same observations were made for obstructive jaundice and also comparable with other studies.

Table 4 shows in cirrhosis of liver, in present study 95% elevation of PT is seen in bleeder in range of 32.3± 14.3. This shows similar results in all the workers, which is comparable with present study showing high prothrombin time. In non

bleeders, results are variable due to 1. Variation in patients population and can be attributed to our exclusion of minor degree of bleeding.

In Viral hepatitis, present study show elevation of PT which is comparable with study of S. Gurdoy et al.[12] In Obstructuve jaundice, all 20 cases(100%) show elevation in our study. Overall results and present study of PT are quite comparable with other worker's results in all liver diseases.

Table 5 shows in cirrhosis, in present study shows elevation in aPTT in 16 cases (80%) in bleeders in range of 44.6± 4.6 and 20 cases (15%) in non bleeders with range of 35.8± 5.8 which is comparable with other study.

In viral hepatitis 22.5% cases show elevation in aPTT by present study. Similar observations were made by above mentioned authors in their studies.

In obstructive jaundice, 55% cases show prolongation of aPTT by present study. No other worker has done similar study. As per above results observed by present study showing elevation value of APTT which is quite comparable with the other results.

Table 6 shows study of fibrinogen in liver disease by comparison of other workers with present study.in cirrhosis, observations show hypofibrigenemia in Norber's study and present study which is quite comparable. The minor variation of results may be due to different number of cases studied and population difference of patients studied.

In viral hepatitis observations show hypofibrigenemia which is comparable with other studies.

In obstructive jaundice. Present study 20 cases studied with results in range of 230± 30 mg% is seen which is in normal range. No other workers have done similar study in obstructive jaundice

Hypofibrigenemia in bleeders noted by all workers are almost similar with present study. Same observations are seen in non bleeders cases.

Table 2: Comparison of bleeding time in liver disease with other studies

Studies	**Cirrhosis Normal range 120-420 sec**				**Hepatitis normal range 120-420 sec**		**Obstructive jaundice normal range 120-420 sec**	
	Bleeder		**Non bleeder**					
	Case	Mean range Sec	case	Mean range Sec	Case	Mean range sec	Case	Mean range sec
Ratnoff et al[7]		Within normal range				Normal		
Donaldson et al[7]	30	Within normal range				Normal		
Singh Dube et al[8]	40	Within normal range				Normal		
Poonam rastogi et al[9]	18	285±55.9	12	206±145.8				
Present study	20	230±70	20	180±60	40	145±25	20	135±15

Table 3: Comparison of clotting time in liver disease with other studies

Studies	**Cirrhosis Normal range 240-600 sec**				**Hepatitis normal range 240-600 sec**		**Obstructive jaundice normal range 240-600 sec**	
	Bleeder		**Non bleeder**					
	Case	Mean range Sec	Case	Mean range Sec	Case	Mean range sec	Case	Mean range sec
Ratnoff et al[6]		Within normal range			Within normal range		Within normal range	
Donaldson et al[7]		Within normal range			Within normal range		Within normal range	
Singh Dube et al[8]	40	Within normal range			Within normal range		Within normal range	
Poonam Rastogi et al[9]	18	285±55.9	12	206±145.8	-	-	-	-
Present study	20	230±70	20	180±60	20	145±25	20	135±15

Table 4: Comparison of Prothrombin time in liver disease with other studies

Studies	**Cirrhosis Normal range 240-600 sec**						**Hepatitis normal range 240-600 sec**			**Obstructive jaundice normal range 240-600 sec**		
	Bleeder			**Non bleeder**								
	Case	Prolonged	%	Case	Prolonged	%	Case	Prolonged	%	Case	Prolonged	%
Israel Spector Milton Cor et al [10]	19	19	100	40	22	55		-			-	
D.S. Singh B. Dube et al 8	40	40	100	-	-	-	-	-	-	-	-	-
Poonam Rastogi et al [9]	18	16	88.8	12	2	18	-	-	-	-	-	-

