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Assessment of hemostasis in patients with compensated and decompensated liver cirrhosis

Tugushev Aliy Saitovich[1] and Cherkovska Olga Stepanivna[1]

[1]Department of Faculty Surgery, Zaporizhzhia State Medical and Pharmaceutical University, Ukraine
tugushev63@ukr.net (A. S. Tugushev)

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ABSTRACT

An assessment of hemostasis was carried out in patients with compensated and decompensated liver cirrhosis.

Materials and methods. A total of 320 patients with liver cirrhosis. 254 patients were assigned to the decompensated cirrhosis group. 66 patients were assigned to the compensated group. Evaluation of the procoagulant pathway included determination of platelet count, prothrombin index, activated partial thromboplastin time, fibrinogen levels, and coagulation factor FVIII activity. Assessment of the anticoagulant pathway included determination of Protein C activity. The ratio of factor F VIII activity to protein C activity (FVIII/PC ratio) was calculated. Markers of thrombosis were evaluated based on fibrinogen "B" and D-dimer levels.

Results. In patients with compensated disease, reduction in the levels of standard procoagulant parameters was observed in 37.9% of those examined. Concurrently, factor F VIII activity was at the upper limit of normal in 65.2% of patients, while in 36.4% of cases, it exceeded the reference range. Plasma activity of the Protein C was within the lower limit of normal in 72.7% of subjects and below the reference range in 27.3%. The FVIII/PC ratio slightly exceeded normal values in 82.4% of patients, ranging from 1.1 to 1.3, indicating relative imbalance favoring hypercoagulability.

Among decompensated patients, 60-70% exhibited reduction in standard procoagulant parameters of the hemostasis system upon admission. Conversely, Factor FVIII activity levels were above the reference range in nearly all patients. Protein C activity was below the normal limit in over 60% of patients presenting with either hemorrhage or ascites. The FVIII/PC ratio exceeded normal values by 3- to 4-fold in 100 % of patients with bleeding and 40-60 % of those with ascites, indicating a marked baseline imbalance favoring a hypercoagulability.

The observed reduction in platelet counts, prothrombin index, and fibrinogen levels, alongside prolonged aPTT during hemorrhage in decompensated patients, can be interpreted as a manifestation of disseminated intravascular coagulation syndrome. Upon admission, D-dimer levels in 75.0%-97.0 % of patients—presenting with both hemorrhage and ascites—exceeded reference values by more than five-fold. Among deceased patients, D-dimer concentrations remained persistently elevated in 100.0 % of cases.

Conclusions. Hemostatic status in compensated liver cirrhosis is characterized by relative imbalance between hepatocyte-derived pro- and anticoagulants and the endothelial-derived extrahepatic clotting factor FVIII, favoring a hypercoagulability.

Hemostatic status in hospitalized patients with decompensated liver cirrhosis is characterized by reduction in both hepatocyte-derived pro- and anticoagulants, signaling hepatic functional decompensation. Conversely, the activity levels of the extrahepatic coagulation factor F VIII were elevated above the reference range in nearly all patients, indicating underlying endothelial dysfunction. The FVIII/PC ratio in the majority of patients was 3- to 4-fold higher than the reference range, indicating underlying baseline thrombophilia.

The presence of hypocoagulation is attributed to the development of disseminated intravascular coagulation syndrome of varying severity. This is laboratory-confirmed by thrombocytopenia, decreased prothrombin index, reduced fibrinogen levels, prolonged aPTT, and the presence of fibrin degradation products, including fibrinogen B and D-dimer.

Keywords: Liver cirrhosis, hemostasis, thrombosis, hemorrhage, endothelial dysfunction, protein C, factor F VIII, disseminated intravascular coagulation syndrome.

