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Original Article

Hypokalemia Correlates with Troponin Levels in Moderate-Severe COVID-19 Patients, Independent to Coagulation Status

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Abstract

Background : Myocardial injury is a common complication of COVID-19, often marked by elevated cardiac troponin and linked to poorer outcomes. Besides recognized causes such as viral injury, inflammation, and coagulopathy, electrolyte disturbances like hypokalemia may also increase cardiac vulnerability. SARS-CoV-2 can promote potassium loss through activation of the renin angiotensin aldosterone system, but the relationship between low potassium and troponin elevation remains unclear.
Aim : To evaluate whether serum potassium levels are associated with troponin elevation in patients hospitalized with moderate to severe COVID-19, and whether this association is influenced by disease severity or D-dimer levels.
Methods : Cross-sectional study of 50 adults with moderate or severe COVID-19. Serum potassium, troponin, and D-dimer were measured once during admission. Associations were tested using independent t-tests, Mann-Whitney tests, and Fisher's exact tests, with $p < 0.05$ considered significant.
Results : Among 50 patients (39 moderate, 11 severe COVID-19), 35 (70%) had normal potassium, 12 (24%) hypokalemia, and 3 (6%) severe hypokalemia; 9 (18%) had elevated troponin. Potassium was lower in patients with elevated troponin than in those with normal levels (3.53 ± 0.53 vs. 3.99 ± 0.58 mmol/L, $p = 0.038$), and potassium status was significantly associated with troponin elevation ($p = 0.0401$). No significant differences were detected when patients were grouped by disease severity, with potassium ($p = 0.44$) and troponin ($p = 0.66$) levels similar in moderate and severe cases. D-dimer levels were not significantly different by severity ($p = 0.175$) and showed no association with potassium ($p = 0.24$) or troponin ($p = 0.91$).
Conclusion : In hospitalized patients with moderate to severe COVID-19, lower potassium levels were associated with elevated troponin, regardless of disease severity and without a detectable link to D-dimer status. These findings suggest hypokalemia may contribute to myocardial injury in COVID-19 and support regular monitoring and timely correction of electrolyte disturbances.

Keywords : COVID-19, D-dimer, Hypokalemia, Myocardial injury, Troponin

INTRODUCTION

Elevated troponin levels have become a critical marker of myocardial injury, drawing significant attention in the management of COVID-19.[1] Studies consistently link troponin elevation in these patients to severe cardiac complications,[1,2] heightened inflammation,[3] and increased mortality.[1–3] The mechanisms behind this are multifaceted, ranging from virus-induced cytokine storms and direct myocardial invasion to systemic hypoxia and a prothrombotic state.[1–3] These factors collectively place immense stress on the heart, increasing the risk of myocardial injury and adverse outcomes. Recognizing and addressing myocardial injury early could be a key step in improving prognosis for high-risk COVID-19 patients.

Among the many potential contributors to myocardial injury in COVID-19, electrolyte imbalances, particularly hypokalemia,[4,5] deserve close investigation. Hypokalemia can impair myocardial repolarization, destabilize cell membrane potentials, and reduce cardiac contractility,[6] thereby predisposing the heart to arrhythmias and ischemic injury.[7] Not only that, Hypokalemia is known to disrupt cellular electrophysiology,[8] create a pro-arrhythmic environment,[9] and potentially worsen myocardial injury.[9] Although the pathophysiological effects of hypokalemia are well recognized,[7–9] the role of hypokalemia in driving troponin elevation in COVID-19 remains unexplored, especially in the context of the frequent coagulopathy observed in these patients.[10,11] While many studies address either coagulation abnormalities[11] or electrolyte disturbances,[12] evidence on the specific interplay between hypokalemia and troponin levels within the broader setting of COVID-19 is lacking.

Building on this gap, our study investigates whether hypokalemia is associated with elevated troponin levels in COVID-19 patients. By exploring this relationship, we aim to provide deeper insight into how hypokalemia contributes to myocardial injury in an already vulnerable population. Our findings could enhance clinical decision-making and guide targeted interventions to mitigate cardiac complications. Ultimately, this work seeks to improve patient outcomes by advancing our understanding of the complex interplay between COVID-19, myocardial injury, and hypokalemia.

