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EVALUATING THE HEMOSTATIC CHARACTERISTICS IN INDIVIDUALS WITH LONG-TERM LIVER ILLNESS- A CLINICAL STUDY

Dr. Sanjay Godbole,[1*] Dr. Chinmay Godbole[2]

[1*]Associate Professor, KJ Somaiya Medical College,Mumbai, Maharashtra

[2]Junior Resident, Bharti Vidyapeeth Deemed University Medical College, Pune, Maharashtra

Corresponding address
Dr. Sanjay Godbole
Email id: dr_sgg@hotmail.com

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ABSTRACT

Background: The frequency of chronic liver disorders is high in developing nations such as India, which places a significant load on the healthcare system. A multitude of hematologic abnormalities are known to be related with and often documented in people with chronic liver disease.

Aim: The current clinical study's objectives were to evaluate the anomalies seen in liver disease patients as their livers gradually deteriorated.

Methods: Eighty individuals with chronic liver disease were included in the current retrospective clinical investigation. Coagulation, hemostatic, and biochemical variables were measured in each research participant and compared to baseline levels found in the healthy subjects.

Results: The mean serum ALT in healthy individuals was 23.2±3.2, indicating a noteworthy decline in categories II a to II b, and II c from 64.2±8.2 to 79.2±11.2 and 50.2±7.2. In cases of hepatocellular carcinoma (HCC), the mean serum ALT was 58.2±6.2. Comparable outcomes were seen for albumin, which decreased dramatically to 3.4±0.4 and 2.7±0.38 in categories II b and II c from 4.2±0.7 in Cirrhosis category II a. In category II a, bilirubin was 0.9±0.4 mg/dL in the controls; it climbed to 0.9±0.3 in category II b and 4.4±1.3 in category II c with $p<0.01$, indicating a substantial increase. In healthy controls, the AST was 23.2±3.2. 70.2±9.2 in cirrhosis individuals. In categories II b and II c, platelet counts dropped dramatically to 87.2±21.2 and 82.2±15.2, respectively, with $p<0.01$. In HCC subjects, With $p<0.01$, there was a substantial decrease in INR, PT, and platelet counts from category II c to 3.4±1.0, 20.3±4.6, and 81.3±12.3, respectively. Calcium levels demonstrated a substantial decrease in cirrhosis category II c and HCC (III) to 9.2±1.8 and 8.5±1.9 with $p<0.001$, and a significant rise in category II a and II b to 14.2±2.4 and 14.6±2.4 mg/dl. With $p<0.001$, fibrinogen levels significantly decreased to category II a, II b, and II c, measuring 1.7±0.6, 1.5±0.7, and 0.7±0.5g/L. Fibrinogen level in category III, HCC, demonstrated a statistically significant difference with 0.97±0.4 and $p<0.01$.

Conclusion: The current study reveals that in individuals with chronic liver disorders, problems related to calcium, fibrinogen, and prothrombin time were detected concurrently with the degradation of liver functions.

Keywords: Calcium, Chronic liver disease (CLD), Fibrinogen, Prothrombin time, Serum bilirubin.

INTRODUCTION

The liver, which also synthesises numerous coagulation proteins, such as factors I, II, V, VII, VIII, IX, X, XI, XII, XIII, several natural proteins (C and S), and anticoagulants, plays a crucial part in the hemostatic system. Liver illnesses, whether acute or chronic, have a significant impact on the hemostatic system. Hemostatic proteins, which are typically produced in the liver, are not as abundant in plasma when liver diseased, which results in bleeding. Additionally, thrombocytopenia, coagulopathy, increased fibrinolysis, and/or portal hypertension can all cause

bleeding. According to statistics from recent literature, deep vein thrombosis or pulmonary artery embolism typically occur in patients with liver problems at a rate of 0.5% to 2%.[1]

Defective hepatic production of coagulation and clotting components is a hallmark of chronic liver disease (CLD). Hemostatic changes brought on by thrombocytopenia are linked to either portal hypertension or hyperfibrinolysis. Liver parenchyma renewal and progressive damage are the causes of liver cirrhosis and fibrosis. Numerous liver pathologies, such as cirrhosis of the liver, hepatocellular carcinoma, and chronic hepatitis, are also brought on by chronic liver illnesses. Protein S, protein C, prothrombin, and coagulation factors are reduced in liver cirrhosis with rising symbiotic activities of vWF (von Willebrand factor) and factor VIII. Factor VIII and vWF promote platelet aggregation, while prostacyclin, elevated nitric oxide, and thrombocytopenia inhibit diminished platelet function (PF).[2] Thrombocytopenia is a result of plenic sequestration brought on by the interaction of glycoprotein IIb/IIIa platelet surface antigen-antibody in portal hypertension or sepsis, immune-mediated platelet destruction, and reduced hepatic synthesis of thromboproteins. Therefore, bleeding problems and thrombotic events are typically observed in people with liver illness.[3]

Previous literature reviews have demonstrated that persons with liver problems have a higher chance of developing venous thrombosis than those in good health. Protein S, protein C, antithrombin, and natural anticoagulants present in plasma are responsible for the thrombotic propensity. Therefore, individuals with chronic liver illnesses are more likely to experience thrombotic events and bleeding problems.[4]

The goal of the current retrospective clinical investigation was to evaluate the anomalies seen in liver disease patients as their livers gradually deteriorated.

