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Intravenous immunoglobulin in severe Crimean-Congo hemorrhagic fever: A retrospective study

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ABSTRACT

Objective: To assess the effectiveness of intravenous immunoglobulin (IVIg) therapy in patients diagnosed with Crimean-Congo hemorrhagic fever (CCHF) disease.

Methods: A single-center retrospective cohort study was conducted on hospitalized patients with confirmed severe CCHF at a tertiary care hospital in Turkey between 2010 and 2022. Cases were categorized into two groups based on whether they received IVIg therapy, with the treatment plan determined by the primary healthcare provider. The clinical, epidemiological, and laboratory parameters of these patients were evaluated. Demographic, laboratory findings, platelet counts on the day of IVIg indication and the third day, bleeding status during follow-up beyond 24 hours after IVIg administration, and prognosis recorded in patient information forms were retrieved.

Results: 72 patients were included in the analysis, with IVIg administered to 42 cases (58.3%) and not given to 30 cases (41.7%). Among the patients, 37 (51.4%) were female. Fever (65.3%) was the most common clinical presentation. The overall mortality rate was 19.4%, and IVIg administration did not significantly impact overall survival outcomes (P=0.48). On Day 3 following IVIg administration or indication, the platelet count was higher in the IVIg-treated group compared to the non-treated group (P=0.02). Furthermore, during follow-up beyond 24 hours after IVIg administration, bleeding was observed in 19.0% of the IVIg-treated group, compared to 46.6% in the non-treated group (P=0.01).

Conclusions: This study underscores the potential advantages of IVIg therapy in managing severe CCHF. Although IVIg administration did not significantly affect overall survival, it was associated with earlier improvement in platelet counts and a notable reduction in bleeding complications. These findings indicate that IVIg may serve as an adjunctive treatment in CCHF, particularly for addressing hemorrhagic manifestations.

KEYWORDS: Intravenous immunoglobulin; Crimean-Congo hemorrhagic fever; Treatment; Clinical improvement

Summary

Question: Is intravenous immunoglobulin (IVIg) therapy associated with improved outcomes in patients with severe Crimean-Congo hemorrhagic fever?

Findings: In this single-center retrospective cohort study of 72 hospitalized patients with severe Crimean-Congo hemorrhagic fever, outcomes were compared between patients who received IVIg and those who did not. IVIg therapy was not associated with a significant reduction in overall mortality. However, patients treated with IVIg showed earlier improvement in platelet counts and experienced fewer bleeding events during follow-up compared with untreated patients.

Meaning: IVIg may be a beneficial adjunctive therapy in severe CCHF by reducing hemorrhagic complications, despite no observed survival benefit.

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1. Introduction

Crimean-Congo Hemorrhagic Fever (CCHF) is a zoonotic, tick-borne viral hemorrhagic fever caused by the Crimean-Congo Hemorrhagic Fever Virus (CCHFV), classified under the genus *Nairovirus*, family Bunyaviridae[1]. This tick-borne virus is one of the most globally widespread, endemic in extensive regions of Africa, Asia, and Europe, with ongoing expansion of its range[2]. Its ability to cause fatal outcomes in up to 40% of cases underscores its significant public health impact[3]. CCHFV leads to diverse clinical manifestations in humans, ranging from asymptomatic or mild infections to life-threatening hemorrhagic syndromes involving shock and multiple organ dysfunction. Severe or fatal outcomes are associated with an excessive cytokine-mediated inflammatory response, resulting in endothelial damage, systemic coagulopathy, and subsequent multiorgan dysfunction. The presence of IgM and IgG antibodies, which correlate with declining viremia, is often absent or significantly delayed in fatal cases of CCHF[4].

Given the absence of specific antiviral therapies, blood and platelet transfusions, fluid and electrolyte replacement, and other supportive measures constitute the cornerstone of current treatment strategies[5-7]. Immunotherapy has emerged as a key therapeutic strategy, particularly when integrated with supportive interventions. Evidence from studies suggests that approaches like intravenous immunoglobulin (IVIg), cytokine modulation, and anti-inflammatory treatments with corticosteroids can significantly enhance disease outcomes[4,8].

