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Analysis of Prothrombin Time in Hepatitis C Patients

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ABSTRACT

Background and Objectives: Various clotting proteins are synthesized in the liver and any impairment in the liver results in multiple coagulation abnormalities. To determine the prevalence of increased level of Prothrombin Time (PT) in patients with cirrhosis and to compare the levels of Prothrombin Time along with International Normalized Ratio (INR) in patients of Hepatitis C with and without Liver Cirrhosis.

METHODOLOGY: A retrospective study was conducted in Sheikh Zaid Hospital, Lahore in the Gastroenterology department. The study was conducted during the 3 months from May to July, 2023. The study involved 80 patients, out of which 43 were females and 37 were males with multiple age groups ranging from 30 to 85 years. These patients were further divided into 55 patients with Hepatitis C without liver cirrhosis and 25 patients with Hepatitis C with liver Cirrhosis. Immuno-Assay Special Chemistry Analyzer (Access 2) and Sysmex CS-1600 were used to detect the HCV positive patients and to analyze the coagulation profile. A self-designed Performa was used to collect the patient data. Data were entered and analyzed by using excel and displayed by using Tables and Bar Charts.

RESULTS: The results indicated that out of 80 patients Prothrombin Time (PT) was normal in 26 patients of Hepatitis C without Cirrhosis, high in 34 patients of Hepatitis C with and without Cirrhosis, and extremely high in 10 patients of Hepatitis C with Cirrhosis. Similarly, International Normalized Ratio (INR) was normal in 14 patients of Hepatitis C without Cirrhosis, high in 59 patients of Hepatitis C with and without Cirrhosis, and abnormally high in 7 patients of Hepatitis C with Cirrhosis.

CONCLUSION: The conclusion of this study is the abnormalities in the coagulation parameter like Prothrombin Time (PT) depend on the severity and intensity of liver disease.

KEYWORDS: Prothrombin Time (PT), International Normalized Ratio (INR), Hepatitis, Cirrhosis, Coagulation Profile.

INTRODUCTION

Hepatitis, a common liver disease, is caused by Hepatitis A, B, and C viruses. In Pakistan, the prevalence of Hepatitis C and B is particularly high, contributing to the overall incidence of the disease. About 10 million population of Pakistan is infected with Hepatitis C carries(1). The Hepatitis C Virus (HCV), which belongs to the Flaviviridae family and has six genotypes, is responsible for causing Hepatitis C. HCV is an enveloped RNA virus with a single-stranded positive polarity(2). Hepatitis C Virus (HCV) affects the liver by destroying the hepatocytes. It is also known as the “Insidious virus” or “silent killer” because the disease usually remains asymptomatic and symptoms appear after 10-15 years of the onset of the disease. It is a “blood borne virus” and can be transmitted through used syringes, unsafe injection practices, piercing, unscreened blood transfusion and sexual contacts. It usually causes chronic illness which leads to Hepatocellular Carcinoma and Liver Cirrhosis(3). The incidence of HCV in the pediatric population is 0.13%(4). In Pakistan, around 6% of the population is infected with HCV, with the predominant genotypes being 3a (58.16%), and 3b (9.05%), followed by un-typable genotypes(5).

When Hepatitis is not treated or prevented the liver becomes damaged and does not come back to its

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normal structure and can lead to Cirrhosis. When normal cells are placed with the scarred tissues (fibrotic tissue and regenerative nodules) then this is called Liver Cirrhosis(18). The chronic phase after Hepatitis is Liver Cirrhosis. Cirrhosis is also caused by high alcohol consumption, non-alcoholic fatty liver disease, autoimmune disorders, obesity, and iron and copper overload(6). Hepatitis C patients are at threat of thrombotic complications, they have high abnormalities in routine tests of coagulation like prolonged Prothrombin Time (PT), International Normalized Ratio (INR) and aPTT along with a mild decrease in platelet count. The severity of coagulation disorder is estimated by Prothrombin Time (PT)(7).

Prothrombin is a protein formed in the liver. The high value of Prothrombin Time (PT) indicates that our liver is not making the right number of clotting proteins, that's why it takes longer for a blood clot. It means that there is serious liver damage(8). Prolonged prothrombin time usually indicates chronic illness of the liver such as advanced liver Cirrhosis and Hepatitis(9). International Normalized Ratio (INR) ensures that your Prothrombin Time (PT) results are standardized or not (20). It is a ratio derived from prothrombin time that can be calculated as the ratio of patient Prothrombin Time (PT) to control Prothrombin Time (PT).(19) The patients with liver failure or injury have elevated International Normalized Ratio (INR). International Normalized Ratio (INR) could reflect the degree of liver dysfunction and predict the mortality of acute and chronic liver disease(10).

