



# Association between D-dimer levels and prognosis in liver cirrhosis

## Povezava med ravnmi D-dimera in prognozo pri cirozi jeter

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**Ključne besede:** tromboza portalne vene, D-dimer, jetrna ciroza, Child-Pughova lestvica

**Abbreviations used in this paper:** D-dimer (a fibrin degradation product), PVT (Portal Vein Thrombosis), CTP (Child-Turcotte-Pugh score), CBC (Complete Blood Count), and PV (Prothrombin Time), Statistical Package for the Social Sciences (SPSS).

### Conflicts of interest

All authors have none to declare.

## ABSTRACT

### Introduction

Liver cirrhosis, a progressive disease with an increased risk of thrombotic events, has sparked interest in D-dimer, a potential biomarker of coagulation abnormalities. This study evaluated the correlation between

## IZVLEČEK

### Uvod

Jetrna ciroza, progresivna bolezen s povečanim tveganjem za trombotične dogodke, je vzbudila zanimanje za D-dimer, potencialni biomarker koagulacijskih nepravilnosti. Ta študija je ocenila korelacijo med

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plasma D-dimer levels and thrombotic complications in cirrhotic patients. More importantly, it sought to assess the potential of D-dimer as a powerful prognostic marker, offering hope for improved diagnosis and treatment strategies.

## Methods

A retrospective analysis was conducted on 61 patients with liver cirrhosis who were admitted to the University Clinical Centre of the Republic of Srpska between January 2022 and January 2024 and had D-dimer testing at admission. Patient data about portal vein thrombosis were analysed and stratified according to Child-Pugh classification.

## Results

Among the patients included in the study, 55 were male and six were female. Portal vein thrombosis was present in 4.92% of cases. The study revealed a robust positive correlation between D-dimer levels and the severity of liver disease, as measured by the Child-Pugh score. Specifically, median D-dimer levels were 0.8 mg/L in Child-Pugh class A, 5.0 mg/L in class B, and 8.25 mg/L in class C patients, providing valuable insights into the disease progression.

## Conclusion

The study's findings underscore the significance of elevated D-dimer levels in advanced stages of liver cirrhosis, suggesting an increased risk of thrombotic complications. These results strongly support the inclusion of D-dimer measurement in the prognostic assessment of patients with liver cirrhosis, offering reassurance about the potential impact on clinical practice.

ravnimi D-dimerja v plazmi in trombotičnimi zapleti pri bolnikih s cirozo. Še pomembneje pa je bilo, da je želela oceniti potencial D-dimerja kot močnega prognostičnega označevalca, ki ponuja upanje za izboljšane diagnostične in terapevtske strategije.

## Metode

Retrospektivna analiza je bila izvedena pri 61 bolnikih z jetrno cirozo, ki so bili sprejeti v Univerzitetni klinični center Republike Srbske med januarjem 2022 in januarjem 2024 in so jim ob sprejemu testirali D-dimer. Podatke bolnikov o trombozi portalne vene so analizirali in stratificirali po Child-Pughovi klasifikaciji.

## Rezultati

Med bolniki, vključenimi v študijo, je bilo 55 moških in šest žensk. Tromboza portalne vene je bila prisotna v 4,92 % primerov. Študija je pokazala močno pozitivno korelacijo med ravnimi D-dimerja in resnostjo bolezni jeter, merjeno s Child-Pughovo lestvico. Natančneje, mediana ravni D-dimerja je bila 0,8 mg/L pri bolnikih z razredom A po Child-Pughu, 5,0 mg/L pri bolnikih z razredom B in 8,25 mg/L pri bolnikih z razredom C, kar zagotavlja dragocen vpogled v napredovanje bolezni.

## Zaključek

Ugotovitve študije poudarjajo pomen povišanih ravni D-dimerja v napredovalih fazah jetrne ciroze, kar kaže na povečano tveganje za trombotične zaplete. Ti rezultati močno podpirajo vključitev merjenja D-dimerja v prognostično oceno bolnikov z jetrno cirozo in zagotavljajo potencialni vpliv na klinično prakso.

