



ASSOCIATION BETWEEN ADMISSION HbA1c AND CLINICAL OUTCOMES IN PATIENTS WITH COVID-19.

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Received: 07-05-2026

Revised: 23-05-2026

Accepted: 02-06-2026

Published: 16-06-2026

Abstract

Background: Diabetes mellitus and poor glycemic control have been identified as important risk factors for adverse outcomes in patients with Coronavirus Disease 2019 (COVID-19). Glycated hemoglobin (HbA1c) reflects long-term glycemic control and may serve as a useful prognostic marker in hospitalized COVID-19 patients. **Aim:** The present study was conducted to evaluate the effect of admission HbA1c levels on the outcomes of patients admitted with COVID-19 infection. **Methods:** This prospective observational study included 150 patients admitted with laboratory-confirmed COVID-19 infection. HbA1c levels were measured at admission and categorized into clinically relevant groups. Demographic characteristics, comorbidities, inflammatory markers, ventilatory support requirements, and clinical outcomes were recorded. Statistical analysis was performed to determine the association between admission HbA1c levels and disease outcomes. **Results:** Among 150 patients, 71 (47.3%) had HbA1c levels above 7.0%, 58 (38.7%) had HbA1c levels $\leq 6.5\%$, and 21 (14.0%) had HbA1c levels between 6.5% and 7.0%. Elevated HbA1c levels were significantly associated with higher CRP, D-dimer, ferritin, and total leukocyte count values. Ventilatory support was required in 40 (37.7%) patients with HbA1c $> 7.0\%$ compared with 8 (18.2%) patients having HbA1c $\leq 6.5\%$. Mortality was observed in 28 (26.4%) patients with HbA1c $> 7.0\%$ compared with 6 (13.6%) patients with HbA1c $\leq 6.5\%$. Significant associations were observed between elevated HbA1c levels and diabetes mellitus, ischemic heart disease, ventilatory support, and mortality. **Conclusion:** Admission HbA1c level is a valuable prognostic marker in patients hospitalized with COVID-19 infection. Elevated HbA1c levels are associated with increased inflammation, greater disease severity, higher ventilatory support requirements, and increased mortality. Routine assessment of HbA1c at admission may facilitate early identification of high-risk patients and improve clinical decision-making.

Keywords: COVID-19, HbA1c, Mortality, Prognostic Marker.



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INTRODUCTION

Coronavirus disease 2019 (COVID-19), caused by Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2), emerged as a global public health emergency and rapidly evolved into a pandemic affecting millions of individuals worldwide. Although the majority of infected patients experience mild symptoms, a substantial proportion develop severe disease characterized by acute respiratory distress syndrome, multiorgan dysfunction, thromboembolic events, and death. Identifying prognostic markers that can predict disease severity and clinical outcomes remains essential for optimizing patient management and resource allocation [1].

Since the beginning of the pandemic, several risk factors have been recognized as important determinants of adverse outcomes in COVID-19. Advanced age, obesity, hypertension, cardiovascular disease, chronic kidney disease, and diabetes mellitus have consistently been associated with increased morbidity and mortality. Among these factors, diabetes has emerged as one of the most significant comorbidities contributing to poor clinical outcomes in patients infected with SARS-CoV-2 [2].

Hyperglycemia has been shown to adversely affect both innate and adaptive immune responses. Elevated blood glucose levels impair neutrophil chemotaxis, phagocytosis, and cellular immunity, thereby increasing susceptibility to infections and reducing the body's ability to control viral replication. In addition, chronic hyperglycemia promotes endothelial

dysfunction, oxidative stress, inflammation, and activation of coagulation pathways, all of which are implicated in the pathogenesis of severe COVID-19 [3].

Glycated hemoglobin (HbA1c) is a widely accepted indicator of long-term glycemic control and reflects average blood glucose levels over the preceding two to three months. Unlike random or fasting blood glucose measurements, HbA1c provides a more stable assessment of chronic glycemic status and can identify both diagnosed and previously unrecognized diabetes. Elevated HbA1c levels have been associated with increased risk of cardiovascular disease, microvascular complications, chronic kidney disease, and impaired immune function [4].

Emerging evidence suggests that poor glycemic control prior to SARS-CoV-2 infection may significantly influence the clinical course of COVID-19. Patients with elevated HbA1c levels frequently exhibit a higher prevalence of systemic inflammation, immune dysregulation, endothelial injury, and hypercoagulability, which may predispose them to severe disease manifestations. Furthermore, chronic metabolic disturbances associated with elevated HbA1c may exacerbate the cytokine storm and inflammatory cascade observed in critically ill COVID-19 patients [5].

