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General Medicine

PROGNOSTIC SIGNIFICANCE OF GLYCATED HEMOGLOBIN(HbA1c) IN DIABETIC PATIENTS WITH SEPSIS

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ABSTRACT **Background:** Sepsis in patients with diabetes mellitus is associated with increased morbidity and mortality due to impaired immune response and poor glycemic control. Glycated hemoglobin (HbA1c) reflects long-term glycemic status and may serve as a potential prognostic marker in septic patients with diabetes.**Objectives:** To evaluate the role of HbA1c as a prognostic factor in diabetic patients with sepsis and to assess its association with severity of illness, ICU admission, and mortality. **Methods:** This was a hospital-based observational study conducted among 100 diabetic patients diagnosed with sepsis. Demographic data, clinical parameters, laboratory investigations, HbA1c levels, and severity scores (GCS and SOFA) were recorded. Patients were followed for clinical outcomes including ICU admission and 30-day mortality. Statistical analysis was performed to assess correlations and associations between HbA1c and clinical outcomes.**Results:** The majority of patients were aged 51–60 years (24%), with a female predominance (61%). Most patients had a diabetes duration of 1–5 years (28%), with a mean duration of 8.91 ± 7.27 years. The mean HbA1c was 9.63 ± 2.03%, with 44% of patients having poor glycemic control (≥9%). Most patients had mild organ dysfunction (58%) with a mean SOFA score of 5.36 ± 3.16. ICU admission was required in 58% of patients, and the 30-day mortality rate was 16%. HbA1c showed a significant negative correlation with GCS ($r = -0.240$, $p = 0.016$) and a non-significant positive correlation with SOFA score ($r = 0.182$, $p = 0.070$). Mean HbA1c was significantly higher in non-survivors (10.66 ± 2.09%) compared to survivors (9.13 ± 2.12%) ($p = 0.009$), while no significant association was found with ICU admission ($p = 0.164$). **Conclusion:** HbA1c is a modest but significant prognostic marker in diabetic patients with sepsis, particularly in predicting mortality. Higher HbA1c levels are associated with poorer neurological status and increased risk of death. However, its role in predicting disease severity and ICU admission is limited. Optimizing long-term glycemic control may improve outcomes in this high-risk population.

KEYWORDS : HbA1c, Sepsis, Diabetes Mellitus, Prognosis, SOFA Score, Mortality, Glycemic Control, ICU Admission

INTRODUCTION

Sepsis is defined as a life-threatening organ dysfunction caused by a dysregulated host response to infection and remains one of the leading causes of morbidity and mortality among critically ill patients.[1] The systemic inflammatory response associated with sepsis profoundly alters metabolic and endocrine regulation, particularly glucose homeostasis. During sepsis, fluctuations in insulin, cortisol, and inflammatory cytokines contribute to stress hyperglycemia, insulin resistance, and impaired glucose utilization.[2] In addition to hyperglycemia, hypoglycemia may also occur in severe sepsis and is considered an indicator of advanced metabolic dysfunction and poor prognosis. Pro-inflammatory cytokines such as tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6) further contribute to glycemic instability by affecting hepatic glucose production and peripheral glucose uptake.[3]

Several scoring systems including the Sequential Organ Failure Assessment (SOFA), Simplified Acute Physiology Score (SAPS), and Acute Physiology and Chronic Health Evaluation (APACHE II) have been developed to assess severity and predict outcomes in critically ill patients. Among these, APACHE II is widely used because of its prognostic accuracy in patients with sepsis.[4–7]

Diabetes mellitus is an important comorbidity influencing the clinical course and outcomes of sepsis. Chronic hyperglycemia impairs immune function through defects in neutrophil chemotaxis, phagocytosis, intracellular killing, opsonization, and cell-mediated immunity, thereby increasing susceptibility to infections.[8–15] Poor glycemic control has been associated with increased severity of infection, prolonged hospitalization, organ dysfunction, and higher mortality among septic patients.