METHODS

This observational study employed a cross-sectional design to assess 50 patients with moderate to severe COVID-19. Patients were selected through purposive sampling from the medical records of inpatients at Dr. Kariadi Hospital, Semarang, between January and December 2021. The inclusion criteria consisted of patients aged 18 years or older with available potassium and troponin data. COVID-19 severity was classified based on clinical presentation: moderate cases included patients without symptoms of severe pneumonia who did not require oxygen supplementation, while severe cases were defined as those exhibiting severe pneumonia symptoms, requiring oxygen therapy, experiencing respiratory failure, sepsis, shock, or requiring admission to the intensive care unit (ICU). Patients with mild COVID-19 were excluded from the study.

Troponin levels were obtained from blood samples and categorized as normal (<0.1 ng/mL) or elevated (≥0.1 ng/mL). Potassium levels were similarly measured and classified as normal (>3.5 mg/dL), hypokalemia (3.0–3.5 mg/dL), or severe hypokalemia (<3.0 mg/dL). One patient with hyperkalemia (>5.0 mg/dL; 5.7 mg/dL) was retained in the dataset and included within the non-hypokalemia group for the primary comparison. Additionally, coagulation status was evaluated using D-dimer levels, with values below 500 ng/mL considered normal and values of 500 ng/mL or higher classified as elevated.

Following data collection, all information underwent a structured process of cleaning, coding, and categorization according to predefined criteria. Statistical analyses were conducted using IBM SPSS Statistics version 24, while data visualization was performed using GraphPad Prism 10.

This study was conducted following ethical guidelines and received approval from the Health Research Ethics Committee of the Faculty of Medicine, Diponegoro University, with ethical clearance number 593/EC/KEPK-RSDK/2020. Additionally, permission was granted by the Director of Dr. Kariadi Hospital. Written informed consent was obtained from all patients before their inclusion in the study. To minimize selection bias, information bias, and confounding variables, the inclusion and exclusion criteria were strictly enforced, with each subject evaluated independently by at least two examiners.

RESULTS

A total of 50 patients were included in the study (Table 1). In terms of COVID-19 severity, 39 patients (78%) presented with moderate disease, while 11 patients (22%) had severe disease. Regarding potassium levels, 35 patients (70%) had normal potassium, 12 patients (24%) had hypokalemia, and 3 patients (6%) had severe hypokalemia. The majority of 41 patients (82%) had normal troponin, whereas 9 patients (18%) had elevated levels. D-dimer was also normal in 43 patients (86%), with the remaining 7 patients (14%) showing elevated D-dimer values.

We first examined the relationship between potassium and troponin levels. Potassium reduction was

TABLE 1
Characteristics of patient data

Patient Characteristic	N	Frequency (%)	Mean ± SD / Median (min – max)
Sex			
Male	23	46	
Female	27	54	
Age			52.14 ± 14.22 years
< 50 years	20	40	
51–75 years	28	56	
>75 years	2	4	
Covid Severity			
Moderate	39	78	
Severe	11	22	
Potassium			3.908 ± 0.603 mg/dL
Normal	35	70	
Hypokalemia	12	24	
Severe Hypokalemia	3	6	
Troponin			0.00895 (0.00099 – 15.101) ng/mL
Normal	41	82	
Increased	9	18	
D-dimer			1455 (270 – 20001) ng/mL
Normal	43	86	
Increased	7	14	

Normally distributed data is shown as Mean ± SD, while Median (min–max) is used for data with abnormal distribution.

more pronounced in patients with increased troponin levels than in those with normal troponin levels. The average potassium level was 3.99 ± 0.58 mg/dL in the normal troponin group and 3.53 ± 0.53 mg/dL in the increased troponin group. Our analysis showed a statistically significant difference between patients with elevated troponin levels than in those with normal troponin levels (Independent t-test, p= 0.038) (Fig. 1A). To further explore this relationship, we compared the distribution of potassium status across troponin groups. Among patients with normal troponin, 31 had normokalemia, 9 had hypokalemia, and 1 had severe hypokalemia. In contrast, among those with elevated troponin, 4 had normokalemia, 3 had hypokalemia, and 2 had severe hypokalemia (Table 2). Fisher's exact analysis revealed a significant association between troponin status and potassium levels (p = 0.0401) (Fig. 1B, Table 2), consistent with the results observed in Figure 1A.