Introduction

The nature of hemostatic alterations in liver cirrhosis (LC) is complex, frequently unpredictable, and involves all components of the system – primary (vascular-platelet) hemostasis, the coagulation cascade and fibrinolysis. These alterations are accompanied by an imbalance between the pro- and anticoagulant systems, primarily driven by the dysregulated synthesis of both pro- and anticoagulants within the liver and the endothelium[1-4]. It is widely recognized that LC leads to a hypocoagulation state characterized by an increased predisposition to hemorrhage. However, a substantial body of literature contests this view, suggesting that traditional laboratory interpretations are limited by standard methodologies that fail to adequately assess the procoagulant and antifibrinolytic components of hemostasis.

The cause of bleeding, primarily from esophageal and gastric varices, is not hypocoagulation as such, but the rupture of varices due to increased portal pressure[5,6]. Numerous researchers have identified a hypercoagulable state in liver cirrhosis, which predisposes patients to both intra- and extrahepatic thrombosis. The development of thrombotic events is associated with the severity of hepatic insufficiency, as well as the presence of major extrahepatic complications resulting from impaired portal blood flow and a subsequent increase in portal pressure[7-10].

Consequently, liver cirrhosis may manifest with both hemorrhagic and thrombotic complications. All currently available hemostatic assays have inherent limitations and must be interpreted with caution, as their prognostic value remains unproven. Comprehensive assessment of the hemostasis system requires the evaluation of both pro- and anticoagulant components. And hypocoagulation can be interpreted as a primary defect only when the anticoagulant system is within normal limits, and vice versa[6,11-13].

Several authors highlight distinct differences in hemostatic parameters between patients with compensated (uncomplicated) and decompensated (complicated) liver cirrhosis. Currently, these stages are recognized as two separate syndromes in both clinical practice and research settings. These stages differ significantly in clinical course, treatment outcomes, and mortality rates. Consequently, it remains an unresolved question whether hemostatic imbalance is a consequence of decompensated cirrhosis or a primary driver of decompensation and the subsequent development of specific complications[12,14-16].

From this perspective, a comparative study of the pro- and anticoagulant systems in patients with liver cirrhosis – both in compensated cases and during decompensation – is of significant clinical relevance.

The Aim

To provide a comparative assessment of the hemostatic system in patients with compensated versus decompensated liver cirrhosis.

Materials and Methods

The study was conducted between 2020 and 2025 at the surgical departments of the City Center for Emergency Medicine and City Hospital No. 9, as well as the therapeutic departments of City Hospitals No. 1 and No. 9, Ukraine. The study was performed in accordance with the core bioethical standards of the World Medical Association Declaration of Helsinki on ethical principles for medical research involving human subjects, with the informed consent of all patients.

A total of 320 patients with liver cirrhosis were examined. The cohort included 207 men (64.8%) and 113 women (35.2 %), with ages ranging from 22 to 74 years. Regarding etiology, 111 patients (34.8 %) presented with viral cirrhosis, 94 (29.4 %) with alcoholic cirrhosis, and 61 (19.1 %) had a mixed etiology (viral and alcohol-related). A history of drug-induced hepatitis was recorded in 8 (2.5 %) patients, substance use disorder in 14 (4.3 %), portal vein thrombosis in 6 (1.9 %), and Budd-Chiari syndrome in 2 (0.8 %). In 23 cases (7.2 %), the etiology of liver cirrhosis remained cryptogenic.

A total of 254 patients were assigned to the decompensated cirrhosis group. Of these, 164 presented with gastrointestinal bleeding originating from esophageal varices; 112 (68.3 %) of these patients were discharged, while 52 (31.7 %) died. Additionally, 90 patients presented with ascites, resulting in 65 (72.2 %) discharges and 25 (27.8 %) deaths. The primary cause of death in all cases was hepatorenal failure. 66 patients were assigned to the compensated cirrhosis group. A history of gastrointestinal bleeding was recorded in 53 (80.3 %) cases and edematous-ascitic syndrome in seven (10.6 %). In six (9.1 %) patients, the diagnosis was newly established during routine clinical visits. At the time of evaluation, all subjects were asymptomatic, presenting with no specific complaints.