METHODOLOGY

It was a retrospective study. Data was collected from Gastroenterology department of Sheikh Zaid Hospital Lahore, Punjab. Total 80 samples of Hepatitis C were collected from Sheikh Zaid Hospital. Patients of Hepatitis C with and without Cirrhosis was included. Intravenous blood samples were collected from the patients of Hepatitis C by using aseptic phlebotomy techniques. A Performa were used to collect patient data of Hepatitis C patients. Different methods were used for detection of HCV positive patients and for the analysis of coagulation profile. The methods and instruments, we used for analysis, were Immuno-Assay Special Chemistry Analyzer (Access 2) and Sysmex CS-1600.

Beckman Coulter Access 2 is an automated immuno-assay system. It works on the principle of enzyme-mediated chemiluminescence. The Sysmex CS-1600 is an automated coagulation analyzer used to perform variety of coagulation tests like Prothrombin Time (PT), aPTT, fibrinogen, D-Dimer. It processes up to 180 samples per hour and has sample capacity of 50 tubes. The principle is based on photo-optical detection and clotting time determination. Data were entered and analyzed by using excel for statistical analysis. Tables and Bar charts were used to display the data.

The study does not include the patients of Hepatitis B and other diseases of liver except Hepatitis C and Liver Cirrhosis. Except Prothrombin Time (PT) and International Normalized Ratio (INR) the other coagulation parameters (aPTT, D-Dimer, fibrinogen, anti-thrombin) are not included in the study.

RESULTS

This study was conducted on patients of Hepatitis C from Gastro-Enterology department of Sheikh Zaid Hospital.Total 80 patients were included in this study. Out of which 43(54%) were females and 37 (46%) were males with multiple age groups. These 80 patients were further divided into two groups: Hepatitis C positive patients without Liver Cirrhosis having 55 patients with 25(45%) males and 30(55%) females and Hepatitis C positive patients with Liver Cirrhosis having 25 patients with 12(48%) males and 13(52%) females.

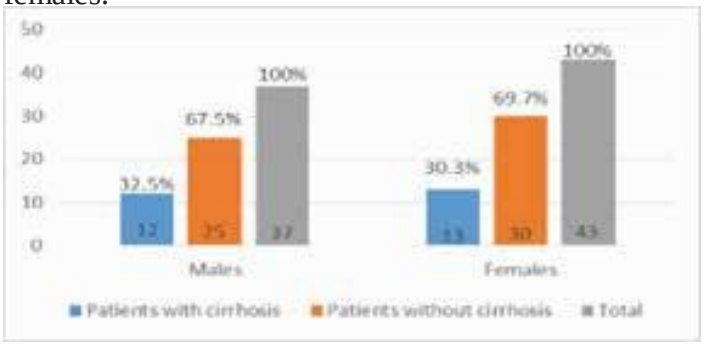

Figure 1 Gender Based Classification of Patients According to Cirrhosis

Out of 80 patients the Prothrombin Time (PT) was normal in 32.5% of patients (without Cirrhosis with range of 10-15 seconds, high in 55% of patients of Hepatitis C with and without Cirrhosis having range of 16-25seaconds and extremely high in 12.5% of patients having range 26-35 seconds with liver Cirrhosis. Prothrombin Time (PT) is affected more in patients with Cirrhosis than without Cirrhosis.

Table 1 Prothrombin Time (PT) range in Hepatitis C patients

PT ranges (seconds)	No. of Patients (Without Cirrhosis)	No. of Patients (With Cirrhosis)	Percentage%
26-35	0	10	12.5%
10-15	26	0	32.5%
16-25	29	15	55%

The results showed that out of total 80 patients International Normalized Ratio (INR) was normal in 18% patients without Cirrhosis (having ratio of 0.8-1.0), high in 73% patients with and without Cirrhosis (having ratio of 1.1-2.0) whereas extremely high in 9% patients with Cirrhosis (having ratio of 2.1-3.0). According to results International Normalized Ratio (INR) was significantly higher in patients with Cirrhosis than in patients without Cirrhosis.