MATERIALS AND METHODS

The goal of the current retrospective clinical investigation was to evaluate the anomalies seen in liver disease patients as their livers gradually deteriorated. The study was carried out with approval from the relevant ethical committee. The individuals who visited the Institute's Department of Medicine made up the study population.

The research included participants with chronic liver disease who came to the outpatient department. Eighty participants of both genders, ranging in age from 30 to 75 years, with a mean age of 46.4±4.26 years, were involved in the study. Following the research subjects' enrollment, a thorough history and demographics were taken, and then a clinical examination was conducted. Assessments were made on anticoagulant, pharmaceutical, and illness histories, as well as end-stage renal disease and its etiology. Subjects with cirrhosis were categorized according to Child's classification: those with mild cirrhosis (Child A) (group IIA), those with moderate cirrhosis (Child B) (group IIB), and those with advanced cirrhosis (Child C) (group IIC). HCC patients (n=10) were included in group III.

No individual received an anticoagulant during the research, and those who were bleeding actively were not included. Furthermore, twenty healthy participants were included as controls. Blood was drawn aseptically and sterilely from the cubital vein.

In addition to serum collection, hematologic evaluations were performed for platelet counts and biochemical markers. Together with AST and ALT (transaminases), serum bilirubin and albumin levels were measured to evaluate the integrity of the liver. Coagulation tests and complete blood counts (CBC) were performed right away. The amounts of plasma fibrinogen were evaluated using the turbidometric technique.

Using SPSS software version 21 (Chicago, IL, USA) for statistical assessment and one-way ANOVA and t-test for result formulation, the gathered data were examined. The data were presented as a mean, standard deviation, percentage, and number. At $p<0.05$, the significance threshold was maintained.

RESULTS

The goal of the current retrospective clinical investigation was to evaluate the anomalies seen in liver disease patients as their livers gradually deteriorated. Eighty participants of both genders, ranging in age from 30 to 75 years, with a mean age of 46.4±4.26 years, participated in the study. The study included 24 female participants and 56 male participants. The ALT value for the biochemical variables was 23.2±3.2 in normal persons, indicating a substantial decrease in values in categories II a to II b, and II c from 64.2±8.2 to 79.2±11.2 and 50.2±7.2; in hepatocellular carcinoma (HCC), the value was 58.2±6.2. Comparable outcomes were seen for albumin, which decreased dramatically to 3.4±0.4 and 2.7±0.38 in categories II b and II c from 4.2±0.7 in Cirrhosis category II a.

Bilirubin in controls was 0.9±0.4 mg/dL, was 0.9±0.3 in II a category, and increased significantly to 2.2±0.8 and 4.4±1.3 in category II b and II c with $p<0.01$. AST in normal controls was 23.2±3.2. In cirrhosis, subjects were 70.2±9.2 for category II a and increased significantly to 78.2±10.2 and decreased significantly to 43.2±6.2.

Regarding the hemostatic characteristics in the research participants, the controls had platelet counts of 230.2±28.2 cells/µl, INR of 1.5±0.05, and PT of 12.3±0.1. For INR, PT, and platelet counts, the corresponding values in the II cirrhosis group were 1.6±0.13, 14.2±1.4, and 190.2±31.2, respectively. With $p<0.01$, the INR considerably rose to 2.4±0.6 and 3.5±1.06 in categories II b and II c. Additionally, with $p<0.01$, platelet counts in categories II b and II c dropped dramatically to 87.2±21.2 and 82.2±15.2, respectively. Table 2 displays a substantial decrease in INR, PT, and platelet counts in HCC participants from category II c to 3.4±1.0, 20.3±4.6, and 81.3±12.3 respectively with $p<0.01$. When the coagulation factors in the research participants with various stages of liver disease were evaluated, it was observed that the levels of calcium and fibrinogen in the controls were 9.35±0.5 mg/dl and 2.9±0.2 g/L, respectively. Calcium levels demonstrated a substantial decrease in cirrhosis category II c and HCC (III) to 9.2±1.8 and 8.5±1.9 with $p<0.001$, and a significant rise in category II a and II b to 14.2±2.4 and 14.6±2.4 mg/dl. With $p<0.001$, fibrinogen levels significantly decreased to category II a, II b, and II c, measuring 1.7±0.6, 1.5±0.7, and 0.7±0.5g/L. Table 3 illustrates the statistical difference in fibrinogen level with $p<0.01$ and 0.97±0.4 in category III, HCC.

Discussion

The goal of the current retrospective clinical investigation was to evaluate the anomalies seen in liver disease patients as their livers gradually deteriorated. Eighty participants of both genders, ranging in age from 30 to 75 years, with a mean age of 46.4±4.26 years, were involved in the study. The study included 24 female participants and 56 male participants. The ALT value for the biochemical variables was 23.2±3.2 in normal persons, indicating a substantial decrease in values in categories II a to II b, and II c from 64.2±8.2 to 79.2±11.2 and 50.2±7.2; in hepatocellular carcinoma (HCC), the value was 58.2±6.2.

