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Laboratory Diagnosis of Coagulation Hemostasis in Chronic Hepatitis And Liver Cirrhosis With Hcv Etiology

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ABSTRACT

In HCV-associated chronic hepatitis blood coagulation system did not show significant changes before or during antiviral therapy. In HCV-associated liver cirrhosis activated partial thromboplastin time, prothrombin time, and thrombin time were prolonged, but showed improvement with AVT. Fibrinogen levels were significantly reduced by 2 times after 3 months of antiviral therapy. These findings suggest that antiviral therapy has a positive impact on coagulation parameters in liver cirrhosis.

KEYWORDS: Chronic Hepatitis, Liver Cirrhosis, Coagulation System, Antiviral Therapy, Activated Partial Thromboplastin Time, Prothrombin Time, Thrombin Time, Fibrinogen.

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INTRODUCTION

The liver plays a crucial role in hemostasis by synthesizing various blood clotting factors, anticoagulant proteins, fibrinolytic components, and platelet production regulators. Consequently, liver dysfunction disrupts the delicate balance of the coagulation system [5].

Hepatitis viruses are known to damage liver cells, potentially leading to chronic hepatitis or liver cirrhosis. While approximately 10–15% of liver cells can still produce clotting factors necessary for maintaining normal hemostasis, this capacity is largely influenced by the severity and duration of the disease. In cases of liver failure, patients may simultaneously exhibit hypercoagulability, hypocoagulability, and hyperfibrinolysis, further complicating the coagulation process.[15]

The body's physiological processes are in a state of constant dynamic equilibrium, and liver diseases disrupt this balance, leading to homeostatic instability. In the advanced stages of liver disease, hemostatic alterations play a critical role in complications related to an increased risk of bleeding [1].

Liver-related pathologies significantly impair hemostatic parameters, often resulting in reduced plasminogen levels and prolonged prothrombin and thrombin times, particularly in cases of liver cirrhosis [7].

Additionally, in liver fibrosis, platelet counts may decrease, while blood clotting tendencies can increase—even when coagulogram parameters exceed normal levels—highlighting the complexity of coagulation disorders in hepatic conditions [12, 16].

Liver dysfunction can contribute to the onset of coagulopathy and hemorrhagic diathesis. In chronic viral hepatitis, platelet reduction and coagulation disturbances play a key role in the development of hemorrhagic syndrome, primarily due to the elevated activity of tissue plasminogen activator. Liver inflammation and fibrosis are closely linked to organ dysfunction. As histological activity and fibrosis progress, there is a rise in endothelial dysfunction, alterations in coagulation parameters, thrombocytopenia, and increased levels of physiological anticoagulants and plasminogen [7].

Research has demonstrated that coagulopathy is elevated in all patients with liver cirrhosis, as evidenced by prolonged International Normalized Ratio (INR), prothrombin index (PTI) and prothrombin time (PT) [13]. Additionally, individuals with liver disease exhibit reduced plasma protein C activity [14].

Although standard tests have been designed to monitor anticoagulant therapy, they remain insufficient for a comprehensive

assessment of hemostasis [6].

Prothrombin time, prothrombin index, and platelet count are valuable indicators for determining the stage of liver disease, monitoring its progression, and selecting appropriate hemostatic therapy in cases of bleeding. However, abnormal prothrombin time and platelet levels do not always correlate with bleeding risk, as these tests alone are insufficient for a comprehensive hemostasis assessment in liver disease [4].

A key factor contributing to bleeding in patients with liver cirrhosis is the reduction of fibrinolysis inhibitors [9]. In liver-related pathologies, tissue plasminogen activator activity and plasminogen activator inhibitor levels serve as crucial parameters for evaluating fibrinolysis [8].

Liver diseases lead to unpredictable disturbances in the hemostasis system, often resulting in serious complications. In liver cirrhosis, complex and irregular changes in coagulation contribute to various complications in patients with impaired liver function. Given these challenges, studying the hemostasis system in patients with chronic hepatitis and cirrhosis is crucial. Monitoring PT, activated partial thromboplastin time (APTT), D-dimer, and fibrinogen levels plays a key role in assessing patient prognosis [11].