Immunoglobulins (Ig) are antibodies produced by B lymphocytes and represent a key component of the immune system. Ig contain specific polyclonal and multifunctional antibodies. For clinical use, Ig are derived from human plasma and administered intravenously or subcutaneously. It is manufactured using components collected from healthy human donors. For therapeutic purposes, it is collected from healthy, immunized individuals who have either recovered from the disease or received a vaccine. The process involves plasmapheresis or the use of donor plasma, with blood cells removed before use[8]. IVIg therapy is widely employed by clinicians in the management of life-threatening conditions, including inflammatory, autoimmune diseases, and viral infections, either to treat the underlying disease or to modulate the immune system[9,10].

IVIg preparations consist of pooled IgG antibodies targeting a wide range of microorganisms. As a pooled product, the specific antimicrobial activity of IVIg depends directly on the pathogens encountered by the donor population contributing to the plasma pool[9-11]. IVIg interacts with Fc gamma receptors, particularly CD32, expressed on various immune cells, including B lymphocytes, dendritic cells, macrophages, neutrophils, and mast cells, thereby suppressing their activity[12], these factors collectively contribute to the reduction of both autoreactive antibody synthesis and inflammatory pathways, while supporting immunomodulatory effects, thus playing a pivotal role in regulating the inflammatory response[8]. This study aimed to investigate the clinical effectiveness of IVIg therapy in individuals diagnosed with CCHF and to evaluate its impact on clinical outcomes such as mortality rates, recovery time and laboratory parameters to provide scientific evidence for a potential adjunctive therapeutic strategy in the management of severe CCHF.

2. Methods

2.1. Study design and patient selection

Patients who received inpatient treatment for CCHF in the Department of Infectious Diseases and Clinical Microbiology between 2010 and 2022 were retrospectively analyzed in this single-center study.

The individuals with a confirmed CCHF diagnosis, determined by positive PCR virus antigen and/or IgM antibody results through IFA methods at the Virology Laboratory of the Ankara Public Health Institution, part of the Turkish Ministry of Health met the inclusion criteria. Participants were excluded if they 1) had a confirmed infectious etiology other than CCHF, 2) were under 18 years of age, 3) were pregnant or lactating, 4) had active malignancies and immunosuppression, and 5) had a mild to moderate severity index (Figure 1).

2.2. Definitions and severity criteria

The disease severity was assessed using the Dokuzo uz *et al.* scoring system[13]. This index includes five parameters: platelet count (0-3 points), activated partial thromboplastin time (aPTT) (0-3 points), fibrinogen level (0-3 points), bleeding (0-3 points), and somnolence (0 or 1 point). Based on the total score, patients were categorized as having mild (0-2 points), moderate (3-9 points), or severe (10-13 points) disease. All patients were clinically evaluated by a physician, and therapeutic decisions were made by the attending healthcare provider.

Mild bleeding was defined as petechiae, ecchymosis, or minor mucosal bleeding (such as mild epistaxis or gingival bleeding) that did not require transfusion or medical intervention. Severe bleeding was defined as gastrointestinal, genitourinary, pulmonary, or intracranial hemorrhage, or any bleeding episode requiring transfusion or resulting in hemodynamic instability. Improvement

