INTERNATIONAL JOURNAL OF
MEDICAL BIOCHEMISTRY

DOI: 10.14744/ijmb.2025.60590
Int J Med Biochem 2025;8(4):300–305

Research Article

Platelet-normalized biomarkers as diagnostic and prognostic indicators in crimean-congo hemorrhagic fever

Serkan Bolat[1], Seyit Ali Buyuktuna[2]

[1]Department of Medical Biochemistry, Sivas Cumhuriyet University Faculty of Medicine, Sivas, Türkiye
[2]Department of Infectious Diseases and Clinical Microbiology, Sivas Cumhuriyet University Faculty of Medicine, Sivas, Türkiye

Abstract

Objectives: Crimean-congo hemorrhagic fever (CCHF) is a viral disease characterized by thrombocytopenia and systemic inflammation. In this study, we evaluated the role of platelet-normalizing biomarkers as diagnostic and prognostic indicators of CCHF.

Methods: This study included 60 patients with CCHF and 30 age-/sex-matched healthy controls. Biochemical parameters, including aspartate aminotransferase, alanine aminotransferase (ALT), gamma-glutamyl transferase, alkaline phosphatase, C-reactive protein and interleukin-6 (IL-6) levels were measured using photometric or electrochemiluminescence methods (Roche Cobas 8000, c702 and e801). Coagulation parameters' levels; activated partial thromboplastin time, international normalized ratio, fibrinogen, and D-dimer were determined using Roche Cobas t511. These parameters were expressed as ratios to platelet count (Plt). Comparisons were performed between the CCHF cohort and control group. Subgroup analyses evaluated associations with intensive care unit (ICU) admission and mortality risk.

Results: Statistically significant differences were observed between CCHF patients and healthy controls in all parameters ($p<0.05$). Patients admitted to the ICU or those who did not survive exhibited a significant increase in all platelet-normalized ratios ($p<0.05$), except ALT/Plt. ROC analysis revealed that IL-6/Plt (AUC=0.998, cut-off>0.018, sensitivity=98.3%, specificity=100%) and D-dimer/Plt (AUC=0.992, cut-off>0.002, sensitivity=95%, specificity=96.7%) had the highest diagnostic accuracy for CCHF. Furthermore, IL-6/Plt and D-dimer/Plt ratios also showed high predictive accuracy for predicting the need for ICU admission and mortality risk.

Conclusion: Platelet-normalized biomarkers, particularly IL-6/Plt and D-dimer/Plt, demonstrate strong diagnostic and prognostic potential for CCHF. Their inclusion in clinical protocols could improve early detection, risk assessment and treatment decisions for CCHF patients.

Keywords: Biomarkers, Crimean-congo hemorrhagic fever, inflammation, mortality prediction, platelet indices

How to cite this article: Bolat S, Buyuktuna SA. Platelet-normalized biomarkers as diagnostic and prognostic indicators in Crimean-congo hemorrhagic fever. Int J Med Biochem 2025;8(4):300–305.

Crimean-congo hemorrhagic fever (CCHF) is a serious viral disease caused by Crimean-congo hemorrhagic fever virus, a member of the Nairoviridae family [1, 2]. CCHF is endemic in several regions, including Africa, the Middle East, Asia and Southeast Europe, and there has been a notable increase in its incidence over the past decade [3]. The disease is characterized by a range of symptoms, including high fever, muscle pain, vomiting and severe hemorrhagic manifestations, and can lead to a mortality rate ranging from 5% to 30%, depending on the outbreak and region [4].