Fibrinogen levels fluctuate in chronic liver disease. As an acute-phase protein, fibrinogen may initially be elevated in newly diagnosed liver disease but declines in the decompensated stage of cirrhosis [2]. In cirrhotic patients, fibrinogen levels below 1 g/L significantly increase bleeding risk [10]. However, bleeding in cirrhosis is not solely due to clotting factor deficiency—it is also linked to portal hypertension, which, when combined with low fibrinogen levels, further exacerbates bleeding risk [3].

Activated Partial Thromboplastin Time (APTT) is a key coagulation parameter that should be monitored in hospitalized patients with chronic liver disease. It plays a crucial role in evaluating coagulation hemostasis, particularly in assessing the intrinsic (factors XII, XI, IX, and VIII) and common (factors X, V, II, and I) pathways of blood clotting. APTT is notably prolonged in patients both with and without chronic liver disease (CLD).To effectively assess hemostasis in chronic liver diseases and determine bleeding risk, measuring Prothrombin Time (PT), International Normalized Ratio (INR), APTT, Thrombin Time (TT), and fibrinogen levels is essential [8].

The main part. The primary of patients was divided as follows: Group 1 included individuals diagnosed with HCV-related diffuse hepatitis who did not receive any antiviral treatment. Group 2 comprised patients with the same condition who were treated with sofosbuvir and velpatasvir. Group 3 consisted of patients suffering from HCV-related liver cirrhosis who did not undergo antiviral therapy, whereas Group 4 included those with HCV-related liver cirrhosis who received treatment with sofosbuvir and velpatasvir.

To evaluate coagulation hemostasis, the following parameters were analyzed: blood clotting time, APTT, PT, PTI, INR, TT, and fibrinogen levels. In HCV-associated chronic hepatitis (CHC), the blood clotting time results were as follows: Group 1: Clotting initiation time – 152 ± 24 sec, completion time – 248 ± 35 sec. Group 2: Clotting initiation time – 160 ± 38 sec, completion time – 254 ± 29 sec. Control group: Clotting initiation time – 140 ± 24 sec, completion time – 236 ± 32 sec. These findings indicate that in HCV-associated chronic hepatitis, blood clotting time did not differ significantly from the control group values. Blood Clotting Time in HCV-Associated Liver Cirrhosis (LC) During Antiviral Therapy (AVT).

In Group 4 patients with HCV-associated liver cirrhosis (LC), blood clotting time remained unchanged during AVT:After 1 month of AVT:Initiation time: 246 ± 30 sec, completion time: 368 ± 40 sec. After 3 months of AVT: Initiation time: 258 ± 25 sec,completion time: 374 ± 41 sec, control group: initiation time: 140 ± 24 sec, completion time: 236 ± 32 sec.

These results indicate that **blood clotting time was significantly prolonged in HCV-associated liver cirrhosis compared to the control group, and AVT did not lead to noticeable changes in this parameter. (table 1).

TABLE 1. IN HCV-INDUCED LIVER CIRRHOSIS, THE BLOOD CLOTTING TIME

Groups	Blood clotting initiation time (seconds).	Blood clotting completion time (seconds).
Control group (n=20)	140 ± 24	236 ± 32
Group 3 (n=30)	244 ± 28**	352 ± 38*
Group 4, n=30 Before treatment	231 ± 22**	347 ± 36*
Group 4, n=30 1 month of AVT	246 ± 30**	368 ± 40*
Group 4, n=25 3 month of AVT	258 ± 25**	374 ± 41*

Note: * - a sign of significant difference from the parameters of healthy pregnant women, ↑ - direction of change, ↔ - no significant difference.

In patients with HCV-associated chronic hepatitis (CHC), comparable alterations were noted in the assessment of activated partial thromboplastin time (APTT), a crucial marker of the initial phase of coagulation hemostasis. The recorded values were as follows:

Group 1 – 30 ± 2.8 seconds, Group 2 – 27 ± 2.2 seconds. Following one month of antiviral therapy (AVT), APTT increased to 32 ± 2.6 seconds, and after three months of AVT, it further extended to 34 ± 2.8 seconds. In the control group, the APTT was measured at 31 ± 2.6 seconds.