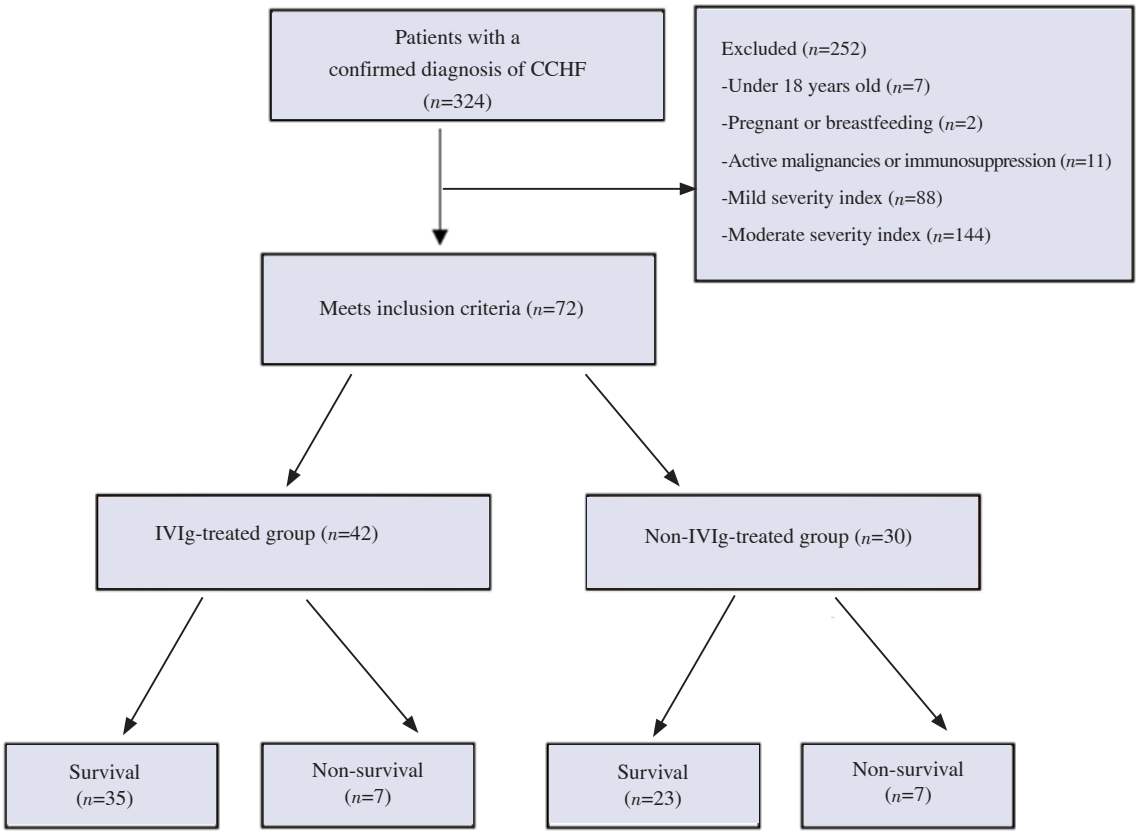

Figure 1. Evaluation algorithm of Crimean-Congo hemorrhagic fever cases from 2010 to 2022. Flow diagram illustrating patient inclusion and exclusion criteria, intravenous immunoglobulin administration, and clinical outcomes (survival or non-survival).

in bleeding manifestations, defined as the cessation or reduction of visible bleeding and stabilization of hemoglobin levels without the need for further transfusion.

Cases were categorized into two groups according to IVIg therapy status. According to the product information, IVIg is generally recommended at a dose exceeding 0.4 g/kg/day. In this study, IVIg was administered at a cumulative dose of 1 g/kg, infused over 1-3 days to achieve the intended immunomodulatory effect. The total infusion time was approximately 5 hours. The infusion was initiated at a slower rate of about 50 mL/h during the first hour (corresponding to 5 g of IVIg) and then gradually increased to approximately 180-190 mL/h, as tolerated and adjusted according to the patient's weight, in accordance with the institutional protocol. IVIg was administered over a period ranging from 1 to 3 days. The timing of IVIg initiation was determined by the attending physician based on the patient's clinical status and laboratory findings.

2.3. Data collection

Demographic, clinical, and laboratory findings, along with platelet counts on the day IVIg was initiated and on the third day, were recorded. Laboratory measurements were obtained on the day of hospital admission. For patients who received IVIg therapy, the subsequent measurements corresponded to 48-72 hours after IVIg administration. For those who did not receive IVIg, the 48-72-hour values reflected routine follow-up during hospitalization. In addition, bleeding status was monitored at intervals exceeding 24 hours post-IVIg administration, and overall prognosis were recorded.