One of the hallmarks of CCHF is thrombocytopenia, a critical indicator of disease severity and progression [5]. Thrombocytopenia in CCHF is often accompanied by life-threatening conditions such as petechiae, ecchymosis, and gastrointestinal bleeding. The pathogenesis of CCHF involves a complex interaction between the virus and the host. Infection triggers an inflammatory response that can develop into a cytokine storm, a hyper-inflammatory condition characterized by excessive release of pro-inflammatory cytokines. This cytokine storm is associated with severe tissue damage and can cause hemorrhag-

Address for correspondence: Serkan Bolat, MD. Department of Medical Biochemistry, Sivas Cumhuriyet University Faculty of Medicine, Sivas, Türkiye
Phone: +90 507 439 00 28 **E-mail:** drsbolat@gmail.com **ORCID:** 0000-0002-8669-8782
Submitted: February 18, 2025 **Accepted:** May 11, 2025 **Available Online:** October 21, 2025

ic symptoms observed in CCHF patients [6, 7]. Studies have shown that CCHF virus can target immune cells, leading to their activation and subsequent cytokine release, which can exacerbate the inflammatory response [6, 8]. The resulting cytokine storm can lead to multiple organ failure, which is a common cause of death in severe cases of CCHF. Liver damage in CCHF is often evaluated through biomarkers such as alanine aminotransferase (ALT) and aspartate aminotransferase (AST), which are indicators of hepatocellular damage. High levels of these enzymes have been consistently reported in CCHF patients, reflecting the degree of liver involvement during infection [9].

Platelet indices are increasingly recognized as potential biomarkers for disease severity and prognosis in a variety of infectious and inflammatory conditions [10, 11]. However, the utility of platelet and liver enzymes, inflammatory markers, and coagulation parameters in assessing the inflammatory and coagulopathic response in CCHF has not been adequately studied. In this study, it aims to determine whether these ratios provide clinically meaningful information about disease progression and severity, potentially improving risk stratification and guiding therapeutic interventions. For this purpose, aspartate aminotransferase to platelet ratio (AST/Plt), alanine aminotransferase to platelet ratio (ALT/Plt), gamma-glutamyl transferase to platelet ratio (GGT/Plt), alkaline phosphatase to platelet ratio (ALP/Plt), C-reactive protein to platelet ratio (CRP/Plt), interleukin-6 to platelet ratio (IL-6/Plt), activated partial thromboplastin time to platelet ratio (APTT/Plt), international normalized ratio to platelet ratio (INR/Plt), fibrinogen to platelet ratio (Fibrinogen/Plt), and D-dimer to platelet ratio (D-dimer/Plt) were evaluated in CCHF patients and healthy controls.

Materials and Methods

Patients

The study included 60 patients aged over 18 years who were admitted to the Infectious Diseases Clinic between March and October 2022 with a preliminary diagnosis of Crimean-congo hemorrhagic fever (CCHF). The diagnosis of CCHF was subsequently confirmed using PCR or serological methods. Additionally, a control group consisting of 30 age-/sex-matched healthy people, with no history of chronic disease or drug use, was included for comparison.

The minimum total sample size required to detect a moderate effect size (Cohen's d=0.65) at a significance level (α) of 5%, with 80% statistical power (1 – β) and a group allocation ratio (N1/N2) of 2, was calculated to be 90. While enlarging the sample size may enhance the detection of statistically significant differences between groups, such differences risk being clinically irrelevant. To prioritize the identification of biologically and clinically meaningful effects, a moderate effect size was selected a priori, balancing statistical sensitivity and practical significance. Power analysis indicated that a total sample size (n=90) would minimize the possibility of overinterpreting insignificant differences and provide sufficient power for the study. All human research protocols were in compliance with relevant national regulations, institutional policies, and the principles outlined in the Declaration of Helsinki. The study was approved by the Institutional Review Board (Ethical Committee approval No: 2025-01/62, Date: 16/01/2025). Informed consent was obtained from all participants involved in the study.

Laboratory analyses

Platelet count, AST, ALT, GGT, ALP, CRP, IL-6, INR, APTT, fibrinogen, and D-dimer levels were measured in both patient and control groups. Additionally, data regarding the need for intensive care unit (ICU) and the survival status of patients were recorded. Laboratory tests for AST, ALT, GGT, ALP, and CRP were conducted using photometric methods on a Roche Cobas c702 analyzer (Roche Diagnostics, Germany), while IL-6 levels were assessed using an electrochemiluminescence method on a Roche Cobas e801 analyzer. Complete blood count tests were performed using a Sysmex XN-1000 (Sysmex Corporation, Japan) analyzer, and coagulation tests were conducted on a Roche Cobas t511 analyzer.