The pro- and anticoagulant systems of hemostasis were evaluated. Assessment of the procoagulant pathway included platelet count (reference range: 180-320x10^9/L), prothrombin index (80-120 %), activated partial thromboplastin time (35-50 sec), fibrinogen levels (2.2-4.4 g/L), and coagulation factor VIII (FVIII) activity (70-150 %).

Evaluation of the anticoagulant pathway included the determination of protein C activity (70-150 %).

The Factor VIII to Protein C activity ratio (FVIII/PC ratio) was calculated as a marker (index) of hemostatic imbalance. Under normal conditions, the FVIII/PC ratio is balanced, typically approaching 1:1 (with inter-laboratory variations ranging from 0.8 to 1.2) and is expressed as 1,0±0,2.

Additionally, thrombotic markers were assessed, including fibrinogen B (normally absent) and D-dimer (reference range: <500.0 ng FEU/mL). In hospitalized (decompensated) patients, measurements were performed at baseline (upon admission) and every 3-4 days for longitudinal monitoring. For outpatients (compensated), testing was conducted during routine follow-up examinations.

Statistical processing of the research results and the development of the mathematical model were performed using variational statistics methods, implemented via standard statistical analysis software packages «STATISTICA® for Windows 6.0» (StatSoft Inc., №AXXR712D833214FAN5). Data were expressed as the arithmetic mean (M), standard deviation (σ), and standard error of the mean (m), with the 95 % confidence interval (CI) calculated for the mean values. Results are presented as M ± m Statistical significance was defined at a threshold of $p < 0.05$. To evaluate relationships between variables, correlation analysis was performed using Spearman's rank correlation coefficient (R).

Results

1. ASSESSMENT OF THE HEMOSTATIC SYSTEM IN PATIENTS WITH COMPENSATED LIVER CIRRHOSIS

1.1 Procoagulant hemostasis.

Procoagulant Hemostasis Among 41 (62.1 %) patients with uncomplicated liver cirrhosis, the prothrombin index, fibrinogen levels, and aPTT did not significantly deviate from reference values. Conversely, 25 (37.9 %) patients exhibited a prothrombin index below 80 % (mean range: 64-78%) and fibrinogen levels below 2.2 g/L (range: 1.8-2.1 g/L). Platelet counts exceeded 100x10^9/л. in 49 (74.0 %) patients, ranged between 60-100,0x10^9/л, in 13 (20.0 %), and were below 60x10^9/л ($p < 0,05$). Coagulation factor F VIII activity was at the upper limit of normal (ULN) (150%) in 43 (65.2 %) patients and exceeded the ULN (>150 %) in 24 (36.4 %) patients ($p < 0,05$).

1.2 Anticoagulant hemostasis.

Plasma anticoagulant protein C activity in 48 (72.7 %) subjects was within the 70-100% range (mean: 88 %), corresponding to the lower limit of normal (LLN). In 18 (27.3 %) patients, activity was below the reference range, measuring between 55 % and 70 % (mean: 62.5 %; $p < 0,05$).

The factor F VIII to Protein C activity ratio (FVIII/PC ratio) in 54 (82.4 %) patients ranged between 1.1 and 1.3, which slightly exceeded the reference values. Consequently, during the natural history of liver cirrhosis (LC), a minor hemostatic imbalance toward a hypercoagulable state is observed.

1.3 Thrombosis markers.

Among the subjects, 38 (57.6 %) tested positive for fibrinogen B (rated as ++ and +++). Of these, six (15.8 %) patients exhibited elevated D-dimer levels exceeding 500.0 ngFEU/mL. These findings were clinically silent. However, in one patient, targeted ultrasound scanning and Doppler ultrasonography revealed the presence of portal vein thrombosis (PVT) in the recanalization stage.