Comparable outcomes were seen for albumin, which decreased dramatically to 3.4±0.4 and 2.7±0.38 in categories II b and II c from 4.2±0.7 in Cirrhosis category II a. AST was 23.2±3.2 in normal controls, whereas bilirubin in controls was 0.9±0.4 mg/dL, 0.9±0.3 in category II a, and substantially rose to 2.2±0.8 and 4.4±1.3 in categories II b and II c with $p<0.01$. Subjects with cirrhosis were 70.2±9.2 for category II a, climbed to 78.2±10.2, and then drastically declined to 43.2±6.2. These biochemical factors aligned with findings from studies by Afdhal N et al. (2008) and Wang FJ et al. (2004), which found similar biochemical parameters to those in the current investigation.

For the hemostatic variables in the study subjects, INR, PT, and platelet counts in controls were 1.5±0.05, 12.3±0.1, 230.2±28.2 cells/µl respectively. For INR, PT, and platelet counts, the corresponding values in the II cirrhosis group were 1.6±0.13, 14.2±1.4, and 190.2±31.2, respectively. With $p<0.01$, the INR considerably rose to 2.4±0.6 and 3.5±1.06 in categories II b and II c. Additionally, with $p<0.01$, platelet counts in categories II b and II c dropped dramatically to 87.2±21.2 and 82.2±15.2, respectively. The HCC participants exhibited a substantial decrease in INR, PT, and platelet counts from category II c to 3.4±1.0, 20.3±4.6, and 81.3±12.3, respectively, with a p-value of less than 0.01. These findings were consistent with research conducted by Shami VM et al[7] and by Pavese P et al[8] which found that people with chronic liver illnesses had comparable results in terms of PT, INR, and platelet counts.

When the coagulation factors of the research participants with various stages of liver disease were evaluated, it was observed that the levels of calcium and fibrinogen in the controls were 9.35±0.5 mg/dl and 2.9±0.2 g/L, respectively. Calcium levels demonstrated a substantial decrease in cirrhosis category II c and HCC (III) to 9.2±1.8 and 8.5±1.9 with $p<0.001$, and a significant rise in category II a and II b to 14.2±2.4 and 14.6±2.4 mg/dl. With $p<0.001$, fibrinogen levels significantly decreased to category II a, II b, and II c, measuring 1.7±0.6, 1.5±0.7, and 0.7±0.5g/L. The fibrinogen level in category III, HCC, demonstrated a statistically significant difference with 0.97±0.4 and $p<0.01$. These results were similar to those of studies by Atkison PR et al[9] in 2013 and Brady KM et al[10] in 2012, the authors of which reported coagulation factors similar to those of the current investigation.

CONCLUSION

Within the bounds of its limitations, the current study finds that in people with chronic liver disorders, anomalies related to prothrombin time, fibrinogen, and calcium were detected concurrently with the degradation of liver function. A few drawbacks of the current study included biases related to geographic areas, a limited sample size, and a short monitoring time. Therefore, further long-term research with bigger sample sizes and longer observation periods will aid in coming to a conclusive result.

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TABLES

S. No	Biochemical variables	Normal (I) (n=20)	Cirrhosis			III (HCC) (n=20)
			II a (n=20)	II b (n=20)	II c (n=20)	
1.	ALT	23.2±3.2	64.2±8.2	79.2±11.2	50.2±7.2	58.2±6.2
2.	AST	30.2±4.2	70.2±9.2	78.2±10.2	43.2±6.2	56.2±7.2
3.	Albumin (grams/dL)	4.5±0.6	4.2±0.7	3.4±0.4	2.7±0.38	2.6±0.4
4.	Bilirubin (mg/dL)	0.9±0.4	0.9±0.3	2.2±0.8	4.4±1.3	3.9±1.5

Table 1: Biochemical variables assessment in the study subjects

S. No	Hemostatic variables	Normal (I) (n=20)	Cirrhosis			III (HCC) (n=20)
			II a (n=20)	II b (n=20)	II c (n=20)	
1.	INR	1.5±0.05	1.6±0.13	2.4±0.6	3.5±1.06	3.4±1.0
2.	PT (Prothrombin Time)	12.3±0.1	14.2±1.4	17.5±2.0	21.5±6.0	20.3±4.6
3.	Platelets (cells/µl)	230.2±28.2	190.2±31.2	87.2±21.2	82.2±15.2	81.3±12.3

Table 2: Hemostatic variables assessment in the study subjects with different liver disease stages

S. No	Hemostatic variables	Normal (I) (n=20)	Cirrhosis			III (HCC) (n=20)
			II a (n=20)	II b (n=20)	II c (n=20)	
1.	Calcium (mg/dl)	9.35±0.5	14.2±2.4	14.6±2.4	9.2±1.8	8.5±1.9
2.	Fibrinogen (g/L)	2.9±0.2	1.7±0.6	1.5±0.7	0.7±0.5	0.97±0.4

Table 3: Coagulation factors in the study subjects with different liver disease stages