Statistical analysis

New indices were derived by dividing the laboratory data by platelet count. These indices were compared between the patient and control groups and, within the patient group, based on the need for intensive care and survival status. The assumption of normality was assessed using the Shapiro-Wilk test. The non-parametric Mann-Whitney U test was used for comparisons between two groups. Furthermore, receiver operating characteristic (ROC) analyses were conducted to evaluate the performance of the indices in predicting CCHF diagnosis and disease prognosis, including the need for intensive care and survival status. The area under the curve (AUC), sensitivity, and specificity were calculated. Data were analyzed using SPSS software (IBM Corp., SPSS Statistics for Windows, Version 23.0, USA), and GraphPad Prism version 8.3.0 (GraphPad Software, www.graphpad.com, USA) was employed for data visualization. A significance level of $p<0.05$ was considered for all statistical tests.

Results

Statistically significant differences were observed between CCHF patients and healthy controls in all parameters studied. All indices were higher in patients than in healthy controls (Table 1, Fig. 1).

INR/Plt, APTT/Plt, D-dimer/Plt, fibrinogen/Plt AST/Plt, GGT/Plt and ALP/Plt, CRP/Plt and IL-6/Plt values of patients admitted to ICU were significantly increased in the ICU group, however, ALT/Plt (p=0.068) was not statistically significant between the groups (Table 2). Similar results were obtained for patients who did not survive.

IL-6/Plt (AUC=0.998), D-dimer/Plt (AUC=0.992), and AST/Plt (AUC=0.990) had the highest predictive values in the ROC analysis to predict the diagnosis of CCHF, with sensitivity and specificity reaching nearly 100% at cut-off values (>0.018, >0.002, and >0.162, respectively). The highest probability

Table 1. Comparison of platelets indexes between CCHF patients and control groups

Parameters	Groups		p
	Control (n=30)	Patient (n=60)	
INR/Plt	0.004 (0.004–0.005)	0.012 (0.009–0.02)	**<0.001**
APTT/Plt	0.118 (0.099–0.146)	0.409 (0.268–0.628)	**<0.001**
D-dimer/Plt	0.001 (0.001–0.001)	0.033 (0.011–0.112)	**<0.001**
Fibrinogen/Plt	1.14 (0.923–1.373)	3.358 (2.287–4.821)	**<0.001**
AST/Plt	0.074 (0.06–0.093)	1.311 (0.38–4.991)	**<0.001**
ALT/Plt	0.077 (0.063–0.097)	0.568 (0.295–2.162)	**<0.001**
GGT/Plt	0.07 (0.047–0.121)	0.587 (0.25–1.137)	**<0.001**
ALP/Plt	0.304 (0.241–0.336)	0.981 (0.589–1.554)	**<0.001**
CRP/Plt	0.005 (0.002–0.009)	0.156 (0.046–0.477)	**<0.001**
IL-6/Plt	0.007 (0.006–0.009)	0.26 (0.15–1.142)	**<0.001**

Continuous variables are expressed as median and quartiles (Q1-Q3). Groups were compared using the Mann-Whitney U test. Significant p-values are shown in bold. CCHF: Crimean-congo hemorrhagic fever; INR: International normalized ratio; Plt: Platelet; APTT: Activated partial thromboplastin time; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; GGT: Gamma-glutamyl transferase; ALP: Alkaline phosphatase; CRP: C-reactive protein; IL-6: Interleukin-6.