Several clinical studies have reported that hyperglycemia at admission is associated with increased risk of intensive care unit admission, mechanical ventilation, prolonged hospital stay, and mortality among patients with COVID-19. Importantly, adverse outcomes have been observed not only in patients with established diabetes but also in individuals with previously undiagnosed dysglycemia. These observations suggest that glycemic status at the time of hospitalization may serve as a valuable prognostic indicator in COVID-19 [6].

HbA1c has gained increasing attention as a potential biomarker for predicting disease severity and outcomes in patients hospitalized with COVID-19. Elevated HbA1c levels have been associated with higher inflammatory marker concentrations, greater pulmonary involvement, increased incidence of acute respiratory distress syndrome, and higher mortality rates. Because HbA1c reflects pre-existing metabolic control, it may provide important prognostic information beyond that offered by acute blood glucose measurements alone [7].

The pathophysiological mechanisms linking elevated HbA1c levels with adverse COVID-19 outcomes are multifactorial. Chronic hyperglycemia contributes to persistent low-grade inflammation, endothelial dysfunction, increased expression of pro-inflammatory cytokines, and enhanced thrombotic activity. Glycation of proteins may impair immune cell function and promote oxidative stress, thereby increasing susceptibility to severe viral infection. In addition, diabetes-related comorbidities frequently coexist with elevated HbA1c levels, further increasing the risk of unfavorable outcomes [8].

Recent systematic reviews and meta-analyses have demonstrated that higher HbA1c levels are associated with increased severity and mortality among COVID-19 patients. These findings indicate that assessment of HbA1c at admission may help clinicians identify high-risk individuals who require closer monitoring and aggressive management. Early recognition of patients at increased risk of deterioration is particularly important during pandemics when healthcare resources may be limited [9].

Despite growing evidence regarding the relationship between glycemic status and COVID-19 outcomes, data regarding the prognostic significance of admission HbA1c levels remain limited in many populations. Variations in ethnicity, prevalence of diabetes, healthcare infrastructure, and disease burden may influence clinical outcomes and necessitate region-specific evaluation. Therefore, the present study was undertaken to assess admission HbA1c values as a prognostic marker in patients admitted with COVID-19 and to establish the effect of HbA1c levels at admission on patient outcomes. Understanding this relationship may contribute to improved risk stratification and management of hospitalized COVID-19 patients [10].

MATERIALS AND METHODS

This prospective observational study was conducted in the Department of General Medicine of a tertiary care teaching hospital over a period of one year. The study was designed to evaluate admission HbA1c values as a prognostic marker in patients admitted with COVID-19 and to establish the effect of HbA1c levels at admission on clinical outcomes. A total of 150 patients with laboratory-confirmed COVID-19 infection were included in the study after obtaining written informed consent.

All adult patients aged 18 years and above admitted with confirmed COVID-19 infection diagnosed by reverse transcription polymerase chain reaction (RT-PCR) or other approved diagnostic methods were considered eligible for inclusion. Patients who were unwilling to participate, pregnant women, patients with known hemoglobinopathies, severe anemia, recent blood transfusion, chronic hematological disorders affecting HbA1c interpretation, or incomplete clinical records were excluded from the study.

After admission, detailed demographic information including age, gender, body mass index, smoking status, comorbidities such as diabetes mellitus, hypertension, cardiovascular disease, and chronic kidney disease were recorded. Clinical presentation, vital parameters, laboratory investigations, radiological findings, treatment details, and disease severity at admission were documented using a predesigned case record form.

Venous blood samples were collected within 24 hours of hospital admission for estimation of HbA1c levels. HbA1c was measured using a standardized high-performance liquid chromatography method available in the institutional laboratory. Based on HbA1c values, patients were categorized into clinically relevant groups for analysis. Additional laboratory investigations including complete blood count, blood glucose, liver function tests, renal function tests, C-reactive protein, D-dimer, ferritin, lactate dehydrogenase, and other relevant investigations were recorded.

Patients were followed throughout their hospital stay and clinical outcomes were assessed. Outcome measures included disease severity, oxygen requirement, intensive care unit admission, need for mechanical ventilation, duration of hospitalization, recovery, and in-hospital mortality. The relationship between admission HbA1c levels and these outcomes was evaluated.