Given this significant association, we next investigated whether disease severity could influence the relationship between potassium and troponin, we analyzed potassium and troponin levels by stratifying patients into moderate vs. severe disease groups. Our observations showed that the average potassium level was 3.86 ± 0.61 mg/dL in the moderate covid group and 4.06 ± 0.50 mg/dL in the severe covid group (Fig. 2A), Our analysis using independent t-test doesn't show any statistically significant difference (p=0.44). When analyzing potassium status categories (normokalemia, hypokalemia, severe hypokalemia), there was no statistically significant difference between COVID-19 severity and potassium status (Fisher's exact, p = 0.69) (Fig. 2A).

Similarly, troponin levels were not significantly influenced by COVID-19 severity. Our data shows that the median troponin levels of moderate covid patients were 0.01 ng/mL (with min 0.001 and max 15.101) and

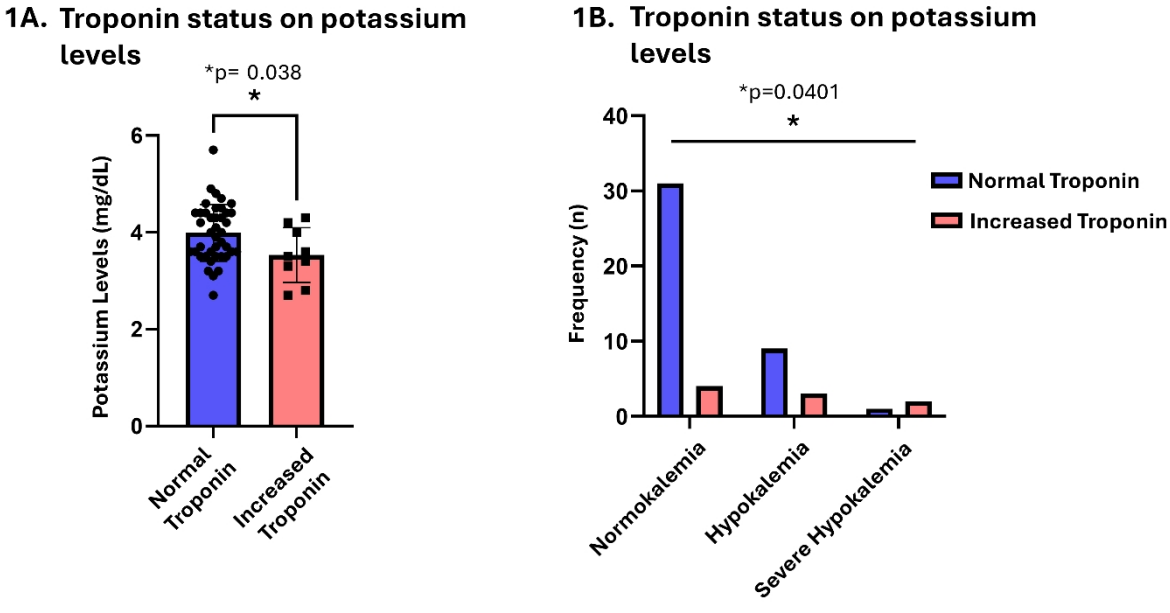

Figure 1. Relationship Between Serum Potassium Levels and Troponin Status in Patients with Moderate to Severe COVID-19. (A) Comparison between mean serum potassium levels in patients with normal vs. increased troponin. The data are presented as the mean values with error bars indicating the standard error of the mean. The analysis showed significant differences in potassium levels between normal and increased troponin groups (Independent t-test, *p= 0.038). (B) Frequency data of different potassium status categories (normokalemia, hypokalemia, and severe hypokalemia) in individuals with normal troponin (blue bars) and those with increased troponin (red bars) shows significant result (fisher's exact, *p=0.0401).

TABLE 2
Analysis of Troponin Status on Potassium Levels

	Normal Troponin (N)	Increased Troponin (N)	Fisher's exact analysis
Normal Potassium	31	4	*p = 0.0401
Hypokalemia	9	3	
Severe Hypokalemia	1	2	
Total	41	9	

Fisher's exact test was used to assess the association between potassium levels and troponin status.
p-value <0.05 was considered statistically significant.

severe covid patients were 0.008 ng/mL (with min 0.001 and max 0.157). Among moderate cases, 31 had normal troponin and 8 had increased troponin, whereas among severe cases, 10 had normal troponin and 1 had increased troponin (Fisher's exact, p = 0.66) (Fig. 2B).