Table 2. Comparison of platelets indexes of CCHF patients according to intensive care unit requirements

Parameters	Intensive care unit requirements		p
	No (n=53)	Yes (n=7)	
INR/Plt	0.012 (0.009–0.016)	0.038 (0.029–0.048)	**<0.001**
APTT/Plt	0.368 (0.259–0.544)	1.364 (0.824–1.524)	**<0.001**
D-dimer/Plt	0.021 (0.01–0.06)	1.273 (0.824–1.524)	**<0.001**
Fibrinogen/Plt	3.2 (2.186–4.548)	6.048 (4.452–7.182)	**0.005**
AST/Plt	0.745 (0.348–3.365)	5.818 (2.843–6.071)	**0.006**
ALT/Plt	0.551 (0.288–1.895)	1.394 (0.832–3.129)	0.068
GGT/Plt	0.472 (0.244–0.947)	1.524 (0.686–13.581)	**0.009**
ALP/Plt	0.875 (0.584–1.275)	2.636 (1.69–3.452)	**<0.001**
CRP/Plt	0.132 (0.036–0.286)	2.806 (0.686–5.952)	**<0.001**
IL-6/Plt	0.24 (0.124–0.688)	7.182 (2.706–15.806)	**<0.001**

Continuous variables are expressed as median and quartiles (Q1-Q3). Groups were compared using the Mann-Whitney U test. Significant p-values are shown in bold.

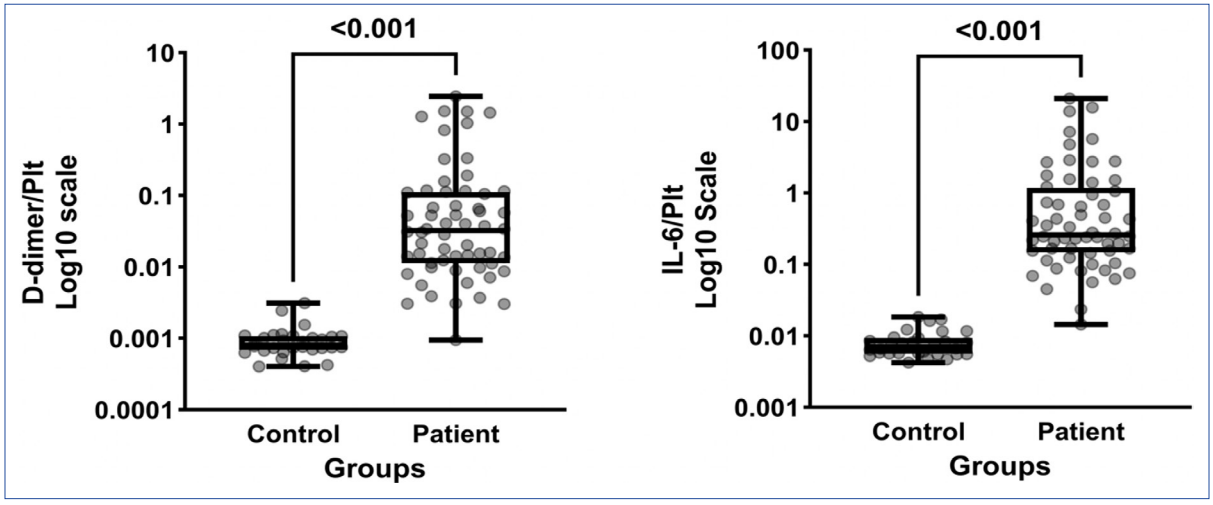

Figure 1. Box-plot comparison of D-dimer/Plt and IL-6/Plt levels between CCHF (Crimean-congo hemorrhagic fever) patients and healthy controls.

Table 3. ROC analysis results for predicting the CCHF diagnosis

Parameters	Cut-off value	AUC	Sensitivity (%)	Specificity (%)	LR (+)	LR (-)
INR/Plt	>0.007	0.973	90 (79.5–96.2)	96.7 (82.8–99.9)	27 (3.92–185)	0.1 (0.048–0.22)
APTT/Plt	>0.196	0.958	93.3 (83.8–98.2)	96.7 (82.8–99.9)	28 (4.07–192)	0.069 (0.027–0.18)
D-dimer/Plt	>0.002	0.992	98.3 (91.1–100)	96.7 (82.8–99.9)	29.5 (4.29–202)	0.017 (0.003–0.12)
Fibrinogen/Plt	>2.03	0.970	88.3 (77.4–95.2)	100 (88.4–100)		0.12 (0.058–0.23)
AST/Plt	>0.162	0.990	96.7 (88.5–99.6)	100 (88.4–100)		0.033 (0.009–0.13)
ALT/Plt	>0.162	0.957	90 (79.5–96.2)	96.7 (82.8–99.9)	27 (3.92–185)	0.1 (0.048–0.22)
GGT/Plt	>0.188	0.930	86.7 (75.4–94.1)	93.3 (77.9–99.2)	13 (3.40–49.8)	0.14 (0.074–0.27)
ALP/Plt	>0.434	0.976	95 (86.1–99.0)	93.3 (77.9–99.2)	14.3 (3.73–54.4)	0.054 (0.018–0.16)
CRP/Plt	>0.014	0.978	93.3 (83.8–98.2)	100 (88.4–100)		0.067 (0.026–0.17)
IL-6/Plt	>0.018	0.998	98.3 (91.1–100)	100 (88.4–100)		0.017 (0.002–0.12)