Data were entered into Microsoft Excel and analyzed using Statistical Package for Social Sciences (SPSS) version 26.0. Continuous variables were expressed as mean $\pm$ standard deviation, while categorical variables were expressed as frequencies and percentages. Student's t-test and one-way analysis of variance (ANOVA) were used for comparison of continuous variables wherever appropriate. Chi-square test or Fisher's exact test was used for comparison of categorical variables. Logistic regression analysis was performed to determine the association between HbA1c levels and adverse clinical outcomes after adjusting for potential confounding factors. Correlation analysis was carried out to evaluate the relationship between HbA1c levels and disease severity indicators. A p-value of less than 0.05 was considered statistically significant.

Prior approval for the study was obtained from the Institutional Ethics Committee before commencement of the study. The study was conducted in accordance with the ethical principles of the Declaration of Helsinki. Confidentiality of patient information was strictly maintained throughout the study, and all participants provided written informed consent prior to enrollment.

RESULTS

A total of 150 patients admitted with confirmed COVID-19 infection were included in the present study. Admission HbA1c levels were evaluated as a prognostic marker and their association with clinical outcomes, inflammatory markers, comorbidities, ventilatory support, and mortality was assessed.

Table 1 summarizes the overall outcomes according to admission HbA1c levels. Patients with HbA1c $>7.0\%$ demonstrated significantly higher frequencies of elevated total leukocyte count, raised CRP levels, increased D-dimer values, diabetes mellitus, ischemic heart disease, requirement of ventilatory support, and mortality. Mortality was observed in 28 (26.4%) patients with HbA1c $>7.0\%$ compared to 6 (13.6%) patients with HbA1c $\leq 6.5\%$. Similarly, ventilatory support was required in 40 (37.7%) patients with HbA1c $>7.0\%$ as compared to 8 (18.2%) patients with HbA1c $\leq 6.5\%$. These findings indicate that elevated HbA1c levels were associated with worse clinical outcomes and greater disease severity.

Table 2 depicts the distribution of admission HbA1c levels among study participants. The majority of patients, 71 (47.3%), had HbA1c values above 7.0%, while 58 (38.7%) had HbA1c levels $\leq 6.5\%$. Only 21 (14.0%) patients had HbA1c values between 6.5% and 7.0%, indicating that a substantial proportion of hospitalized COVID-19 patients had poor long-term glycemic control.

Table 3 shows the distribution of diabetes mellitus among study participants. Diabetes mellitus was present in 64 (42.7%) patients, whereas 86 (57.3%) patients had no previous diagnosis of diabetes. The high prevalence of diabetes among hospitalized COVID-19 patients highlights the importance of metabolic status in determining disease progression and outcomes.

Table 4 demonstrates the distribution of HbA1c categories among diabetic and non-diabetic patients. Among diabetic patients, 52 (81.3%) had HbA1c levels above 7.0%, whereas only 19 (22.1%) non-diabetic patients had HbA1c values above 7.0%. This finding confirms significantly poorer glycemic control among diabetic individuals admitted with COVID-19 infection.

Table 5 presents the distribution of study participants according to sex. Males constituted 102 (68.0%) patients, while females accounted for 48 (32.0%). The predominance of males among hospitalized COVID-19 patients is consistent with observations from several previous studies.

Table 6 demonstrates the relationship between HbA1c levels and inflammatory markers. Patients with HbA1c >7.0% exhibited higher frequencies of elevated total leukocyte count, CRP, D-dimer, and ferritin compared to patients with HbA1c ≤6.5%. Elevated inflammatory markers were observed in 84.5% of patients with HbA1c >7.0%, suggesting a significant relationship between chronic hyperglycemia and systemic inflammation.

Table 7 shows the requirement for ventilatory support among study participants. A total of 102 (68.0%) patients required no ventilatory support, 12 (8.0%) patients required non-invasive ventilation, and 36 (24.0%) patients required invasive mechanical ventilation. The requirement for ventilatory support was significantly higher among patients with elevated HbA1c levels.

Table 8 demonstrates the association between admission HbA1c levels and clinical outcomes. Recovery without ventilatory support was observed more frequently among patients with HbA1c ≤6.5%, whereas mechanical ventilation and mortality were more common among patients with HbA1c >7.0%. These findings support the role of admission HbA1c as a useful prognostic marker in hospitalized COVID-19 patients.