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## INTRODUCTION

D-dimer is a fibrin degradation product found in the blood following clot breakdown. Currently, tests for measuring D-dimer concentrations are widely used across various areas of clinical practice. When combi-

ned with clinical probability assessment, D-dimer testing is a well-established tool for safely ruling out pulmonary embolism (1–3). Additionally, D-dimer levels are used to predict the risk of recurrent venous thromboembolism and to guide the duration of anticoagulation therapy in affected patients (4–6).

D-dimer levels are significantly elevated in patients with liver cirrhosis and tend to increase progressively with the severity of liver dysfunction (7). It has also been suggested that D-dimer levels are influenced by the presence and management of ascites (8). Specifically, patients with ascites show significantly higher D-dimer levels than those without, and these levels tend to decrease following the resolution of ascites. The incidence of venous thromboembolism, particularly portal vein thrombosis, increases over time in patients with cirrhosis, from 5% at one year to 40% at ten years. This trend is attributed to complex mechanisms including thrombophilia, reduced portal vein blood flow, intra-abdominal infections, malignancies, and recent interventions (9).

A recent meta-analysis conducted by our research group demonstrated a significant association between elevated D-dimer levels and portal vein thrombosis in cirrhotic patients, as well as the potential of D-dimer to predict the development of portal vein thrombosis following splenectomy (10). Therefore, D-dimer may serve as a prognostic biomarker negatively associated with clinical outcomes in liver cirrhosis.

In our study, we retrospectively analysed the correlation between D-dimer levels and Child-Pugh scores, and the predictive value of D-dimer for thrombotic complications and overall prognosis in patients with liver cirrhosis.

## **MATERIALS AND METHODS**

This retrospective, descriptive, and analytical study was conducted at the University Clinical Centre of the Republic of Srpska, Department of Gastroenterology and Hepatology. It focused on patients admitted between January 2022 and January 2024 who were diagnosed with liver cirrhosis. The aim of this study was to investigate the relationship between D-dimer levels and the severity of liver cirrhosis, and assess the predictive value of D-dimer for thrombotic complications and overall prognosis.

The study included 61 patients with confirmed liver cirrhosis who underwent D-dimer testing upon hospital admission.

**Inclusion criteria** were as follows:

1. A confirmed diagnosis of liver cirrhosis based on clinical presentation, routine laboratory tests, imaging, and, when necessary, liver biopsy.
2. Availability of D-dimer level measurements at admission.

**Exclusion criteria** were:

1. Pre-existing thromboembolic complications.
2. Presence of malignant tumours.

Clinical data were collected retrospectively from electronic medical records, including demographic information, clinical characteristics, and laboratory findings. Demographic data encompassed patient age, sex, and relevant medical history. Clinical evaluation included an assessment of liver cirrhosis severity using the Child-Pugh score, which categorises the disease into Class A, B, or C. This scoring system is based on five parameters: serum bilirubin, serum albumin, prothrombin time, presence of ascites, and grade of hepatic encephalopathy. Data were analysed using Statistical Package for the Social Sciences (SPSS) version 29.

Laboratory data primarily focused on D-dimer levels, and other key laboratory parameters such as serum bilirubin, serum albumin, prothrombin time (PT), and complete blood count (CBC). Additional data from medical records included the aetiology of liver disease, presence of ascites, hepatic encephalopathy, and other relevant clinical findings. In cases where D-dimer levels were measured multiple times during hospitalisation, the highest recorded value was used for analysis to ensure consistency and accuracy.

## **RESULTS**

The study included 61 patients with liver cirrhosis, comprising 55 males (90.16%) and six females (9.84%). Alcohol consumption was identified as the leading aetiology, accounting for 52 cases (85.25%) (Table 1).

Table 1. Demographic data and etiology of liver cirrhosis

<b>Mean age</b>	<b>57,41</b>
<b>Gender</b>	
Male	55 (90.16%)
Female	6 (9.84%)
<b>Etiology of liver cirrhosis</b>	
Alcoholic	52 (85.25%)
Viral	6 (9.84%)
Unknown	3 (4.91%)

The average D-dimer level in the study cohort was 6.17 mg/L, markedly exceeding the reference range of <0.5 mg/L. This elevation indicates ongoing fibrinolytic activity, a well-documented characteristic of liver cirrhosis. The mean Child-Pugh score among the patients was 9.20, reflecting a predominantly advanced stage of liver dysfunction. The most cirrhotic patients had Child-Pugh score B, presented in Figure 1.