All medications taken during their hospital stay, and adverse events potentially associated with IVIg therapy were monitored and documented throughout the study. The mortality rate, duration from treatment initiation to death, and hospital stay length among recovered patients were assessed.

The study's primary outcome was defined as the resolution of clinical symptoms associated with CCHF. Time to improvement,

discharge/death, and the reduction or absence of transfusion requirements constituted the primary endpoints.

2.4. Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics version 22 (IBM Corp., Armonk, NY, USA). Categorical variables were expressed as frequencies (n) and percentages (%), while continuous variables were summarized as means with standard deviations. The *Chi*-square test or Fisher's exact test was applied to assess associations between categorical variables. Normal distribution of continuous data was evaluated using the Kolmogorov-Smirnov test. Depending on data distribution, comparisons between IVIg-treated and non-IVIg-treated groups were performed using either Student's t-test or the Mann-Whitney U test. A two-tailed P-value of less than 0.05 was considered statistically significant.

3. Results

A total of 324 patients hospitalized with CCHF between April 1, 2010, and October 1, 2022, were initially identified as the study cohort. Following the application of predefined inclusion and exclusion criteria, 72 patients with severe CCHF were included in the final analysis.

The study population was stratified into IVIg-treated and non-IVIg-treated groups. Of the 72 patients, 35 (48.6%) were male, and 37 (51.4%) were female. IVIg was administered to 42 patients (58.3%), while 30 patients (41.7%) did not receive it. IVIg was administered on average (3.0±1.4) days after hospital admission (range: 1-6 days). The decision to initiate IVIg therapy was made by the primary physician based on the presence of bleeding manifestations and the need for platelet support.

The mean age of patients who received IVIg was (47.7±18.1) years (range, 18-78 years), while the mean age of those who did not receive IVIg was (51.7±13.5) years (range, 22-88 years) (P=0.37). The overall mortality rate in the study was 19.4% (n=14). There were no differences in mortality rates between the IVIg-treated and non-treated groups, indicating that IVIg administration did not impact overall survival outcomes (P=0.48).

The most common symptom was fever (65.3%, 47/72). Comorbidities were present in 27 patients (37.5%), with neurological diseases as the most common (23.6%, 17/72), followed

Table 1. Evaluation of epidemiological, clinical, and outcome characteristics between intravenous immunoglobulin-treated and non-intravenous immunoglobulin groups of Crimean-Congo hemorrhagic fever patients (n=72).

Characteristics	IVIg-treated group (n=42)	Non-IVIg treated group (n=30)	P value
Age, year, mean±SD	47.7±18.1	51.7±13.5	0.37[&]
Sex			
Female	20 (48.0)	17 (57.0)	
Male	22 (52.0)	13 (43.0)	0.45
Comorbidities			
Diabetes mellitus	1 (2.4)	0 (0)	>0.05
Hypertension	5 (11.9)	4 (13.3)	
Neurological diseases	9 (21.4)	8 (26.7)	
Symptoms			
Fever	28 (66.7)	19 (63.3)	0.55
Mild bleeding	6 (14.2)	1 (3.3)	0.23
Severe bleeding	25 (59.5)	21 (70.0)	0.36
Laboratory parameters			
White blood cell counts, /μL, normal range: 4-10×10^3	1 820 (1 310-3 000)	2 055 (1 230-2 620)	0.67[#]
Hemoglobin, g/dL, mean±SD, normal range: 11-17	13.6±2.0	14.6±2.0	0.04[&]
Platelets, ×1 000 U/L, normal range: 150-450	29 (19-42)	23.5 (17-31)	0.31[#]
Aspartate aminotransferase, U/L, normal range: 0-35	344 (237-663)	392 (165-577)	0.78[#]
Alanine aminotransferase, U/L, normal range: 0-45	147 (82-240)	143.5 (88-231)	0.85[#]
Creatinine, mg/dL, normal range: 0.8-1.5	0.8 (0.7-1.3)	0.8 (0.6-1)	0.58[#]
Lactate dehydrogenase, U/L, normal range: 0-248	1 179 (741-1 841)	1 275 (935-1 869)	0.78[#]
Creatine kinase, 20-200 U/L	511 (284-1 085)	765 (444-2 519)	0.12[#]
Total bilirubin, mg/L, normal range: 0.1-1.2	0.5 (0.4-0.7)	0.6 (0.4-0.8)	0.69[#]
International normalized ratio	1.1 (1-1.3)	1.1 (1-1.2)	0.49[#]
D-dimer, μg/L, normal range: 0-550	7.8 (5.6-25.3)	15.1 (2.4-34.5)	0.66[#]