ROC: Receiver operating characteristic; CCHF: Crimean-congo hemorrhagic fever; AUC: Area under the curve; LR: Likelihood ratio; INR: International normalized ratio; Plt: Platelet; APTT: Activated partial thromboplastin time; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; GGT: Gamma-glutamyl transferase; ALP: Alkaline phosphatase; CRP: C-reactive protein; IL-6: Interleukin-6.

Table 4. ROC analysis results for predicting the intensive care unit requirements of CCHF patients

Parameters	Cut-off value	AUC	Sensitivity (%)	Specificity (%)	LR (+)	LR (-)
INR/Plt	>0.025	0.895	85.7 (42.1–99.6)	94.3 (84.3–98.8)	15.1 (4.84–47.4)	0.15 (0.025–0.93)
APTT/Plt	>0.762	0.895	85.7 (42.1–99.6)	92.5 (81.8–97.9)	11.4 (4.22–30.6)	0.15 (0.025–0.95)
D-dimer/Plt	>0.118	0.978	100 (59.0–100)	92.5 (81.8–97.9)	13.3 (5.16–34.0)	0
Fibrinogen/Plt	>4.43	0.819	85.7 (42.1–99.6)	73.6 (59.7–84.7)	3.24 (1.89–5.58)	0.19 (0.031–1.20)
AST/Plt	>1.94	0.814	85.7 (42.1–99.6)	66.0 (51.7–78.5)	2.52 (1.56–4.09)	0.22 (0.035–1.34)
ALT/Plt	>0.569	0.714	100 (59.0–100)	58.5 (44.1–71.9)	2.41 (1.75–3.32)	0
GGT/Plt	>0.590	0.798	100 (59.0–100)	58.5 (44.1–71.9)	2.41 (1.75–3.32)	0
ALP/Plt	>1.23	0.900	100 (59.0–100)	73.6 (59.7–84.7)	3.79 (2.42–5.93)	0
CRP/Plt	>0.529	0.914	85.7 (42.1–99.6)	88.7 (77.0–95.7)	7.57 (3.36–17.1)	0.16 (0.026–0.99)
IL-6/Plt	>1.77	0.946	85.7 (42.1–99.6)	92.5 (81.8–97.9)	11.4 (4.22–30.6)	0.15 (0.025–0.95)

rates for positive outcomes were observed for D-dimer/Plt (LR+=29.5) and APTT/Plt (LR+=28) (Table 3, Fig. 2).

In the ROC analysis to estimate ICU requirements, D-dimer/Plt (AUC=0.978, cut-off >0.118) and IL-6/Plt (AUC=0.946, cut-off >1.77) showed the highest predictive accuracy with sensitivity and specificity exceeding 85% in most cases. The highest positivity rates were observed for INR/Plt (LR+=15.1) and D-dimer/Plt (LR+=13.3) (Table 4, Fig. 2).