These findings indicate that APTT values in HCV-associated chronic hepatitis showed no significant deviations from the control group, both before and during AVT. (Figure 1)

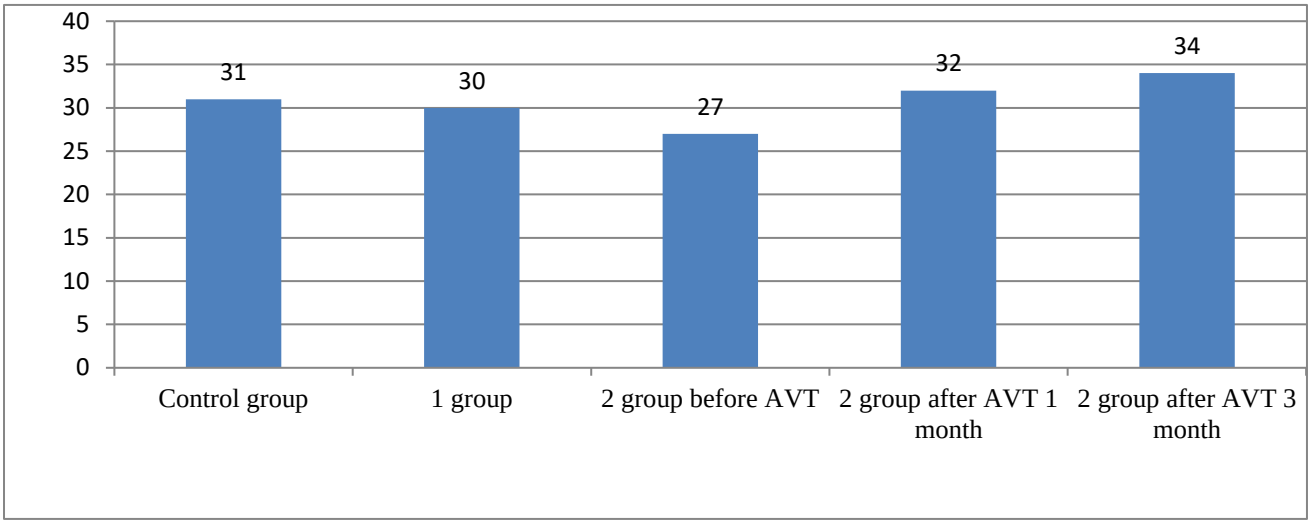

Fig. 1. APTT in HCV-induced chronic hepatitis, sec.

In HCV-associated liver cirrhosis (LC), a slight shortening of APTT was observed: Group 3: 40 ± 3.2 sec, group 4 (before treatment): 42 ± 3.4 sec, after 1 month of AVT: 38 ± 3.5 sec and after 3 months of AVT: 36 ± 2.8 sec. Control group: 31 ± 2.6 sec. These findings suggest that APTT was markedly prolonged in patients with HCV-related liver cirrhosis compared to the control group but showed a progressive improvement during AVT.

The clinical study results revealed that activated partial thromboplastin time (APTT) was significantly prolonged by 29–35% in HCV-associated liver cirrhosis (LC) compared to the control group**.. (Figure 2)**