Glycated hemoglobin (HbA1c) reflects the average blood glucose level over the preceding 2–3 months and serves as a reliable marker of long-term glycemic control.[16] Both the American Diabetes Association and the World Health Organization recommend HbA1c for diagnosis and monitoring of diabetes mellitus.[17] [18] Recent studies have highlighted the prognostic significance of HbA1c in patients with sepsis. Elevated HbA1c levels have been associated with increased mortality, organ dysfunction, inflammatory marker elevation, and worse clinical outcomes in diabetic patients with sepsis.[19–23] In contrast, some studies suggest that diabetes alone may not independently increase mortality, but poor chronic glycemic control contributes substantially to adverse outcomes.[24]

Recent evidence has also demonstrated a complex relationship between HbA1c and sepsis outcomes. Balintescu et al.[25] reported a U-shaped association between HbA1c levels and sepsis risk, suggesting that both poor glycemic control and excessively strict glycemic control may increase susceptibility to infection and mortality.

Considering the increasing burden of diabetes mellitus and the high mortality associated with sepsis, assessment of HbA1c may provide valuable prognostic information in diabetic patients presenting with sepsis. Therefore, the present study was undertaken to evaluate the prognostic significance of HbA1c in patients with type 2 diabetes mellitus admitted with sepsis and to assess its relationship with mortality, length of hospital stay, blood glucose levels, inflammatory markers, and severity scores. The aims of the study were to evaluate the predictive value of HbA1c for hospital mortality and length of hospital stay in diabetic patients admitted with sepsis, and to study the correlation of HbA1c with admission blood sugar, C-reactive protein (CRP), SOFA score, and its efficacy as a prognostic marker in sepsis.

MATERIALS AND METHODS

This hospital-based prospective study was conducted in the Department of General Medicine at Al-Ameen Medical College and Hospital over a period of 18 months. A total of 100 adult patients with type 2 diabetes mellitus admitted with sepsis were included in the study.

Adult patients aged more than 18 years with previously diagnosed or newly detected type 2 diabetes mellitus and fulfilling the Sepsis-3 criteria for sepsis were included. Patients with chronic kidney disease, end-stage malignancy, immunosuppressive therapy, decompensated liver disease, moderate to severe anemia, recent surgery, trauma, burns, or pregnancy were excluded from the study.

Convenience sampling was used to recruit eligible patients admitted to the medical wards and intensive care unit during the study period. After obtaining approval from the Institutional Ethics Committee and written informed consent, all enrolled patients underwent detailed clinical evaluation including history of diabetes, comorbidities, medication use, and presenting symptoms. General physical examination and systemic examination were performed for all patients.

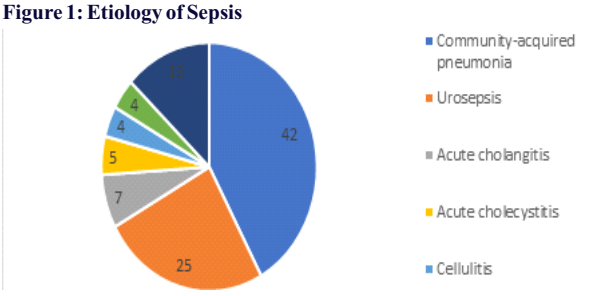
Baseline investigations included complete blood count, liver and renal function tests, serum electrolytes, urine analysis, fasting and random blood glucose levels, coagulation profile, and inflammatory markers including C-reactive protein (CRP). Glycated hemoglobin (HbA1c) was measured to assess long-term glycemic control. Additional investigations such as chest radiography, electrocardiography, and ultrasonography were performed when clinically indicated. Severity of illness was assessed at admission using the Acute Physiology and Chronic Health Evaluation II (APACHE II) score and Sequential Organ Failure Assessment (SOFA) score. Patients were monitored throughout hospitalization and followed up for 30 days after admission. The primary outcomes assessed were hospital mortality and length of hospital stay. Secondary outcomes included correlation of HbA1c with admission blood glucose levels, CRP, APACHE II score, and SOFA score to evaluate its prognostic significance in sepsis. Statistical analysis was performed using SPSS version 25.0 and Epi Info software. Continuous variables were expressed as mean ± standard deviation, while categorical variables were presented as frequencies and percentages. Independent sample t-test or Mann–Whitney U test was used for comparison of continuous variables, and Chi-square test or Fisher's exact test for categorical variables. Pearson or Spearman correlation analysis was performed to assess the relationship between HbA1c and prognostic markers. A p-value <0.05 was considered statistically significant.

RESULTS

A total of 100 patients with type 2 diabetes mellitus admitted with sepsis were included in the study. The majority of patients belonged to the 51–60 years age group (24%), followed by 41–50 years (22%), indicating that sepsis was more common among middle-aged and elderly individuals. Females constituted 61% of the study population, while males accounted for 39%.