Data are expressed as n (%), and *chi*-square test or Fisher's exact test was used unless otherwise indicated. IVIg: intravenous immunoglobulin. [#]Data are expressed as median (Q1, Q3), and Mann-Whitney U test was used. [&]Data are expressed as mean±SD, and Student's t-test was used.

by hypertension (12.5%, 9/72, Table 1). The exact time of symptom onset was not available for the patients.

An analysis of bleeding status after hospital admission revealed that 6 cases exhibited mild bleeding (such as epistaxis or petechiae), and 25 cases had severe bleeding (such as gastrointestinal hemorrhage or hematuria) among patients who were scheduled to receive IVIg. In contrast, the other group, 1 patient experienced mild bleeding, and 21 had severe bleeding. There were no significant differences in bleeding status between the two groups (P>0.05). These findings suggest that both groups exhibited a similar bleeding profile before the initiation of IVIg therapy.

All patients in both groups received platelet transfusions. Additionally, fresh frozen plasma was administered to 25 out of 42 patients (59.5%) who received IVIg, while 15 out of 30 patients (50.0%) who did not receive IVIg also received fresh frozen plasma (P=0.42). We found that following IVIg administration, bleeding occurred in 19.0% of patients in the IVIg-treated group, compared to 46.6% in the non-IVIg group (P=0.01). This suggests that IVIg treatment can reduce the incidence of bleeding in this patient population. No adverse events attributable to IVIg were documented, but this may also be due to incomplete records. The data are summarized in Table 2.

Table 2. Treatment and outcomes of the study population (n=72).

Treatment	IVIg-treated group (n=42)	Non-IVIg treated group (n=30)	P value
Medication			
Fresh frozen plasma	25 (59.5)	15 (50.0)	0.42
Platelet suspension	42 (100.0)	30 (100.0)	>0.99
Erythrocyte suspension	9 (21.4)	2 (6.7)	0.09
Outcome			
Length of hospital stay, days, median (Q1-Q3)	9 (6-11)	9 (6-12)	0.59
Mortality	7 (16.6)	7 (23.3)	0.48
Bleeding status after 24 hours of post-intervention	8 (19.0)	14 (46.6)	0.01

Data are expressed as n (%) unless otherwise indicated. IVIg: intravenous immunoglobulin.

Table 3. Demographic and baseline characteristics of Crimean-Congo hemorrhagic fever patients according to intravenous immunoglobulin treatment status (n=72).