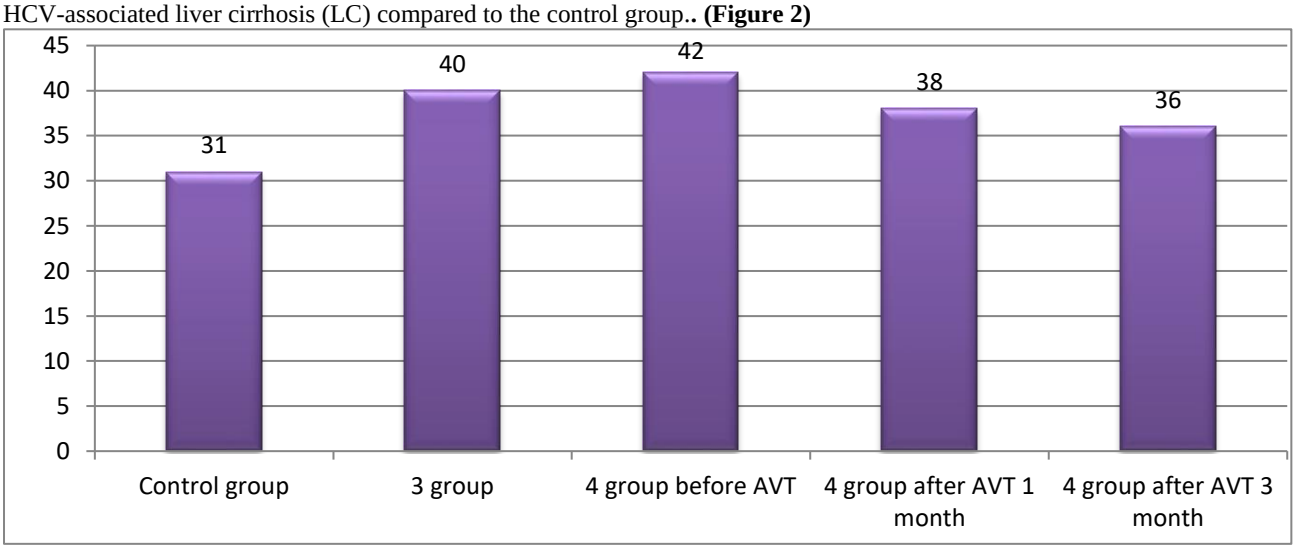

Fig. 2. APTT in HCV-induced liver cirrhosis, sec.

The evaluation of prothrombin time (PT) and its associated indices, including the Prothrombin Index (PTI) and International Normalized Ratio (INR), in chronic hepatitis C (CHC) of HCV etiology revealed no statistically significant differences compared to the control group.

In the control group, PT (Prothrombin Time) was 12.5 ± 1.0 sec, PTI (Prothrombin Index) was 104 ± 10%, and INR (International Normalized Ratio) was 0.96 ± 0.07. In the first group, PT was 13.0 ± 1.2 sec, PTI was 92 ± 8%, and INR was 1.08 ± 0.09. In the second group, PT was 12.8 ± 1.1 sec, PTI was 94 ± 7%, and INR was 1.07 ± 0.08. In the second group of patients with chronic hepatitis C (CHC) of HCV etiology, these indicators remained almost unchanged during antiviral therapy (AVT). One month after AVT, PT was 13.4 ± 1.2 sec, PTI was 90 ± 8%, and INR was 1.12 ± 0.09. Three months later, PT was 13.5 ± 1.1 sec, PTI was 89 ± 7%, and INR was 1.12 ± 0.08 (Table 2).

TABLE 2. PT, PTI, AND INR IN HCV-INDUCED CHRONIC HEPATITIS

Groups	PT (sec)	PTI (%)	INR
Control group (n=20)	12,5 ± 1,0	104 ± 10	0,96± 0,07
Group 1 (n=30	13,0 ± 1,2	92 ± 8	1,08 ± 0,09
Group 2 (n=30) (Before treatment)	12,8 ± 1,1	94 ± 7	1,07 ± 0,08
Group 2 (n=30) (1 month after AVT)	13,4 ± 1,2	90 ± 8	1,12 ± 0,09
Group 2 (n=28) (3 months after AVT)	13,5 ± 1,1	89 ± 7	1,12 ± 0,08

Clinical studies have shown that no significant changes were detected in thrombin time (TT) in patients from Groups 1 and 2. In the control group, TT was 24.3 ± 2.1 sec, while in Group 1, it was 26.7 ± 2.4 sec, and in Group 2, it was 27.9 ± 2.6 sec. In Group 2 patients undergoing antiviral therapy (AVT), TT values were as follows: One month after AVT:28.4 ± 2.6 sec, three months after AVT: 27.7 ± 2.4 sec (figure 3).