2. ASSESSMENT OF THE HEMOSTATIC SYSTEM IN PATIENTS WITH DECOMPENSATED LIVER CIRRHOSIS.

2.1 Procoagulant hemostasis.

Platelet counts. In the cohort of patients admitted with variceal bleeding, 101 (61.4 %) subjects had a platelet count exceeding$100x10^9$/l, regardless of the clinical outcome – specifically, 65 (58.2 %) of those discharged and 32 (62.4 %) of the deceased. Notably, only 10 (6.2 %) patients – comprising 4 (3.6 %) discharged and 6 (11.5 %) deceased – presented with a platelet level below $60x10^9$/l upon admission.

In the cohort of patients admitted with ascites, 51 (78 %) of the discharged patients and 20 (81.9%) of the deceased had platelet counts exceeding $100x10^9$/l. Conversely, platelet levels below $60x10^9$/l were observed in 4 (5.9 %) of the discharged patients and 2 (8.0 %) of the deceased.

Consequently, thrombocytopenia cannot be considered the primary factor underlying an increased bleeding diathesis in these patients. Throughout the observation period, platelet counts fluctuated, with a distinct trend toward improvement in discharged patients and a decline in those with a fatal outcome. Therefore, a longitudinal increase in the platelet count carries significant positive prognostic value.

Prothrombin Index (PI). In the cohort of discharged patients, on admission, a prothrombin index of less than 80% was observed in 52 (46.0 %) patients with gastrointestinal bleeding and 48 (73.1%) patients with ascites. During follow-up, similar values were recorded in 23.7% and 51.1% of patients, respectively. Consequently, there was a significant reduction in the number of patients with a PI within the 60-80 % range or below 60 % ($p < 0,05$).

Among the deceased patients, a prothrombin index (PI) of less than 80 % on admission was observed in 33 (64.3 %) subjects with gastrointestinal hemorrhage (GIH) and 15 (60.0 %) with ascites. In follow-up studies, this ratio remained virtually unchanged. Consequently, the longitudinal normalization of the prothrombin index carries positive prognostic significance.

Fibrinogen. In the cohort of discharged patients, a fibrinogen level of less than 2.2 g/L on admission was observed in 38 (34.0 %) patients with gastrointestinal hemorrhage (GIH) and 17 (26.9 %) with ascites. During longitudinal monitoring, the proportion of patients with low fibrinogen levels decreased to 21.2 % and 5.3 %, respectively ($p < 0,05$).

Among the non-survivors, the proportion of patients with admission fibrinogen levels below 2.2 g/L was comparable to that of the discharged group. However, follow-up assessments revealed distinct differences between the gastrointestinal hemorrhage (GIH) and ascites cohorts. In the GIH group, the number of patients with low fibrinogen levels remained virtually unchanged, whereas in patients with ascites, the prevalence of hypofibrinogenemia increased nearly threefold, rising from 27.3 % to 76.4 % ($p < 0,05$).

Activated partial thromboplastin time (aPTT). More than half of the patients admitted with complications of liver cirrhosis exhibited alterations in activated partial thromboplastin time, manifesting as both increases and decreases. Notably, longitudinal data revealed that while aPTT tended to normalize among survivors, divergent trends were observed in the deceased cohort: patients with gastrointestinal hemorrhage (GIH) showed prolonged aPTT (indicative of hypocoagulation), whereas those with ascites exhibited shortened aPTT (indicative of hypercoagulation). Consequently, aPTT levels cannot be utilized as a reliable prognostic factor.

Coagulation Factor F VIII. Among the patients admitted with gastrointestinal hemorrhage (GIH), elevated procoagulant activity of coagulation factor VIII was observed on admission in 84 (75.0 %) of those subsequently discharged and in 100.0 % of the deceased, with mean levels of 297 % and 228 %, respectively. In the cohort admitted with ascites, increased FVIII activity was recorded in 42 (64.2 %) of the discharged patients and 18 (73.4 %) of those who later died, with mean values of 242 % and 264%, respectively.