Laboratory parameters	48th/72nd hour of follow-up			Last day of follow-up (discharge/death)		
	IVIg-treated (n=42)	non-IVIg groups (n=30)	P value	IVIg-treated (n=42)	non-IVIg groups (n=30)	P value
White blood cell counts, /μL, normal range: 4-10×10^3	2 020 (1 250-3 600)	2 200 (10.30-3 110)	0.82	5 350 (3 910-6 940)	4 745 (3 200-6 265)	0.17
Hemoglobin, g/dL, normal range: 11-17	12.0 (10.7-13.5)	13.4 (12.1-14.2)	0.12	10.7±2.1	11.4±1.9	0.25[&]
Platelets, ×1 000 U/L, normal range: 150-450	28 (20-45)	19 (15-27)	0.02	171 (129-223)	131.0 (119.5-174.5)	0.15
Aspartate aminotransferase, U/L, normal range: 0-35	549 (374-1 458)	545 (382-1 133)	0.71	84 (51-154)	91.5 (31-131)	0.79
Alanine aminotransferase, U/L, normal range: 0-45	278 (171-430)	213 (133-478)	0.48	108 (32-171)	98.5 (45-180)	0.99
Creatinine, mg/dL, normal range: 0.8-1.5	0.8 (0.5-1.1)	0.7 (0.6-1.0)	0.77	0.6 (0.5-0.8)	0.6 (0.5-0.7)	0.47
Lactate dehydrogenase, U/L, normal range: 0-248	1 177 (732-2 205)	1 268 (1 049-2 381)	0.20	476 (384-541)	822 (559-891)	0.16
Creatine kinase, 20-200 U/L	1 483 (698-2 621)	531.5 (306.5-2 002.0)	0.35	65 (42-200)	780 (405-1 274)	0.71
Total bilirubin, mg/L, normal range: 0.1-1.2	1.0 (0.7-2.0)	0.7 (0.5-1.6)	0.49	0.8 (0.6-1.1)	0.8 (0.7-1.3)	0.39
International normalized ratio	1.0 (0.9-1.1)	1.1 (0.9-1.2)	0.34	0.9 (0.9-1.0)	0.9 (0.9-1.0)	0.99
D-dimer, μg/L, normal range: 0-550	2.7 (1.9-7.1)	3.3 (1.7-6.0)	0.80	2.8 (1.5-15.5)	2.7 (1.9-4.0)	0.76

Data were expressed as median (Q1-Q3) unless otherwise indicated. IVIg: intravenous immunoglobulin. Mann-Whitney U test was used unless otherwise indicated. [&]Student's t-test was used.

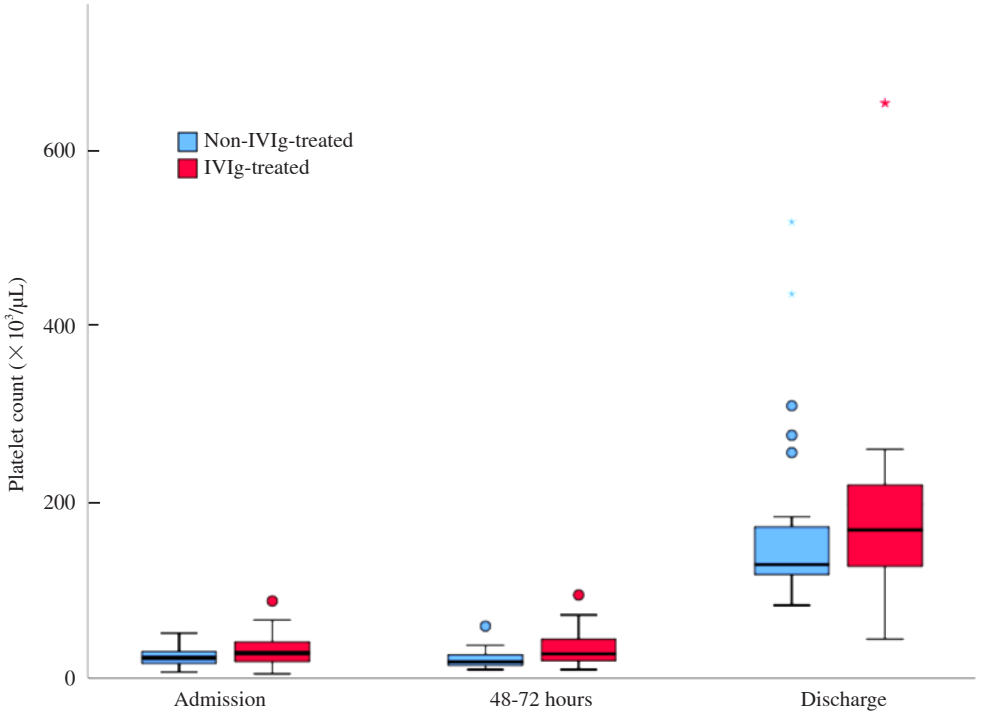

Figure 2. Distribution of platelet counts at admission, 48-72 hours, and discharge among IVIg-treated and non-IVIg-treated patients, presented as boxplots. The boxes indicate the median and interquartile range (Q1-Q3), the whiskers represent the range, and individual points denote outliers. IVIg: intravenous immunoglobulin.