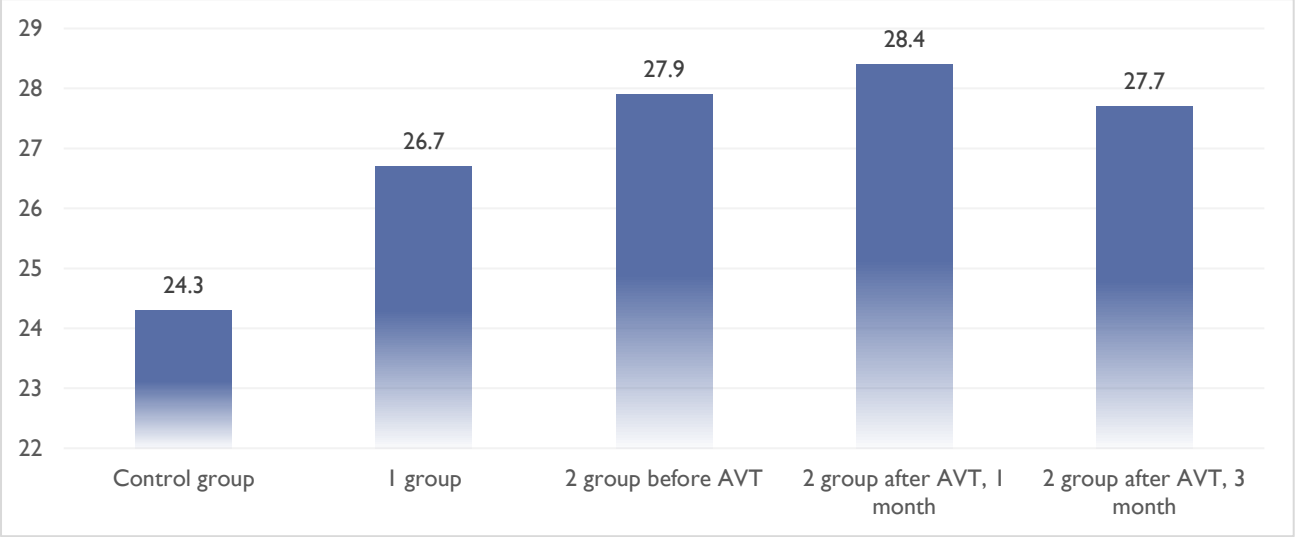

Fig. 3. Thrombin time in HCV-induced chronic hepatitis, sec.

In patients with HCV-associated liver cirrhosis (LC), substantial differences were identified in Prothrombin Time (PT), Prothrombin Index (PTI), and International Normalized Ratio (INR) when compared to the control group. In Group 3, PT was 18.3 ± 1.6 sec, PTI was 66 ± 5%, and INR was 1.52 ± 0.18. In Group 4, before treatment, PT was 17.6 ± 1.6 sec, PTI was 68 ± 7%, and INR was 1.46 ± 0.16.-In the control group, PT was 12.5 ± 1.0 sec, PTI was 104 ± 10%, and INR was 0.96 ± 0.07. In Group 4 patients undergoing antiviral therapy (AVT), these indicators changed as follows:- One month after AVT: PT 16.1 ± 1.3 sec, PTI 74 ± 5%, INR 1.34 ± 0.16. Three months after AVT: PT 14.5 ± 1.0 sec, PTI 83 ± 6%, INR 1.21 ± 0.10. (table 3).

TABLE 3.PT, PTI, AND INR IN HCV-ASSOCIATED LIVER CIRRHOSIS

Groups	PT, sec	PTI, %	INR
Control group (n=20)	12,5 ± 1,0	104 ± 10	0,96 ± 0,07
Group 3 (n=30)	18,3±1,6**	66 ± 5**	1,52± 0,18**
Group 4 (n=30) Before treatment	17,6±1,6**	68±7**	1,46± 0,16**
Group 4, n=30 1 month after AVT	16,1 ± 1,3*	74 ± 5*	1,34 ± 0,14*
Group 4, n=30 3 month after AVT	14,5 ± 1,0^	83 ± 6^	1,21±0,10

Note: * - a sign of significant difference from the parameters of healthy pregnant women, ↑ - direction of change, ↔ - no significant difference.

In liver cirrhosis (LC) associated with HCV, notable variations were detected in Prothrombin Time (PT), Prothrombin Index (PTI), and International Normalized Ratio (INR), showing a 1.26-fold discrepancy in comparison to the control group.

In patients from Groups 3 and 4 with HCV-associated liver cirrhosis (LC), thrombin time (TT) was significantly reduced compared to the control group.