Similar to the results in patients admitted to the ICU, ROC analysis to estimate mortality risk exhibited high predictive accura-

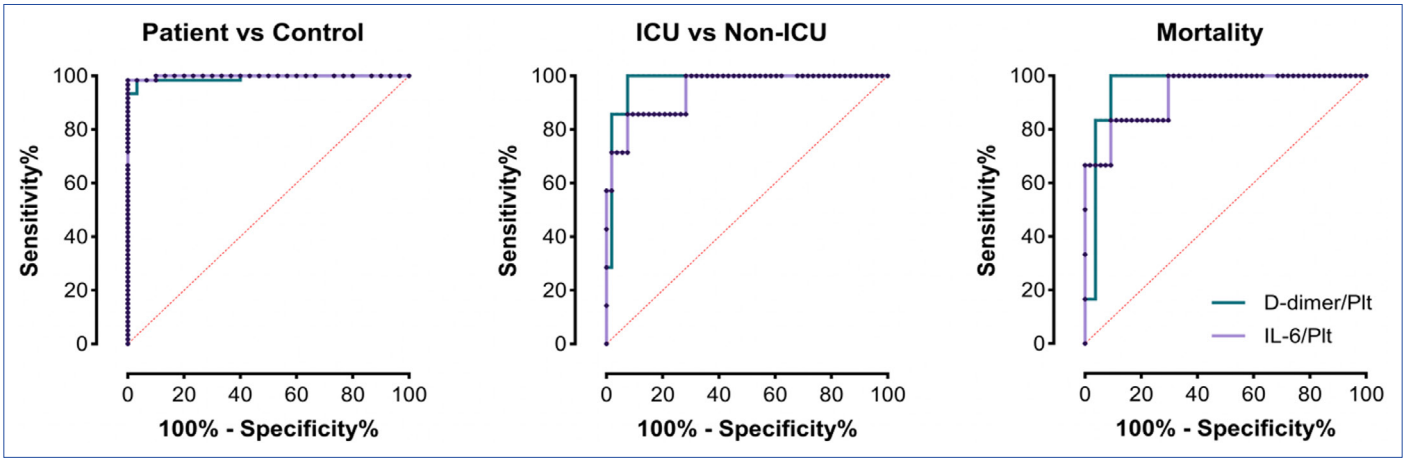

Figure 2. Diagnostic accuracy of D-dimer/Plt and IL-6/Plt levels in CCHF (Crimean-congo hemorrhagic fever) prediction, ICU (intensive care unit) requirements and mortality risk.

cy with sensitivity and specificity exceeding 80% for D-dimer/Plt (AUC=0.960, cut-off >0.118) and IL-6/Plt (AUC=0.935, cut-off >1.77) (Fig. 2). The highest positivity rates were observed for INR/Plt (LR+=11.3) and D-dimer/Plt (LR+=10.8).

Discussion

Viral hemorrhagic fevers are a group of serious, often fatal illnesses caused by several different families of viruses. Among these illnesses is CCHF, which is characterized by systemic inflammation, vascular instability, and coagulation abnormalities, frequently leading to hemorrhage, multiple organ failure, and death [12]. Thrombocytopenia is an important feature of CCHF and plays a critical role in the prognosis of the disease. Platelet count below 20,000/μL has been associated with severe bleeding and poor outcomes [13]. An important factor that plays a role in the pathogenesis of CCHF is uncontrolled immune response and cytokine storm [14]. IL-6 is an important proinflammatory cytokine involved in the acute phase response and has been widely studied as a biomarker of disease severity in a variety of infectious and inflammatory conditions [15]. Studies have reported increased levels of IL-6 in patients with CCHF [14, 16]. In a study conducted in Türkiye, serum IL-6 levels were found to be high in CCHF patients and positively correlated with disease severity [16]. Another study highlighted that high levels of IL-6 are associated with disseminated intravascular coagulation (DIC) in CCHF patients, and high levels of IL-6 are observed in fatal cases [3]. Our results in this study show that the IL-6/Plt ratio is significantly higher in CCHF patients compared to healthy controls. We think that thrombocytopenia and an increased level of IL-6 reflect the complex interplay between viral infection, immune activation, and clotting disorders. The elevation of IL-6/Plt level showed high diagnostic accuracy with an AUC of 0.998, specificity of 100%, and sensitivity of 98.3%. These findings suggest that IL-6/Plt ratio is a valuable biomarker in the early detection of CCHF.