Analysis of D-dimer levels according to Child-Pugh classification revealed a clear association between the severity of liver dysfunction and the extent of fibrinolytic activity. Patients in Child-Pugh Class A had a median D-dimer level of 0.8 mg/L, those in Class B had a median level of 5.0 mg/L, while patients in Class C exhibited the highest median D-dimer level at 8.25 mg/L. This progressive increase in D-dimer levels with advancing Child-Pugh class underscores the link between deteriorating liver function and enhanced fibrinolysis (Figure 2).

These findings reflect a progressive increase in D-dimer levels with advancing severity of liver cirrhosis, as classified by the Child-Pugh score. Portal vein thrombosis (PVT) was identified in 4.92% of patients, including hospitalised individuals and those previously discharged. This incidence underscores the thrombotic risk associated with advanced stages of liver cirrhosis. Notably, elevated D-dimer levels were observed in patients with PVT. However, they were also present in

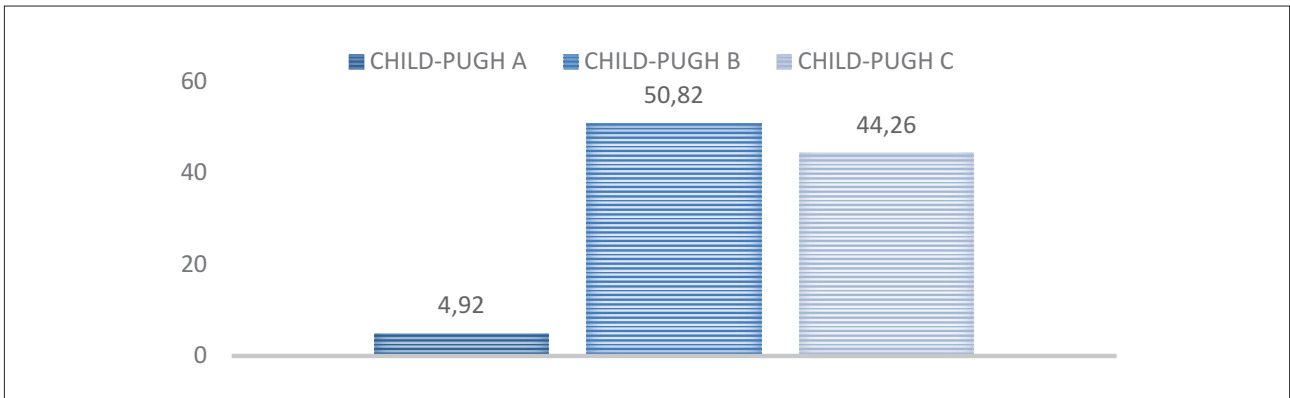


Figure 1. Frequency (%) of Child-Pugh score class

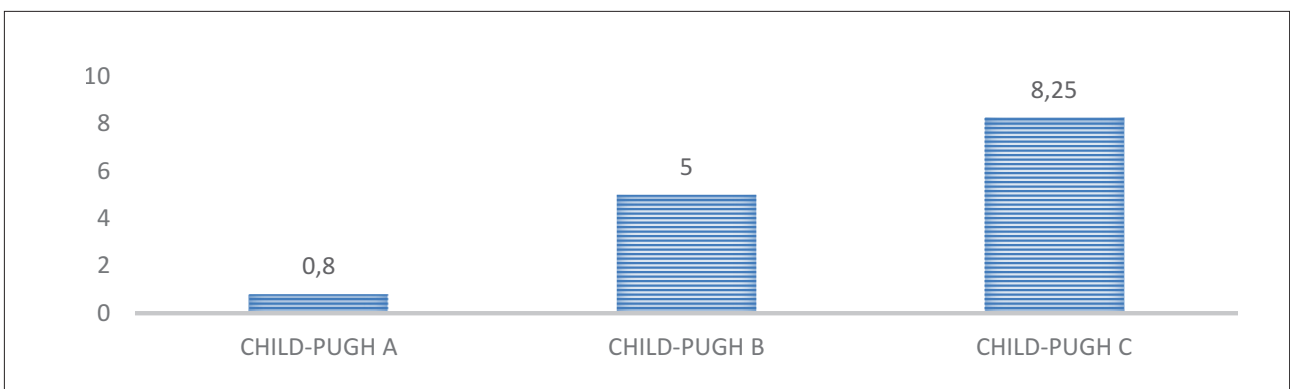


Figure 2. Mean D-dimer levels in different Child-Pugh class

those without thrombosis, suggesting a broader association between D-dimer elevation and the hypercoagulable state in cirrhosis.

## DISCUSSION

Our analysis revealed a significant correlation between D-dimer levels and the severity of liver cirrhosis, as assessed by the Child-Pugh score. The average D-dimer level across the cohort was 6.17 mg/L, notably higher than the <0.5 mg/L reference range. D-dimer levels were analysed according to the Child-Pugh classification: for Class A, the median D-dimer level was 0.8 mg/L; for Class B, the median level was 5.0 mg/L; for Class C, the median level was 8.25 mg/L.

An Egyptian study by El-Sayed et al. investigated D-dimer levels in 67 patients with chronic liver diseases and 30 healthy controls (11). The study found that cirrhotic patients with Child-Pugh Class A and B had significantly higher D-dimer levels compared to non-cirrhotic patients and healthy controls (Class B,  $147.32 \pm 114.16$  ng/ml; Class A,  $115.3 \pm 138.4$  ng/ml; non-cirrhotic liver disease,  $28.86 \pm 40.03$  ng/ml; healthy controls,  $17.6 \pm 11.7$  ng/ml). Similarly, a Chinese study by Cong et al. analysed D-dimer levels in 43 cirrhotic patients categorised according to their Child-Pugh scores, and 16 healthy controls (12).