Aspsia Sdoultati et al [11]	34	34	100	-	-	-	-	-	-	-	-	+
S. Gurdoy et al [12]	35	33 26.5±13.5	94	-	-	-	15	12.8±0.6	-	-	-	-
Present Study	20	19 32.3±14.3	95	20	10 25.1±12.9	50	40	30 23.54± 13.5	75	20	16 27.1±9.15	80

Table 5: Comparison of activated partial prothrombin time in liver disease

Studies	Cirrhosis Normal range 240-600 sec						Hepatitis normal range 240-600 sec			Obstructive jaundice normal range 240-600 sec		
	Bleeder			Non bleeder								
	Case	Prolonged	%	Case	Prolonged	%	Case	Prolonged	%	Case	Prolonged	%
Israel Spector Milton Cor et al[10]	19	9	64.3	-	-	-		-			-	
D. S. Singh B. Dube et al[8]	40	32	80	-	-	-	-	-	-	-	-	-
Poonam Rastogi et al [9]	18	14	77.7	-	-	-	-	-	-	-	-	-
Talat Naheed et al[13]	100	75 39.68±7.15	75	-	-	-	90	36 ±0.68	40	-	-	-
Present study	20	16 44.6±4.6	80	20	3 35.8±5.8	15	40	9 39.0± 2.0	22.5	20	11 42.5± 2.5	55

Table 6: Comparison of fibrinogen level in liver disease in present study with other studies

Studies	Control Mg%	Cirrhosis Normal range 240-600 sec					Hepatitis normal range 240-600 sec			Obstructive jaundice normal range 240-600 sec		
		Bleeder		Non bleeder								
		Case	Count in mg%	Case	Count in mg%		Case	Count in mg%	%	Case	Count in mg %	%
Israel Spector Milton Cor et al[10]	325±160	19	253±35	22	22 55			-			-	
Sidney Stain et al [15]	285±22	60	271±104	-	- -		-	-	-	-	-	-
Poonam Rastogi et al [9]	281±28	18	196±25	12	2 18		-	-	-	-	-	-
Aspsia Sdoultati et al [11]	250±5	34	289±52	-	- -		-	-	-	-	-	+
S. Gurdoy et al[12]	303.8±75.6	35	233.4±76.1	-	-	-	15	12.8±0.6	-	-	-	-
Present study	225±25	20	155±65	20	10 25.1±12.9	50	40	30 23.54± 13.5	75	20	16 27.1±9.15	80

Conclusion

Present study of 100 cases of various liver diseases for various coagulation tests was done. Efforts were made to find out the importance and diagnostic significance of various coagulation tests in various liver diseases. The following conclusions were made.

Bleeding Time and Clotting Time: In cirrhosis of liver, BT and CT show normal range but mean value for bleeders is higher than non bleeders. In viral hepatitis and obstructive jaundice, BT and CT shows normal range.

Prothrombin Time: Prothrombin time shows marked significant value in all liver diseases. In cirrhosis bleeder shows elevation of Prothrombin time in 90-100% cases and non bleeders show 50-55 % cases.

In viral hepatitis, PT value is elevated in 75% cases. In obstructive jaundice, 80% cases show rise in PT.

Activated Partial Thromboplastin Time: aPTT is quite significant in cirrhosis. Bleeders show elevation of aPTT in 80% cases and non bleeders show 15% cases. In viral hepatitis, decreased number of cases i.e.22.5% rise in aPTT. In obstructive jaundice, moderate number of cases i.e. 55% cases show rise in aPTT.

Fibrinogen

Hypofibrinogenemia Observed: In cirrhosis, bleeders show moderate to severe degree of hypofibrigenemia in 55% cases. Non bleeders show moderate degree of hypofibrigenemia in 25% cases.