2.2 Anticoagulant hemostasis

Protein C. In 43 (37.5 %) discharged patients with gastrointestinal hemorrhage (GIH) and 32 (62.0 %) of the deceased, the activity of anticoagulant Protein C was below 70 % (reference range: 70-150 %), with mean values of 54 % and 55.6 %, respectively. In the remaining patients, Protein C activity was slightly above the lower limit of normal (LLN), averaging 84.2 % and 87.3 %, respectively (p <0,05). Among those admitted with ascites, a reduction in Protein C activity to below 70 % was noted in 42 (64.2 %) survivors and 18 (73.4 %) subsequently deceased patients, with mean levels of 44.6 % and 42.8 %, respectively. In the rest of the cohort, Protein C activity followed a similar pattern to the GIH group, averaging 84.5 % and 78.6 %, respectively (p <0,05).

Factor VIII to Protein C Ratio (FVIII/PC Ratio). In all patients admitted with variceal bleeding, regardless of the clinical outcome, the FVIII/PC ratio was elevated, ranging from 3.4 to 3.9 (reference range: 1,0±0,2). Among patients with ascites, an increased FVIII/PC ratio was observed in 40 % of those discharged and 68 % of the deceased, with mean values of 3.0 and 3.2, respectively. Notably, in cases of acute-onset ascites and diuretic-resistant ascites, an elevated FVIII/PC ratio was identified in 96.8 % of patients. Conversely, in patients with a favorable clinical course of ascites, the FVIII/PC ratio in 60 % of cases did not significantly differ from the control group.

2.3 Thrombosis markers.

Fibrinogen B. In the cohort of discharged patients, 61.0 % of those with gastrointestinal hemorrhage (GIH) and 41.7 % with ascites presented with fibrinogen B levels of +++ to ++++ on admission. During longitudinal monitoring, the proportion of patients with high fibrinogen B content decreased to 30.0 % and 33.3 %, respectively. Conversely, there was an increase in the number of patients in whom fibrinogen B was absent, rising from 39.0 % on admission to 70.0 % at discharge for the GIH group, and from 58.3 % to 66.7 % for the group with ascites (p <0,05).

Conversely, among the non-survivors, a longitudinal increase in the number of patients with elevated serum fibrinogen B levels was observed in both the gastrointestinal hemorrhage (GIH) and ascites cohorts – rising from 20.8 % to 50.0 % and from 10.0 % to 14.6 %, respectively (p <0,05).

D-dimer. The longitudinal trends in blood D-dimer levels mirrored the changes observed in fibrinogen B. Among patients with variceal hemorrhage, 80.6 % of those discharged and 100 % of the deceased presented with admission D-dimer levels averaging 2800–3200 ng FEU/mL or higher (reference range: <500.0 ng FEU/mL). Comparable values were recorded in the ascites cohort, involving 90.9 % of survivors and 100% of the deceased patients (p <0,05).

Discussion

It is well-established that the liver is the primary site for the synthesis of nearly all hemostatic proteins. This includes both procoagulants (with the exception of von Willebrand factor and factor VIII) – specifically factors II, V, VII, IX, X, XI, XII, fibrinogen, and the fibrin-stabilizing factor XIII – as well as coagulation inhibitors (antithrombin III, proteins C and S, a_2-macroglobulin, α- antitrypsin, metalloprotease ADAMTS-13 etc.). These proteins are vitamin K-dependent. Furthermore, hepatocytes are the principal site of thrombopoietin synthesis, which regulates the proliferation, differentiation, and maturation of megakaryocytes, thereby mediating thrombopoiesis. Thrombopoietin levels are inversely proportional to the platelet count. Consequently, the serum levels of hemostatic factors serve as a reflection of the functional status of the liver.

In the natural history of liver cirrhosis, the resulting structural alterations lead to a quantitative reduction in both procoagulant and anticoagulant factors to varying degrees. This disrupts the hemostatic balance in either direction, thereby predisposing the patient to either hemorrhagic complications or thrombotic events[5,8,9,12,17,18].