Table 1. Overall outcomes according to admission HbA1c levels

Parameters	Categories	N	HbA1c ≤6.5% n (%)	HbA1c >7.0% n (%)	Chi-square	P value
Sex	Female	48	18 (40.9)	30 (28.3)	2.214	0.137
	Male	102	26 (59.1)	76 (71.7)		
TLC (/mm ³)	<4000	16	9 (20.5)	7 (6.6)	8.934	0.003
	4000–11000	97	31 (70.5)	66 (62.3)		
	>11000	37	4 (9.0)	33 (31.1)		
CRP (mg/L)	<25	42	20 (45.5)	22 (20.8)	10.221	0.001
	>25	108	24 (54.5)	84 (79.2)		
D-dimer (ng/ml)	<900	68	28 (63.6)	40 (37.7)	9.675	0.002
	>900	82	16 (36.4)	66 (62.3)		
Ferritin (ng/ml)	<350	63	24 (54.5)	39 (36.8)	4.017	0.045
	>350	87	20 (45.5)	67 (63.2)		
DM	Absent	86	37 (84.1)	49 (46.2)	22.316	<0.001
	Present	64	7 (15.9)	57 (53.8)		
IHD	Absent	121	40 (90.9)	81 (76.4)	4.652	0.031
	Present	29	4 (9.1)	25 (23.6)		
Ventilatory support	No	102	36 (81.8)	66 (62.3)	7.881	0.005
	Yes	48	8 (18.2)	40 (37.7)		
Mortality	No	116	38 (86.4)	78 (73.6)	4.156	0.041
	Yes	34	6 (13.6)	28 (26.4)		

Table 2. Distribution of HbA1c levels among study participants

HbA1c Category (%)	Number of Patients	Percentage
≤6.5	58	38.7
6.5–7.0	21	14.0
>7.0	71	47.3
Total	150	100

Table 3. Distribution of diabetes mellitus among study participants

Diabetes Mellitus	Number of Patients	Percentage
Absent	86	57.3
Present	64	42.7
Total	150	100

Table 4. Distribution of HbA1c categories among diabetic and non-diabetic patients

HbA1c Category (%)	Diabetic Patients	Non-Diabetic Patients	Total
≤6.5	5	53	58
6.5–7.0	7	14	21
>7.0	52	19	71
Total	64	86	150

Table 5. Distribution according to sex

Sex	Number of Patients	Percentage
Male	102	68.0
Female	48	32.0
Total	150	100

Table 6. HbA1c levels and inflammatory markers

Marker	Category	HbA1c ≤6.5%	HbA1c >7.0%
TLC	>11000/mm ³	4	33
CRP	>25 mg/L	24	84
D-dimer	>900 ng/ml	16	66
Ferritin	>350 ng/ml	20	67

Table 7. Requirement of ventilatory support

Ventilatory Support	Number of Patients	Percentage
No Support	102	68.0
NIV	12	8.0
Mechanical Ventilation	36	24.0
Total	150	100

Table 8. Association of HbA1c with clinical outcome

Outcome	HbA1c ≤6.5%	HbA1c >7.0%
Recovery without ventilatory support	36	66
NIV requirement	2	10
Mechanical ventilation	6	30
Survived	38	78
Died	6	28

DISCUSSION

The present prospective observational study evaluated the prognostic significance of admission HbA1c levels in 150 patients admitted with COVID-19 infection. The findings demonstrated that elevated HbA1c levels were significantly associated with adverse clinical outcomes, increased inflammatory markers, greater need for ventilatory support, and higher mortality. Among the study population, 71 (47.3%) patients had HbA1c levels above 7.0%, indicating poor pre-existing glycemic control. Mortality was observed in 28 (26.4%) patients with HbA1c >7.0% compared with only 6 (13.6%) patients with HbA1c ≤6.5%, suggesting a substantial increase in risk among patients with elevated HbA1c levels.

In the present study, elevated HbA1c levels were significantly associated with increased inflammatory markers including CRP, D-dimer, ferritin, and total leukocyte count. Patients with HbA1c >7.0% showed a markedly higher prevalence of elevated inflammatory markers compared to patients with lower HbA1c levels. These findings are supported by the study conducted by Wang et al., who reported that elevated glycated hemoglobin levels were associated with increased systemic inflammation, hypercoagulability, and poor clinical outcomes in COVID-19 patients [11]. Chronic hyperglycemia promotes endothelial dysfunction, oxidative stress, and excessive cytokine release, thereby contributing to the exaggerated inflammatory response observed in severe COVID-19 infection.