As presented in Table 3, laboratory parameters were generally comparable between the IVIg-treated and non-treated groups. Notably, platelet counts on Day 3 post-treatment were significantly higher (P=0.02) and returned to normal range at the day of final follow up in the IVIg group. No other laboratory parameters exhibited statistically significant differences between the groups. The temporal changes in platelet counts from admission to Day 3 and the final follow-up in both the IVIg-treated and non-treated groups are shown in Figure 2.

4. Discussion

IVIg, used in the treatment of various conditions, continues to be utilized in the management of infectious diseases caused by numerous pathogens that are difficult to control and for which specific treatments are unavailable. IVIg is administered to manage and protect against various infections, particularly in immunocompromised patients or in cases where the immune system has a weak response. Although ribavirin has been historically used in the treatment of CCHF in Turkiye, recent studies have shown inconsistent results regarding its clinical benefit[6,14,15]. None of the patients in our study received ribavirin therapy, which excluded its potential confounding effect on outcomes. Current management in our center focuses on supportive care and, in selected cases, adjunctive IVIg therapy.

IVIg treatment is utilized for a range of viral infections among various medical conditions. IVIg treatment is used as an immunomodulatory or immunosuppressive therapy against viral infections[9,10]. The therapeutic effects of IVIg are mediated through several mechanisms, including the regulation of antigen-presenting cell maturation and function, and broad immunomodulatory effects on inflammatory responses[9–11,16,17]. The development of CCHF is attributed to both the direct cytopathic and indirect immunopathogenic effects of the virus, which impact endothelial cells and immune system cells.

Key factors playing a pivotal role in the pathogenesis include the extent of endothelial injury, hyperinflammatory cytokine response, platelet depletion, disseminated intravascular coagulation, hemophagocytic activity, and hepatocellular necrosis[5–7,18]. IVIg

promotes cellular and tissue homeostasis by engaging cell surface receptors through natural antibody-mediated stimulation. IVIg interacts with multiple components of the immune system at different levels, demonstrating its activity against infections[11,17,19].

In our study, IVIg was administered to CCHF patients to utilize its immunosuppressive and immunomodulatory properties. We proposed that IVIg may significantly modulate the immune response, thereby facilitating infection control and potentially improving disease outcomes.

The timing and route of IVIg administration in CCHF may be particularly important; to our knowledge, no previous studies have specifically addressed this aspect. In our study, patients diagnosed with refractory thrombocytopenia who received IVIg treatment showed a reduction in the need for blood transfusions and an increase in platelet counts. Consequently, a decrease in hemorrhagic complications was noted among these cases. In a study conducted in Iran comparing Ribavirin plus 30-50 g IVIg as adjuvant therapy to ribavirin alone, it was demonstrated that IVIg may reduce the clinical burden and shorten the disease duration. However, the two groups had no significant difference in mortality rates[20]. Similarly, in a study carried out in Turkiye the same year involving pediatric patients, it was suggested that IVIg might be effective during the hemorrhagic phase of CCHF[21]. It was reported that IVIg was administered to treat severe thrombocytopenia, and ribavirin was not used in that cohort. IVIg was given to manage severe thrombocytopenia and coagulopathy during the hemorrhagic phase. Although the patient population and clinical context differ from our cohort, both studies suggest that IVIg may contribute to hematologic recovery and stabilization of coagulopathy in severe CCHF cases, supporting its potential role as an adjunctive therapeutic modality. Additionally, in other viral infections, such as in moderate-to-severe hospitalized COVID-19 patients, studies have documented that the use of IVIg has resulted in clinical improvement[22].