Because coagulation abnormalities are a common complication of COVID-19 and may contribute to myocardial injury, we also examined whether D-dimer levels differed by disease severity. D-dimer levels tended to be higher in severe COVID-19 than in moderate cases. However, the difference did not reach statistical significance. The median D-dimer levels of moderate covid patients were 1230 ng/mL (with min 270 and max 20001) and severe covid patients were 3280 ng/mL (with min 410 and max 18910) Mann-Whitney test, p = 0.1750) (Fig. 2C). Elevated D-dimer levels were common in both groups, with no significant difference in distribution (Fisher's exact test, p = 0.99).

To further explore potential links between coagulation status and myocardial injury, we next analyzed biomarker levels according to D-dimer categories (normal vs. elevated). When troponin levels were compared between patients with normal and elevated D-dimer, the median values were similar

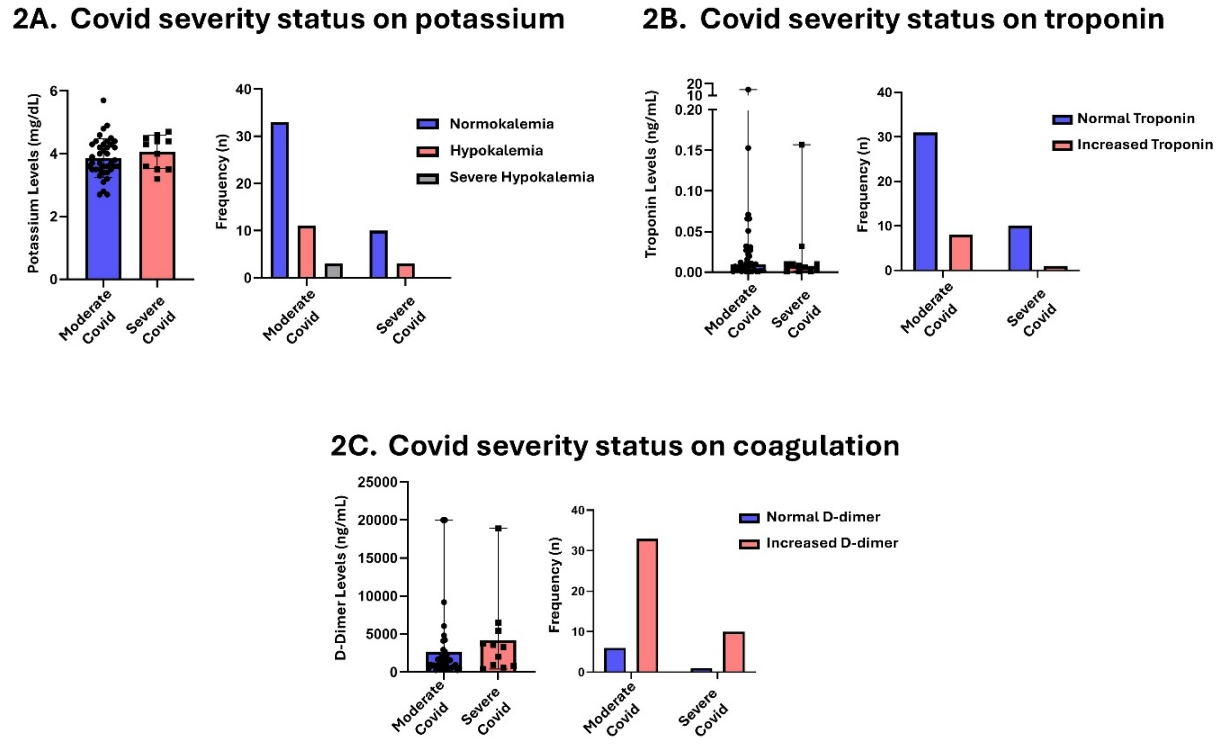

Figure 2. Association of COVID-19 Severity with Hypokalemia and Elevated Troponin. **(A) Left panel:** Comparison of serum potassium levels in moderate vs. severe COVID-19 patients. The data are presented as the mean values with error bars indicating the standard error of the mean. (Independent t-test, $p = 0.44$). The right panel further breaks down the distribution, showing how many patients with their potassium status in both groups. (Fisher's exact, $p = 0.69$). **(B) Left panel:** Comparison of serum troponin levels in moderate vs. severe COVID-19 patients. The data are shown as median number of factors with error bars representing max - min value. (Mann-Whitney, $p = 0.29$). The right panel further illustrate the distribution of patient troponin status, showing how many patients with normal or increased troponin in both groups. (Fisher's exact, $p = 0.66$). **(C) Left panel:** Comparison of D-dimer levels between patients with moderate and severe COVID-19. Data are shown as median values with error bars representing the minimum and maximum values (Mann-Whitney test, $p = 0.1750$). Right panel: Distribution of normal and increased D-dimer levels across COVID-19 severity categories (Fisher's exact test, $p = 0.99$).