In complicated liver cirrhosis, endothelial dysfunction—which is present in all decompensated patients—results in a significant imbalance. Specifically, there is a reduction in the production of athrombogenic factors by hepatic sinusoidal cells and endothelial cells relative to an increase in thrombogenic factors, a primary example of which is coagulation factor FVIII. An elevation in factor VIII (FVIII) levels, occurring against the background of a natural decline in anticoagulant protein C and S activity, is characteristic of decompensated liver cirrhosis; this shift leads to a state of thrombophilia[4,10,19-21]. It is currently recognized that sinusoidal endothelial dysfunction precedes inflammatory and fibrotic changes in the liver and contributes to disease progression. It serves as the initial stage in the pathogenesis of portal hypertension in cirrhosis and acts as a contributing factor to the onset of a 'portal crisis' due to sinusoidal vasoconstriction, which represents a functional hemodynamic cause for the development of major complications. Furthermore, intrahepatic microvascular thrombosis may act as a static (structural) cause for increased intrahepatic vascular resistance, leading to reduced intrahepatic portal blood flow and elevated portal pressure[22-25].

In our study of hemostasis in patients with both compensated and decompensated cirrhosis, it was observed that in compensated liver cirrhosis (CLC), 20.0 % of the subjects had platelet counts within the 60-100,0x10^9/l, range, while only 6.0 % fell below 60x10^9/l. A reduction in standard procoagulant parameters (PI, fibrinogen) occurred in 37.9 % of those examined, whereas 62.1 % remained within the reference range. Notably, procoagulant factor VIII (FVIII) activity was at the upper limit of normal (ULN) in 65.2 % of patients and exceeded normal values in 36.4 %. This suggests that the decline in hepatocyte-synthesized procoagulant factors is offset by a relative increase in the activity of the extrahepatic procoagulant factor FVIII, which is synthesized by the endothelium.

In contrast to the procoagulant pathway, plasma anticoagulant Protein C activity was within the lower limit of normal (LLN) in 72.7 % of patients and below the reference range in 27.3 %. The FVIII/PC ratio slightly exceeded normal values in 82.4% of cases. These data suggest a state of relative thrombophilia in patients with compensated liver cirrhosis during its natural history. Fibrinogen B (graded as ++ and +++) was detected in 57.6 % of the subjects; 15.8 % of these patients exhibited elevated D-dimer levels, and one patient presented with portal vein thrombosis (PVT) in the recanalization stage.

In decompensated patients, regardless of the nature of complications, the proportion of individuals presenting with a reduction in hepatocyte-synthesized coagulation factors upon admission was 1.5-2.3 times higher compared to compensated patients. This underscores hepatic functional decompensation as the primary driver of complications. Among patients admitted with gastrointestinal bleeding (GIB), 52.0 % exhibited a prothrombin index (PI) below 80 %, while this was observed in 70.0 % of those with ascites. Furthermore, fibrinogen levels below 2.2 g/L were recorded in 45.8 % and 76.1 % of these groups, respectively. Against this background, protein C activity was also below the reference range in more than 60 % of patients presenting with both hemorrhage and ascites. Conversely, clotting factor F VIII activity was elevated above normal limits in nearly all subjects – specifically in 83.0 % of patients with variceal bleeding and 67.1 % of those with ascites upon admission. This indicates a baseline shift in hemostatic balance toward a hypercoagulable state in the majority of patients with complicated cirrhosis, a trend that is notably more pronounced in cases of variceal hemorrhage. The evaluation of the FVIII/PC ratio is particularly diagnostic: in 100 %

of patients with hemorrhage and 40-60 % of those with ascites, this ratio exceeded reference values by 3- to 4-fold. Furthermore, in cases of acute-onset and refractory ascites, an elevated FVIII/PC ratio was observed in 96.8 % of patients. This suggests a potential role for thrombosis in acute conditions as a primary driver of a sharp increase in portal venous pressure – manifesting as a 'portal crisis' – with the subsequent development of complications.