In **Group 3**, TT was **35.7 ± 4.2 sec**.,In **Group 4**, TT was **34.6 ± 3.3 sec**. In the **control group**, TT was **24.3 ± 2.1 sec**. For **Group 4 patients undergoing antiviral therapy (AVT)**, TT changed as follows: **One month after AVT: 32.4 ± 3.8 sec**., t**hree months after AVT: 28.6 ± 3.5 sec**. These findings indicate that **HCV-related liver cirrhosis significantly prolongs thrombin time**, but **AVT may help in reducing this prolongation over time**.

In individuals with HCV-related liver cirrhosis (LC), thrombin time (TT) showed a 1.25-fold reduction after undergoing antiviral therapy (AVT). (figure 4)

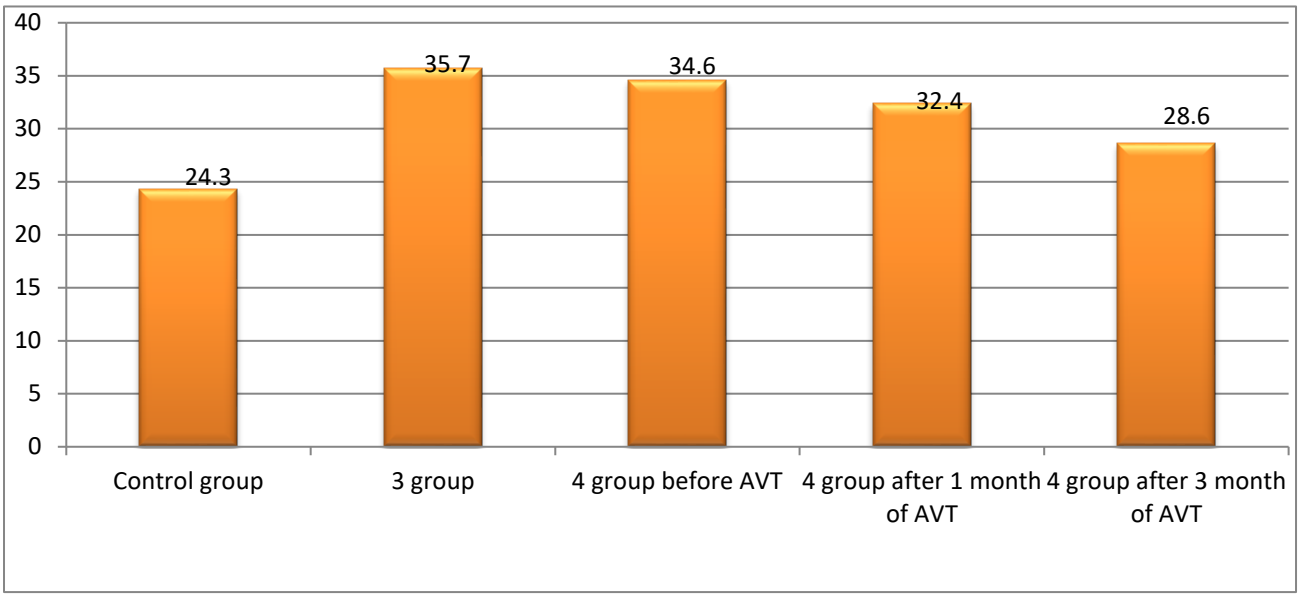

Fig. 4. Thrombin Time (TT) in HCV-associated liver cirrhosis (measurede in seconds).

In **HCV-associated chronic hepatitis (CHC)**, the **fibrinogen level did not show significant changes** during AVT. These findings suggest that **AVT may help improve coagulation parameters in cirrhosis**, while **fibrinogen levels remain stable in chronic hepatitis C**. (figure 5)