(Normal D-dimer group were 0.01 ng/mL vs Elevated D-dimer group were 0.008 ng/mL), and the difference was not statistically significant (Mann-Whitney, $p = 0.91$). The proportion of patients with elevated troponin was also similar in both groups (Fisher's exact test, $p = 0.99$) (Fig. 3A).

A parallel analysis was performed for potassium levels. Mean concentrations were similar between the two D-dimer categories (Normal D-dimer group were 3.87 ± 0.61 mg/dL vs Elevated D-dimer group 4.16 ± 0.46 mg/dL) (Independent t-test $p = 0.24$), and the distribution of normokalemia, hypokalemia, and severe hypokalemia showed no meaningful variation (Fisher's exact $p = 0.79$) (Fig. 3B). These findings suggest that, within this cohort of moderate-to-severe COVID-19 patients, neither troponin nor potassium levels were influenced by coagulation status.

DISCUSSION

In this cross-sectional study of hospitalized patients with moderate to severe COVID-19, we found a notable association between hypokalemia and elevated troponin levels. This relationship persisted regardless of whether patients had severe or moderate disease, and it was not influenced by D-dimer status. These findings suggest that, for some patients, myocardial injury in COVID-19 may be linked to electrolyte disturbances rather than to the severity of respiratory illness or to overt coagulation abnormalities.

The biological link between hypokalemia and myocardial injury is well established.(8,9) SARS-CoV-2 infection can activate the renin angiotensin aldosterone system through ACE2 downregulation, leading to increased renal potassium loss.[12] Potassium depletion

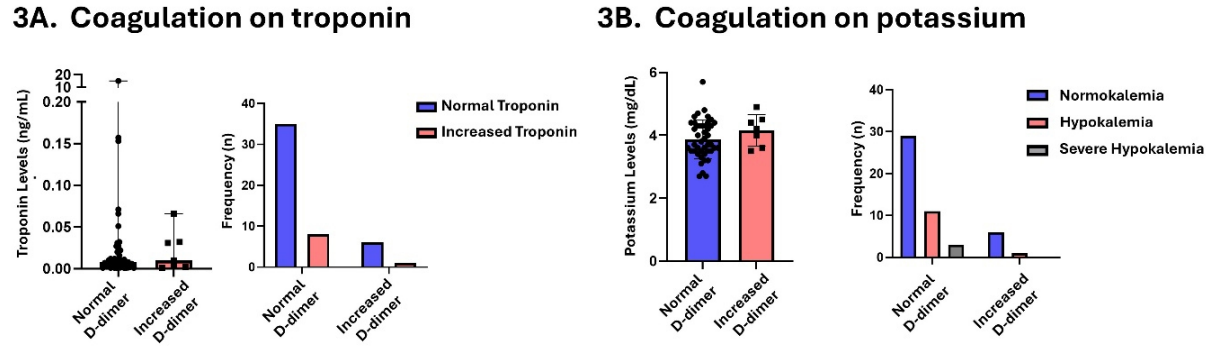

Figure 3. Association Between D-Dimer Status and Both Troponin and Serum Potassium in COVID-19 Patients. **(A) Left panel:** Comparison of serum Troponin levels in normal and increased D-dimer Covid-19 patients. The data are shown as median values with error bars representing max – min value. (Mann-Whitney, $p = 0.91$). The right panel further breaks down the distribution, showing how many patients with either normal or increased troponin. (Fisher's exact, $p = 0.99$). **(B) Left panel:** Comparison of serum potassium levels in normal vs. increased D-dimer groups. The data are presented as the mean values with error bars indicating the standard error of the mean. (Independent t-test, $p = 0.24$). The right panel further breaks down the distribution, illustrates the distribution of normokalemia, hypokalemia, and severe hypokalemia in each D-dimer category. (Fisher's exact, $p = 0.79$).