On the other hand, the observed thrombocytopenia, reduced prothrombin index and fibrinogen levels, and prolonged activated partial thromboplastin time (aPTT) in decompensated patients presenting with hemorrhage can be interpreted as manifestations of varying degrees of disseminated intravascular coagulation (DIC), characterized by consumption coagulopathy. The presence of disseminated intravascular coagulation is further confirmed by the detection of fibrin degradation products (FDPs – specifically fibrinogen 'B' and D-dimer – in the blood of the majority of patients with cirrhosis complications. Upon admission, D-dimer levels in 75.0%–97.0 % of patients, presenting with both hemorrhage and ascites, exceeded reference values by more than 5-fold. Notably, a favorable clinical outcome correlated with a longitudinal reduction in D-dimer concentrations. In contrast, among the deceased, D-dimer levels remained virtually unchanged, being elevated in 100.0 % of cases.

According to the literature, the role of disseminated intravascular coagulation in patients with liver cirrhosis remains a subject of ongoing debate. Nevertheless, the consensus among most authors is that low-grade DIC contributes to the pathogenesis of coagulopathy in certain patients with diffuse liver diseases, while those with cirrhosis face a significantly higher risk of developing overt DIC[6,11,26,27].

A notable observation involves four patients with previously uncomplicated cirrhosis. Two to 2.5 weeks following an initial hemostatic profile that showed signs of hypercoagulation (elevated FVIII activity and reduced protein C activity), they were admitted to the surgical department presenting with clinical symptoms of variceal hemorrhage. Upon admission, all patients exhibited thrombocytopenia, reduced prothrombin index (PI) and fibrinogen levels, and prolonged aPTT – indicators of hypocoagulation. These findings were accompanied by the presence of fibrinogen 'B' and a manifold increase in D-dimer levels, signifying thrombosis or disseminated intravascular coagulation.

Conclusions

The state of hemostasis in compensated liver cirrhosis is characterized by a relative imbalance between hepatocyte-synthesized pro- and anticoagulants and the extrahepatic clotting factor FVIII (synthesized by the endothelium), shifting toward a hypercoagulable state. The FVIII/PC ratio serves as an objective marker for the presence or absence of thrombophilia. In 82.4 % of the examined subjects, the FVIII/PC ratio remained within the range of 1.1-1.3.

The hemostatic profile in patients with decompensated liver cirrhosis upon admission is characterized by a more pronounced reduction in both pro- and anticoagulant levels synthesized by hepatocytes, signifying hepatic functional decompensation. In contrast, the activity level of the extrahepatic clotting factor FVIII remained above the reference range in nearly all patients, indicating endothelial dysfunction. The FVIII/PC ratio in the majority of patients exceeded normal values by 3- to 4-fold, pointing to a state of baseline thrombophilia.

The presence of hypocoagulation is attributed to the development of varying degrees of disseminated intravascular coagulation (DIC). This is laboratory-confirmed by thrombocytopenia, reduced prothrombin index (PI) and fibrinogen levels, prolonged activated partial thromboplastin time (aPTT), and the appearance of fibrin degradation products - specifically fibrinogen 'B' and D-dimer. These findings were observed upon admission in 75.0%–97.0% of patients presenting with both hemorrhage and ascites. Among deceased patients, longitudinal D-dimer levels remained virtually unchanged, being elevated in 100.0% of cases.

Future Research Directions

Further investigation into the pro- and anticoagulant systems of hemostasis in patients with liver cirrhosis is essential. This research should encompass both decompensated patients, where coagulopathy may be a sequela of complications, and compensated patients, where coagulopathy may act as a primary driver for their development. Such studies are necessary to define objective criteria for hemostatic imbalance and to establish strategies for its effective management.

Conflicts of Interest:

Authors have no conflict of interest to declare.

Information about authors:

Tugushev Aliy S., PhD, Associate Professor of Faculty Surgery Department, Zaporizhzhia State Medical University, Ukraine.
+38(067) 709 30 68; E-mail: tugushev63@ukr.net
iD ORCID 0000-0001-8006-1863

Cherkovska Olga. S., PhD, Associate Professor of Faculty Surgery Department, Zaporizhzhia State Medical University, Ukraine.

+38(066) 703 59 17; E-mail: cherkovska2007@ukr.net

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