Understanding the mechanisms underlying this finding in CCHF is also important for developing targeted therapies to improve the management and outcomes of this life-threatening disease and to mitigate its impact in CCHF.

D-dimers are produced as a result of the breakdown of cross-linked fibrin by plasmin during the fibrinolysis process. D-dimer is elevated in conditions associated with coagulation activation and fibrinolysis, such as DIC. High levels of D-dimers indicate activation of coagulation and fibrinolytic systems, which are hallmarks of viral hemorrhagic fever. In CCHF, elevated D-dimer levels are a common finding and are closely related to disease severity and outcomes. Many studies have documented elevated D-dimer levels in CCHF patients. Büyüktuna et al. [17] found that D-dimer levels were significantly higher in severe CCHF cases compared to mild and moderate groups. Similarly, Ergönül et al. [18] reported that D-dimer levels were strongly associated with coagulopathy and bleeding severity in CCHF patients [18]. Our findings demonstrate that the D-dimer/Plt ratio is significantly higher among patients requiring ICU care and in those who did not survive, compared with non-ICU and surviving patients. Notably, the high AUC, sensitivity, and specificity values (AUC=0.978 for ICU requirement and AUC=0.960 for mortality) underscore the potential of the D-dimer/platelet ratio as a reliable biomarker for predicting both critical care needs and mortality risk.

This study has some limitations. First, the sample size (60 patients and 30 controls) may restrict the statistical power of subgroup analyses, particularly for rare outcomes like ICU requirement or mortality risk. Second, the single-center design introduces potential selection bias. Third, the cross-sectional nature of the study limits causal inference. Future multicenter studies with larger cohorts are needed to validate these findings.

Conclusion

Our findings highlight the diagnostic and prognostic value of platelet-based ratios in CCHF. A significantly higher IL-6/Plt ratio in patients compared to healthy controls indicates that it can be used as an early detection biomarker with its high sensitivity and specificity. Furthermore, the D-dimer/platelet ratio was found to be higher among patients requiring intensive care and non-survivors, underscoring its potential role in predicting both critical care needs and mortality risk. These results reflect the complex interaction between viral infection, immune activation, and coagulation disorders, highlighting the importance of thrombocytopenia and inflammatory cytokines in the pathophysiology of CCHF. Going forward, mechanistic investigations focusing on the specific pathways by which IL-6 and D-dimer affect coagulation and immune responses in CCHF could guide the development of targeted therapies. The incorporation of these biomarkers into existing clinical protocols can improve early diagnosis, risk stratification, and therapeutic decision-making, ultimately improving patient outcomes in this life-threatening disease.

Ethics Committee Approval: The study was approved by the Sivas Cumhuriyet University Non-interventional Clinical Research Ethics Committee (no: 2025-01/62, date: 16/01/2025).

Informed Consent: Informed consent was obtained from all participants.

Conflict of Interest Statement: All authors declared no conflict of interest.

Funding: The authors declared that this study received no financial support.

Use of AI for Writing Assistance: No AI technologies utilized.

Authorship Contributions: Concept – S.B., S.A.B.; Design – S.B.; Supervision – S.A.B.; Materials – S.A.B.; Data collection and/or processing – S.A.B.; Data analysis and/or interpretation – S.B.; Literature search – S.A.B.; Writing – S.B.; Critical review – S.A.B.

Peer-review: Externally peer-reviewed.