D-dimer is a fibrin degradation product, a small protein fragment found in the blood after a clot is degraded through fibrinolysis (13). Hyperfibrinolysis in cirrhotic patients is thought to represent a state of low-grade disseminated intravascular coagulation (DIC) (14) and is a frequently observed clinical feature. This condition likely results from primary clotting activation, impaired synthesis of fibrinolytic protein inhibitors, and the liver's delayed hepatic clearance of tissue plasminogen activator (15, 16). In our study, the D-dimer level was notably higher in the portal vein thrombosis (PVT) group compared to the control group. In line with our findings, a previous study demonstrated a significant correlation between D-dimer levels and the formation of PVT (17). However, several other studies found that D-dimer levels did not differ

between cirrhotic patients with and without PVT (14, 18–20).

Moreover, the current study did not find a significant association between D-dimer levels and the Child-Turcotte-Pugh (CTP) score. In contrast, other studies have reported that D-dimer positively correlates with the degree of liver dysfunction (17, 21, 22). These discrepancies could be attributed to differences in study design, sample size, or patient characteristics. The discrepancies suggest further investigation is needed to clarify the relationship between D-dimer levels and liver function severity.

Our study also found that higher D-dimer levels were associated with an increased incidence of thrombotic events, including PVT. With a PVT incidence of 4.92% in our cohort, it is evident that patients with advanced liver cirrhosis are at significant risk for thrombotic complications. Elevated D-dimer levels may indicate thrombotic risk early, allowing for timely interventions to prevent or manage such complications.

While our findings provide important insights, several limitations should be considered. The retrospective nature and the relatively small sample size may limit the generalizability and accuracy of the results. Future studies with larger, prospective cohorts are needed to validate these findings and explore the longitudinal relationship between D-dimer levels and disease progression in liver cirrhosis.

## CONCLUSION

This study demonstrates a significant correlation between elevated D-dimer levels and the severity of liver cirrhosis, as assessed by the Child-Pugh score. Our findings suggest that D-dimer could be a valuable biomarker for assessing disease severity and predicting thrombotic risk. However, the small sample size limits the generalizability of these results, underscoring the need for further research with larger, more diverse cohorts. Confirming these findings will establish their clinical relevance and improve prognostic evaluations in liver cirrhosis.

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