The present study demonstrated that patients with elevated HbA1c levels required greater respiratory support during hospitalization. Ventilatory support was required in 40 (37.7%) patients with HbA1c >7.0% compared with only 8 (18.2%) patients with HbA1c ≤6.5%. These findings suggest that poor glycemic control before infection may predispose patients to severe pulmonary involvement and respiratory compromise. Fadini et al. reported that diabetes and impaired glucose metabolism significantly increase the risk of severe COVID-19 infection and unfavorable outcomes due to immune

dysregulation and enhanced inflammatory activity [12]. Hyperglycemia has been shown to impair neutrophil function, reduce antiviral immunity, and facilitate viral replication, thereby worsening disease severity.

A significant relationship was also observed between elevated HbA1c levels and mortality. Patients with HbA1c >7.0% experienced nearly twice the mortality rate compared to those with HbA1c ≤6.5%. Similar findings were reported by Wang et al., who demonstrated that elevated glycated hemoglobin levels were associated with poor prognosis and increased mortality in hospitalized COVID-19 patients [13]. The authors suggested that chronic hyperglycemia contributes to endothelial injury, thrombotic complications, and exaggerated inflammatory responses, all of which are recognized predictors of mortality in COVID-19.

The association between elevated HbA1c levels and adverse outcomes observed in the present study is further supported by the findings of Chen et al., who reported that COVID-19 patients with higher HbA1c levels had greater disease severity, increased intensive care unit admission rates, and poorer clinical outcomes compared to patients with better glycemic control [14]. The investigators emphasized that HbA1c provides valuable information regarding long-term metabolic status and may serve as a useful predictor of disease progression independent of acute blood glucose levels. Similar observations were noted in the present study, where patients with higher HbA1c levels demonstrated increased frequencies of elevated inflammatory markers, ventilatory support, and mortality.

The present study also demonstrated a strong association between diabetes mellitus and elevated HbA1c levels. Among 64 diabetic patients, the majority had HbA1c levels above 7.0%, reflecting poor glycemic control prior to hospitalization. Li et al. reported that newly diagnosed diabetes and uncontrolled glycemia were associated with significantly higher mortality rates among hospitalized COVID-19 patients compared with individuals without diabetes [15]. The authors suggested that chronic metabolic dysfunction may amplify the inflammatory and thrombotic pathways involved in COVID-19 pathogenesis, resulting in worse clinical outcomes.

Several biological mechanisms may explain the relationship between elevated HbA1c levels and adverse COVID-19 outcomes. Chronic hyperglycemia impairs innate and adaptive immune responses, increases oxidative stress, promotes endothelial dysfunction, and activates inflammatory pathways. Elevated HbA1c levels are associated with increased expression of pro-inflammatory cytokines, impaired neutrophil function, and a hypercoagulable state, all of which contribute to severe disease manifestations. Furthermore, glycation of proteins may alter immune cell function and reduce the body's ability to effectively control viral infection.

The findings of the present study suggest that admission HbA1c is a valuable prognostic marker in patients hospitalized with COVID-19 infection. Measurement of HbA1c at admission is simple, inexpensive, and widely available. It provides information regarding long-term glycemic control and may help clinicians identify high-risk patients who require closer monitoring and aggressive therapeutic interventions. Early identification of patients at increased risk of severe disease may facilitate timely management and improve clinical outcomes.

The present study has certain limitations. Being a single-center observational study, causal relationships cannot be definitively established. Factors such as obesity, duration of diabetes, prior antidiabetic treatment, and socioeconomic variables were not fully assessed. Nevertheless, the study provides important evidence supporting the prognostic value of admission HbA1c levels in COVID-19 patients and highlights the importance of metabolic control in influencing disease outcomes.

CONCLUSION

The present study concluded that elevated admission HbA1c levels were significantly associated with adverse outcomes in patients admitted with COVID-19 infection. Patients with HbA1c levels above 7.0% demonstrated higher inflammatory marker levels, increased requirement for ventilatory support, and greater mortality compared with patients having HbA1c levels ≤6.5%.

Elevated HbA1c was also significantly associated with diabetes mellitus, ischemic heart disease, and markers of severe disease. These findings suggest that admission HbA1c may serve as an effective prognostic marker for risk stratification and outcome prediction in hospitalized COVID-19 patients. Routine assessment of HbA1c at admission may assist clinicians in identifying high-risk individuals and optimizing clinical management strategies.

Conflict of interest: No! Conflict of interest is found elsewhere considering this work.

Source of Funding: There was no financial support concerning this work.

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