In viral hepatitis and obstructive jaundice mild degree of hypofibrigenemia is seen i.e. 2.5% cases it suggests fibrinogen has not much significant value in viral hepatitis and obstructive jaundice.

Conflict of Interest: None.

References

1. Pallor C. Blood coagulation recent advances 2, Churchill Livingstone Edinburgh, London and New York, page no.267-292.
2. Coagulation disorders in liver disease. *Haema* 2006;9(1):31-44.
3. Cowling DC. coagulation defects in liver disease. *J Clinical Pathol* 9:347.
4. Leon Schiff, Eugene R. Schiff Miami, Florida. Disease of the liver sixth Edition, Page No. 219-252.
5. Shella Sherlock, The Hematology of Liver disease 9th edition, Oxford, London, Page No.45-48.
6. Ratnoft O.D. cook. Haemostasis mechanism of Liver disease. Medical Clinics of North America,47-721.
7. Donaldson GWK. Coagulation factors in chronic liver disease. *J Clin Pathol* 1969;22:199
8. Singh D, Dube B, Gupta P. Hepatic Cirrhosis in Varansi A. haemostatic approsial *JIMA* 69:26-30.
9. Poonam Rastogi, Gupta S.C. Dipti Bhishi. Coagulation studies in patients with Cirrhosis of Liver, Bleeder Vs. Non Bleeders. *Indian J Pathol Microbiol* 33:4,323-327
10. Israelispector, Corn Milton. Lab, Test of hemostasis. The relationship to haemorrhage in liver disease. *Arch Intern Med* 119:577-582
11. Aspasia S. Soultati, SP Dourkis. Predicating utility of a model for end stage liver disease in echologic liver disease. *World J Gastroenterol* 2006;12(25):4020-4025.
12. Sebnen Gurdey, M. Baskal case records of coagulation defects in liver disease. *Turk J Gastroenterol* 2005;16(3):129-133.
13. Talat Naweed, Nabeel, cirrhotic or Non Cirrhotic portal hypertension. *Pak J Med* 2001:17(3):133-141.
14. Rao P.C. Manorama Shared, (1974). Platelet function in liver disorders. *Indian J Med Res* 62
15. Sidney Stein harker (1982). Kinetics and functional studies of platelets, fibrinogen in patient of hepatic cirhhosis. *J Lab Clin Med* 1982;99:217-222.
16. Rake MO, William (1970). IVC in hepatic failure Lancet,1:533.
17. Clark, Rake. Coagulation abnormality in acute liver failure. *Scand J Gastroentol Suppl* 1973-6;19-63.
18. Tytgat C. Collen D. (1968). 265 Investigation of Fibrinolytic system in liver cirrhosis. *Acta Haemat* 40.
19. Mac Farlane RG. An enzyme cascade in blood clotting mechanism and its function as a biochemical amplifier Nature.1964, 498-499.
20. Liq, Wang, BE, Cong. YL. carticle in Chienese. The value of coagulation factors in Hepatitis B related cirrhosis. 2005,44(3):188-190.
21. Bloom AL. (1975). Annotation: Intravascular coagulation and the liver. *Br J Hematol* 30:1
22. Innerfield, Ingrist, Boyd (1952). The plasma antithrombin time in incipient and advanced liver diseases Gastroentrol.20:247.
23. Ekynoyn (1969) Platelet function in renal failure. *N Eng J Med* 233:677-681
24. Hillbrand, Partho, Jedrichowski, Sherlock. Significance of intravascular coagulation and fibrinolysis in acute hepatic failure. *Scand J Gastroentrol Suppl.*1973;19:133.
25. Bergstrom and Kleon (1960) Studies on the plasma fibrinolytic activity in a case of liver cirrhosis. *Acta Medica Scandinaria* 168:291, Quoted Ref.no 1.

How to cite this article: Kotadiya TP, Khant V, Prajapati B. A study of coagulation profile in diseases of liver: At tertiary care center hospital. *Indian J Pathol Oncol* 2019;6(1):107-111.