References

1. Baysal AÇ, Kıymaz YÇ, Şahin NÖ, Bakır M. Investigation of long noncoding RNA-NRAV and long noncoding RNA-lethe expression in Crimean-Congo hemorrhagic fever. J Med Virol 2024;96(12):e70142. Erratum in: J Med Virol 2025;97(2):e70245. [CrossRef]
2. Khan ST, Hashim H, Hamid W, Mehmood S, Qamar F. Crimean-Congo hemorrhagic fever--Distribution, diagnosis, treatment and control measures. Lahore Garrison Univ J Life Sci 2017;1:152–67. [CrossRef]
3. Hawman DW, Feldmann H. Crimean-Congo haemorrhagic fever virus. Nat Rev Microbiol 2023;21(7):463–77. [CrossRef]
4. Büyüktuna SA, Doğan HO. Diagnosis, prognosis and clinical trial in Crimean-Congo hemorrhagic fever. In: Human Viruses: Diseases, Treatments and Vaccines: The New Insights. Springer International Publishing; 2021. p. 207–19. [CrossRef]
5. Yilmaz H, Yilmaz G, Kostakoğlu U, Yaman H, Örem A, Köksal İ. The prognostic significance of serum troponin T levels in Crimean-Congo hemorrhagic fever patients. J Med Virol 2017;89(3):408–12. [CrossRef]
6. Frank MG, Weaver G, Raabe V; State of the Clinical Science Working Group of the National Emerging Pathogens Training and Education Center's Special Pathogens Research Network. Crimean Congo hemorrhagic fever virus for clinicians-Virology, pathogenesis, and pathology. Emerg Infect Dis 2024;30(5):847–53. [CrossRef]
7. Akinci E, Bodur H, Sunbul M, Leblebicioglu H. Prognostic factors, pathophysiology and novel biomarkers in Crimean-Congo hemorrhagic fever. Antiviral Res 2016;132:233–43. [CrossRef]
8. Welch SR, Ritter JM, McElroy AK, Harmon JR, Coleman-McCray JD, Scholte FEM, et al. Fluorescent Crimean-Congo hemorrhagic fever virus illuminates tissue tropism patterns and identifies early mononuclear phagocytic cell targets in Ifnar-/- mice. PLoS Pathog 2019;15(12):e1008183. [CrossRef]
9. Rathore SS, Manju AH, Wen Q, Sondhi M, Pydi R, Haddad I, et al. Crimean-Congo haemorrhagic fever-induced liver injury: A systematic review and meta-analysis. Int J Clin Pract 2021;75(11):e14775. [CrossRef]
10. Viswanathan S, Saravanakumari V. Are platelet indices useful in diagnosis of tropical acute febrile illnesses? J Local Global Health Sci 2016;2016:3. [CrossRef]
11. Incir S, Calti HK, Palaoglu KE. The role of immature granulocytes and inflammatory hemogram indices in the inflammation. Int J Med Biochem 2020;3:125–30. [CrossRef]
12. Muzammil K, Rayyani S, Abbas Sahib A, Gholizadeh O, Naji Sameer H, Jwad Kazem T, et al. Recenta in Crimean-Congo hemorrhagic fever virus detection, treatment, and vaccination: Overview of current status and challenges. Biol Proced Online 2024;26(1):20. [CrossRef]
13. Doğan HO, Büyüktuna SA, Kapancik S, Bakir S. Evaluation of the associations between endothelial dysfunction, inflammation and coagulation in Crimean-Congo hemorrhagic fever patients. Arch Virol 2018;163(3):609–16. [CrossRef]
14. Doğan K, Bolat S, Öksüz C, Büyüktuna SA. Leukotriene metabolism and proiflammatory cytokines in Crimean Congo hemorrhagic fever. J Med Virol 2023;95(1):e28199. [CrossRef]
15. McElvaney OJ, Curley GF, Rose-John S, McElvaney NG. Interleukin-6: Obstacles to targeting a complex cytokine in critical illness. Lancet Respir Med 2021;9(6):643–54. [CrossRef]
16. Onuk S, Sipahioglu H, Beştepe Dursun Z, Eren E, Aslan Sırakaya H, Kuzugüden S, et al. The relationship between cytokine concentrations and severity scoring index for Crimean-Congo hemorrhagic fever. Cureus 2023;15(2):e34882. [CrossRef]
17. Büyüktuna SA, Yerlitaş Sİ, Zararsız GE, Doğan K, Kablan D, Bağcı G, et al. Exploring free amino acid profiles in Crimean-Congo hemorrhagic fever patients: Implications for disease progression. J Med Virol 2024;96(5):e29637. [CrossRef]
18. Ergönül O. Crimean-Congo haemorrhagic fever. Lancet Infect Dis 2006;6(4):203–14. [CrossRef]