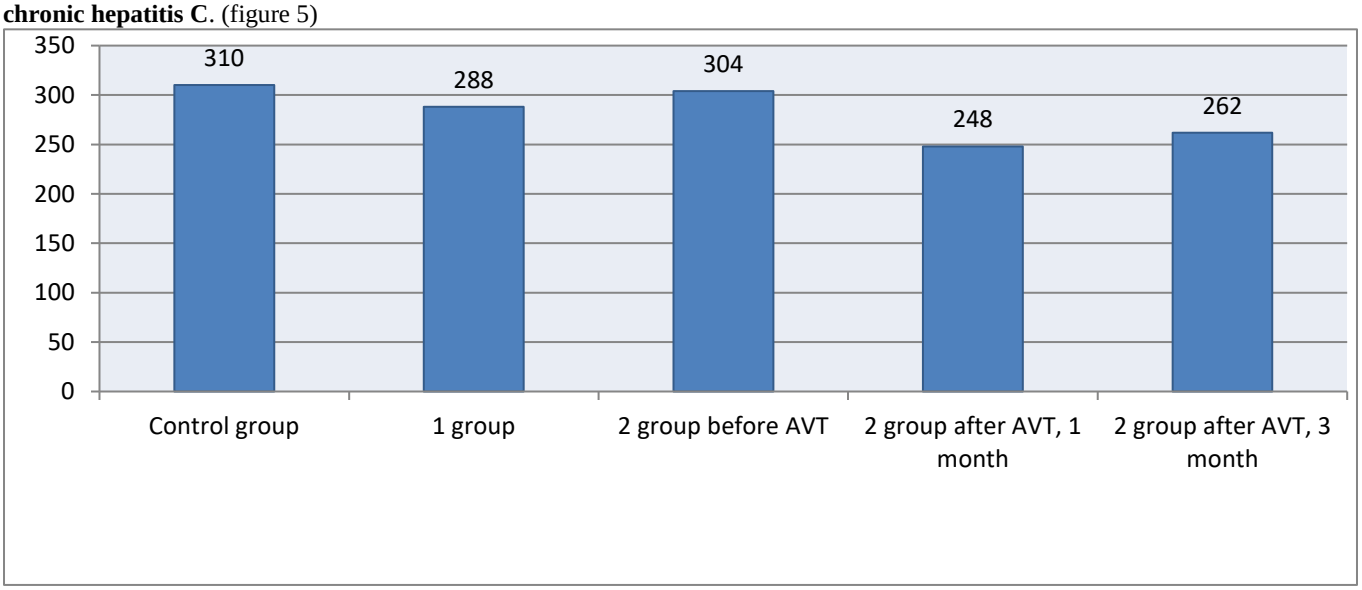

Fig. 5. Fibrinogen in HCV-related chronic hepatitis, mg/dL.

As shown in Figure 5, fibrinogen levels varied across groups:control group: 310 ± 26 mg/dL, Group 1: 288 ± 31 mg/dL, Group 2 (before treatment): 304 ± 28 mg/dL, Group 2 (1 month after AVT): 248 ± 26 mg/dL, Group 2 (3 months after AVT): 262 ± 28 mg/dL. These findings indicate that fibrinogen levels decreased after one month of AVT but showed partial recovery by the third month.

In **HCV-associated liver cirrhosis (LC)**, fibrinogen levels **did not show significant changes** compared to the control group. However, during **AVT**, a gradual **increase in fibrinogen levels** was observed: c**ontrol group: 310 ± 26 mg/dL, group 3: 158 ± 36 mg/dL, group 4 (before treatment): 152 ± 18 mg/dL, group 4 (1 month after AVT): 166 ± 18 mg/dL, group 4 (3 months after AVT): 189 ± 11 mg/dL.** The results indicate that fibrinogen levels are considerably reduced in liver cirrhosis compared to

healthy individuals, but antiviral therapy (AVT) may aid in its gradual restoration over time. (figure 6)