Table No.2 International Normalized Ratio (INR) range in Hepatitis C patients

INR Ratio Range	No. of Patients (Without Cirrhosis)	No. of Patients (With Cirrhosis)	Percentage%
2.1-3.0	0	7	9%
0.8-1.0	14	0	18%
1.1-2.0	41	18	73%

DISCUSSION

Various diseases which effect the liver are Hepatitis, Cirrhosis, non-alcoholic fatty liver disease and liver failure. The most common disease of liver is Hepatitis B; Hepatitis C whose chronic stage is liver Cirrhosis if these left untreated severity level increases. In the mid-20th century, the Prothrombin Time (PT) and International Normalized Ratio (INR) are used for the prognosis and progression of liver disease. The liver synthesis almost all clotting factors and their inhibitors and the disease is characterized by reduced production of pro-coagulants and anti-coagulants proteins. The deficiency in these proteins or coagulants affects the coagulation parameters like Prothrombin Time (PT), International Normalized Ratio (INR) and to a lesser extent aPTT. The patients of Hepatitis C and Cirrhosis indicates the prolonged Prothrombin Time (PT), International Normalized Ratio (INR) with mild decrease in platelets.

The study in 2013 conducted by Sura O. Al-Dewanchi and colleagues had revealed that there was a significant increase in the coagulation parameters of liver diseases. He took 50 patients with 38 of Cirrhosis and 12 of chronic Hepatitis. The results showed Prothrombin Time (PT), and International Normalized Ratio (INR) was high in patients of Hepatitis and Cirrhosis up to 3 folds. And the fibrinogen level reduced in patients with chronic liver diseases(11). The previous studies revealed significant prolongation of Prothrombin Time (PT), and increasing International Normalized Ratio (INR) in patients with chronic liver disease. These findings are similar with other medical researches(12, 13). Ratika Pramod et al. in 2020 conducted study on 102 patients with liver disease. The study assessed Prothrombin Time (PT), D-Dimer levels, and platelet count. The results revealed abnormal PT values in the patients. It was observed that PT levels and positive plasma D-Dimer levels significantly increased with the severity of liver disease(14).

Another similar study conducted in 2019 by Tarun Kotadiya et al. concluded that out of 100 patients of various liver disease (40 with Cirrhosis, 40 with Hepatitis and 20 with obstructive jaundice) 75% of patients had prolonged Prothrombin Time (PT)(15). Faut H. Saner and Carmen Kirchner both studied on monitoring and treating coagulation disorder in End Stage Liver Disease in 2016. Patients with ESLD (end stage liver disease) were subjected to perform their standard lab tests. Pathological values of these test indicating high risk of bleeding in these patients. Results showed that there was 1.5-fold increase in INR, PT, aPTT and platelets was <50/nl(16).

Ozlem kandemir et al. in 2009 studied the role of AST level, prothrombin time and platelet count in Hepatitis C patients with liver fibrosis. Over-all 68 patients are included in this study. All cases had increased ALT and AST level, platelet count was found to be significantly lower which means increased in degree of fibrosis of liver and prolonged PT in chronic Hepatitis C patients(17).

Our study is comparable to these studies as our results indicated that out of 80 patient's PT was normal in 26 patients of Hepatitis C without Cirrhosis, high in 34 patients of Hepatitis C with and without Cirrhosis and extremely high in 10 patients of Hepatitis C with Cirrhosis. Similarly, International Normalized Ratio (INR) was normal in 14 patients of Hepatitis C without Cirrhosis, high in 59 patients of Hepatitis C with and without Cirrhosis and abnormally high in 7 patients of Hepatitis C with Cirrhosis.

CONCLUSION

The conclusion of this study reveals that Prothrombin Time (PT) and International Normalized Ratio (INR) are severely affected and prolonged in chronic liver diseases (Hepatitis C, Cirrhosis). The range of coagulation abnormalities depends on the severity of liver disease. The raised levels of coagulation parameters indicate that our liver is not working properly, there is severe damage to liver cells, it means that liver is not making the right amount of clotting proteins so that's why it takes longer for blood to clot.

Recommendations

Patients should be provided with proper precautions and awareness of Hepatitis C and its chronic phases so that it will helpful in overcome disease. Routine monitoring of coagulation parameters of Hepatitis C

patients is necessary for diagnosis of liver function and stage of disease. Follow up should be needed and well explained for early diagnosis and proper treatment of disease. Future researches can be conducted on different types of liver diseases correlated with Coagulation parameters and on liver diseases that can further lead to other body organ disorders.

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Authors Contribution

Taha Sahar was involved in study design and conception. Jawaria Alvi and Muhammad Raza both were involved in study design, conception, literature search, data collection, data analysis and interpretation. Alia Bibi and Muhammad Kamran were involved in literature search, data analysis, and generation of figures and writing of menuscript. Final draft was approved by Taha Sahar.

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Authors Contributions:

Jawaria Alvi, Taha Sahar, Alia Bibi: Substantial contributions to the conception and design of the work.

Muhammad Usman , Muhammad Raza Ul Hasnain: Design of the work and the acquisition. Drafting the work. Final approval of the version to be published.

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