alters the electrical stability of the myocardium, delays repolarization, and increases the risk of arrhythmias.[8,9] In the setting of systemic illness and hypoxia, even modest potassium reductions can lower the threshold for myocardial injury. Our data support the possibility that correcting potassium early could reduce the risk of cardiac complications in hospitalized COVID-19 patients. Troponin serves not only as a biomarker of myocardial infarction but also of non-ischemic myocardial stress, frequently observed in systemic illness.[13,14] In the context of COVID-19, several mechanisms can lead to elevated troponin levels, including direct viral infiltration of cardiomyocytes,[3] cytokine-induced myocardial dysfunction and impaired microvascular perfusion,[3,15] oxygen supply-demand mismatch due to respiratory compromise, and coagulopathy associated with endothelial dysfunction and microthrombosis.[3,16] Our findings suggest that hypokalemia may contribute an additional myocardial stress, distinct from the classic ischemic or thrombotic pathways, by increasing cardiac vulnerability to electrical injury during systemic illness.

Interestingly, we did not find an association between D-dimer levels and troponin or potassium concentrations. While D-dimer is widely used as a marker of coagulopathy in COVID-19 on prior review,[11] is non-specific and can be influenced by many factors. In this study, most patients had D-dimer values within the normal range, which may explain the lack of statistical association. It is also possible that in moderately to severely ill but non-ICU patients, coagulation abnormalities are not the main driver of myocardial injury although our data didn't specifically analyze this possibility.

Clinically, our results suggest that checking electrolyte levels should be a routine part of caring for patients with COVID-19. An increase in troponin is not always caused by a blocked heart artery or a blood clot; sometimes, it can be due to general body stress combined with chemical imbalances in the blood, such as low potassium. Finding and fixing these correctable problems may help lower the risk of heart injury without the need for unnecessary treatments.[3]

The clinical impact of these findings is significant because hypokalemia is a treatable condition. Unlike complications such as cytokine storms[1,16] or viral myocarditis,[3] low potassium can be identified and corrected with standard care. Early detection and correction may reduce the risk of heart injury in patients with COVID-19.[17,18] These results support routine potassium monitoring in hospitalized patients, careful use of medicines that can lower potassium such as diuretics, and, for those at high risk, consideration of preventive potassium supplementation.[4,19] The fact that this association appears even in moderate illness highlights the value of intervening early, before the disease progresses to a level that requires intensive care.

Previous reports have linked hypokalemia to worse COVID-19 outcomes, although most emphasized global severity rather than cardiac injury. The multicenter study from China showed that hypokalemia was common and tracked with poorer prognosis,[18] but it did not specifically evaluate cardiac biomarkers such as

troponin. Another study examining electrolyte imbalance in COVID-19 patients similarly found hypokalemia to be frequent and related to increased morbidity, yet it focused more broadly on metabolic disturbances rather than their relationship with myocardial injury.[12] Our analysis complements these findings by demonstrating that lower potassium is also associated with troponin elevation, and that this signal persists irrespective of disease severity and D-dimer status. Taken together, prior work underscores prevalence and prognostic relevance, while our data connect hypokalemia to a concrete marker of myocardial injury.

This study has limitations. It was conducted at a single center with a relatively small number of patients, which may limit generalizability. We did not use regression modeling, as our aim was to examine individual associations rather than adjust for multiple variables, so the influence of confounding factors cannot be excluded. Information on comorbidities, chronic medications, and baseline organ function was not available, which restricts interpretation of the results. Laboratory measurements were obtained only once, preventing assessment of temporal trends or treatment effects. Even so, the analysis provides a clear, direct view of the statistical association between potassium and troponin in COVID-19 and offers insights that may be useful in clinical care.

CONCLUSION

In hospitalized patients with moderate to severe COVID-19, lower potassium levels were associated with higher troponin concentrations, independent of disease severity and without a clear relationship to D-dimer status. These findings suggest that hypokalemia may contribute to myocardial injury through mechanisms other than coagulopathy. Given that hypokalemia is readily identifiable and correctable, routine electrolyte monitoring and timely potassium repletion should be considered as part of comprehensive inpatient management to mitigate cardiac risk.

This study did not incorporate regression modeling or adjustment for potential confounders such as ICU admission, comorbidities, medication use, or baseline organ function, and laboratory values were obtained at a single time point. Further multicenter, prospective studies with larger sample sizes, comprehensive clinical data, and serial biomarker measurements are warranted to validate these findings and to clarify the interplay between potassium balance, coagulation abnormalities, and myocardial injury in COVID-19.

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CONFLICT OF INTEREST

All the authors declare that they have no conflicts of interest that might be perceived as influencing the impartiality of the reported research.

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