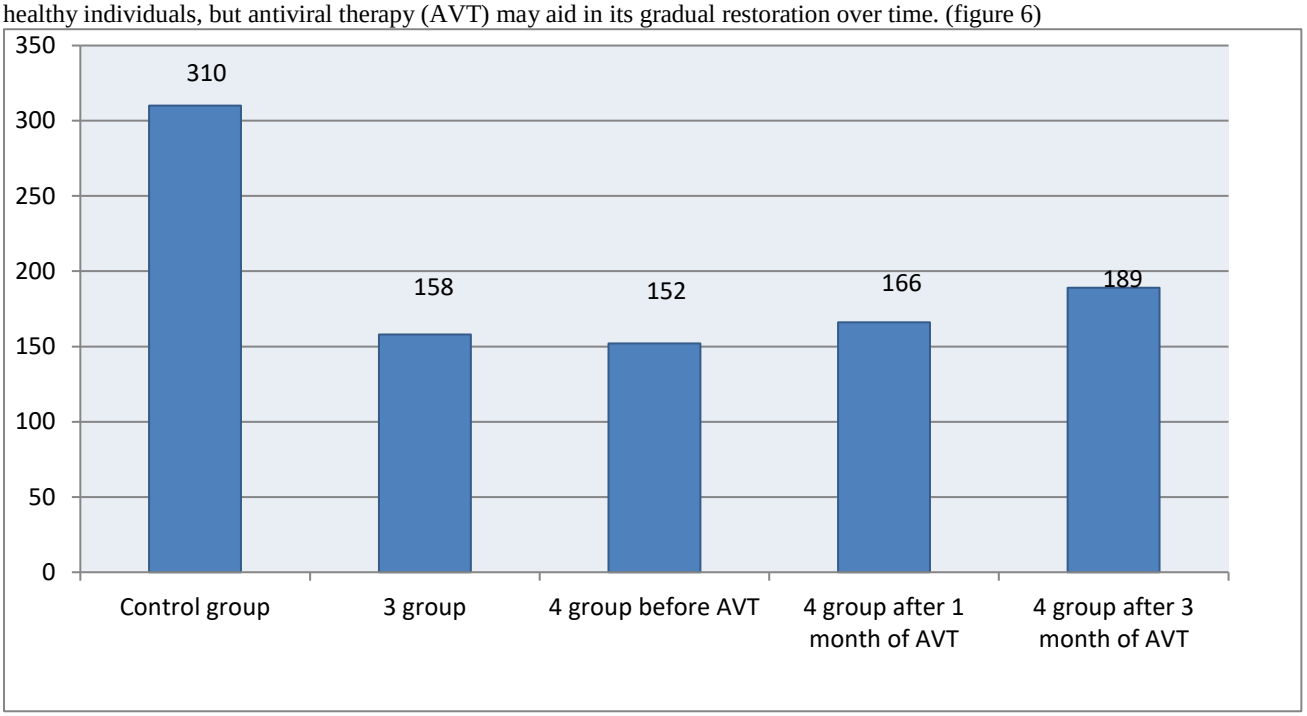

Fig. 6. Fibrinogen levels in HCV-associated liver cirrhosis (mg/dL).

In HCV-related liver cirrhosis (LC), fibrinogen levels were found to be notably lower, showing a twofold decrease in comparison to the control group.**.** However, during **antiviral therapy (AVT), a gradual increase in fibrinogen levels was observed, reaching a 1.2-fold increase after 3 months.**

In **HCV-associated liver cirrhosis (LC), fibrinogen levels did not show significant changes initially**, but a gradual **increase was observed during AVT**: **Group 3: 158 ± 36 mg/dL, group 4 (before treatment): 152 ± 18 mg/dL, group 4 (1 month after AVT): 166 ± 18 mg/dL, group 4 (3 months after AVT): 189 ± 11 mg/dL** (a **1.2-fold increase** from baseline). C**ontrol group: 310 ± 26 mg/Dl.** These findings indicate that **although fibrinogen levels remained significantly lower than in the control group, AVT contributed to a progressive increase in fibrinogen levels over time**.

CONCLUSION

In HCV-associated chronic hepatitis (CHC), blood coagulation time, APTT, PT, PTI, INR, TT, and fibrinogen levels did not show significant changes before or during antiviral therapy (AVT). In HCV-related liver cirrhosis (LC), blood coagulation time was significantly extended and remained unchanged throughout AVT. APTT, PT, and TT were also prolonged but showed signs of improvement with AVT. Fibrinogen levels were notably lower, reduced by half compared to the control group, but increased 1.2 times after three months of AVT.These findings suggest that AVT has a positive impact on coagulation parameters in liver cirrhosis, while no significant changes were observed in chronic hepatitis C.

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