Laboratory findings play a crucial role in the diagnosis, clinical assessment, and prognosis of CCHF. Previous studies have shown that elevated alanine aminotransferase, aspartate aminotransferase, creatine kinase (CK), and lactate dehydrogenase (LDH) levels, along with leukopenia and thrombocytopenia, are common and well-documented features of the disease[23,24]. Elevated CK and LDH levels are considered to reflect widespread tissue injury, muscle involvement, and endothelial damage, which are characteristic of severe CCHF. In our study, the majority of patients exhibited elevated CK and LDH levels, indicating tissue and endothelial injury. These findings are consistent with previous studies reporting a correlation between increased CK and LDH levels and greater disease severity in CCHF[13,25,26].

In studies, the mortality rate in CCHF patients varies between 3% and 30%[5–7,27]. Consistent with the current literature, our study observed the mortality rate of 19.4%. Our findings revealed no significant statistical difference between patients who received IVIg and those who did not. However, a larger sample size would be necessary to draw definitive conclusions on this matter. Based on our findings, which show an earlier increase in platelet count in the IVIg-treated group, it is suggested that if IVIg treatment had been administered to the patients in the non-treated group, the mortality rate might have been lower.

IVIg usage, particularly the hyperimmune preparations, which are derived from donors with high titers of the desired antibodies, continues to be utilized in the treatment of various infectious diseases and infection-related disorders. It has also been reported to exhibit antiviral effects against numerous viruses[11,28]. However, hyperimmune IVIg specific to CCHF is not currently available in our country; therefore, standard pooled IVIg was used in this study. The rationale for its use was based on its known immunomodulatory properties, including the modulation of cytokine responses, attenuation of systemic inflammation, and potential stabilization of the vascular endothelium in severe cases. According to the *Platelet Transfusion: 2025 Association for the Advancement of Blood and Biotherapies and International Collaboration for Transfusion Medicine Guidelines International Clinical Practice Guidelines*[29], transfusion services are increasingly facing challenges in meeting platelet demands. In the context of CCHF, where bleeding and thrombocytopenia are major clinical concerns, there is a growing need for novel therapies that can reduce transfusion requirements. IVIg, by potentially mitigating endothelial injury and modulating immune responses, may serve as a promising therapeutic alternative that could help reduce the need for platelet transfusions in these patients.

Our study provides valuable and unique data regarding the use of IVIg treatment in CCHF patients and its role in bleeding management, contributing to the existing literature. However, there are some limitations. First, the retrospective nature of the study restricts the capacity to draw definitive causal inferences. It was carried out at a single institution, which may not fully represent other patient populations in different geographic regions. The exact time of symptom onset was uncertain, as patients could not accurately recall when their symptoms began. The timing of IVIg administration was not standardized across patients. Furthermore, the short follow-up period and absence of long-term outcome assessments are also notable limitations.

In conclusion, the antiviral and anti-inflammatory activities of IVIg suggest that it may demonstrate a beneficial therapeutic effect in CCHF. This study demonstrated that the administration of IVIg in patients with CCHF led to a more rapid normalization of platelet

counts and a significant reduction in bleeding episodes. The results of our study suggest that IVIg may have a favorable impact on the prognosis of CCHF. Until a specific treatment is identified, IVIg is considered a promising therapeutic option and may also serve as supportive therapy. Further studies of larger sample sizes are needed to determine the effect of IVIg on mortality.

Conflict of interest statement

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Data availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Ethical approval and informed consent

This study was conducted in accordance with the principles of the Declaration of Helsinki and was approved by the Clinical Research Ethics Committee of Karadeniz Technical University (approval number: 2025/24, dated on 3 March 2025). Informed consent was waived due to the retrospective nature of the study, and anonymous clinical data were used in the analysis.

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Authors' contributions

Conceptualization: FA; Methodology: FA, HNKP; Software: HNKP; Formal analysis: HNKP, GY; Investigation: FA and DCY, FAK; Data curation: DCY, FAK; Writing-original draft preparation: FA and HNKP; Writing-review and editing: GY; Visualization: HNKP; Supervision: GY. All authors have read and approved the final version of the manuscript.

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