Community-acquired pneumonia was the most common source of sepsis (42%), followed by urosepsis (25%). Other etiologies included acute cholangitis (7%), acute cholecystitis (5%), cellulitis (4%), gluteal abscess (4%), CAP with ARDS (3%), necrotising fasciitis (2%), necrotising pancreatitis (2%), pyogenic liver abscess (2%), diabetic foot infection (1%), perianal abscess (1%), peritonitis (1%), and secondary bacterial peritonitis (1%).

Figure 1: Etiology of Sepsis



According to the WHO South-East Asia BMI classification, 40% of patients had normal BMI, while 31% were overweight and 26% were obese. Only 3% of participants were underweight. The duration of diabetes mellitus ranged widely among participants, with the majority having diabetes for 1–5 years (28%) or 6–10 years (25%). The mean duration of diabetes was 8.91 ± 7.27 years.

Table 1. Baseline Demographic and Clinical Characteristics of Study Participants (n = 100)

Variable	Frequency (n)	Percentage (%)
Age Group (years)		
≤30	7	7.0
31–40	14	14.0
41–50	22	22.0
51–60	24	24.0
61–70	14	14.0
71–80	14	14.0
>80	5	5.0
Gender		
Male	39	39.0
Female	61	61.0
BMI Classification		
Underweight	3	3.0
Normal	40	40.0
Overweight	31	31.0
Obese Class I	24	24.0
Obese Class II	2	2.0
Duration of Diabetes		
Newly diagnosed	18	18.0
1–5 years	28	28.0
6–10 years	25	25.0
11–15 years	15	15.0
>15 years	14	14.0

Assessment of glycemic control revealed poor long-term diabetic control in most patients. More than half of the participants (55%) had HbA1c values between 7–8.9%, while 44% had HbA1c ≥9%. The mean HbA1c level was 9.63 ± 2.03%.

Table 2. Clinical Severity Profile of Sepsis (n = 100)

Variable	Frequency (n)	Percentage (%)
GCS Category		
Severe (≤8)	13	13.0
Moderate (9–12)	9	9.0
Mild/Normal (13–15)	78	78.0
SOFA Score Category		
Mild dysfunction (2–4)	58	58.0
Severe dysfunction (≥9)	16	16.0
MAP/Vasopressor Requirement		
No hypotension	29	29.0
MAP <70 mmHg	48	48.0
Dopamine <5 or dobutamine	11	11.0
Dopamine 5–15 or epinephrine <0.1	10	10.0
Dopamine >15 or epinephrine >0.1	2	2.0

Baseline laboratory investigations demonstrated evidence of systemic inflammation and organ dysfunction. The mean WBC count was markedly elevated (18,636.92 ± 4,159.04/µL). Mean serum creatinine was 1.77 ± 0.57 mg/dL, indicating mild renal dysfunction. Liver enzymes were elevated with mean ALT and AST values of 72.94 ± 37.48 U/L and 82.75 ± 38.79 U/L respectively. Mean platelet count was 181,600 ± 72,526/µL, while the average PaO_2/FiO_2 ratio was 367.94 ± 62.88.

Table 3. Glycemic Status and Baseline Laboratory Parameters (n = 100)

Parameter	Mean ± SD
HbA1c (%)	9.63 ± 2.03
Duration of diabetes (years)	8.91 ± 7.27
PaO_2/FiO_2 ratio	367.94 ± 62.88
Hemoglobin (g/dL)	12.65 ± 1.20
WBC count (/µL)	18,636.92 ± 4,159.04
Serum creatinine (mg/dL)	1.77 ± 0.57
ALT (U/L)	72.94 ± 37.48
AST (U/L)	82.75 ± 38.79
Total bilirubin (mg/dL)	1.47 ± 0.51
Platelet count (/µL)	181,600 ± 72,526
Potassium (mEq/L)	4.20 ± 0.58
Mean GCS score	13.09 ± 2.56
Mean SOFA score	5.36 ± 3.16
Mean hospital stay (days)	7.36 ± 3.19

Hemodynamic assessment showed that only 29% of patients maintained normal blood pressure without hypotension. Nearly half of the patients (48%) had MAP <70 mmHg, while the remainder required

varying degrees of vasopressor support, reflecting different severities of septic shock.

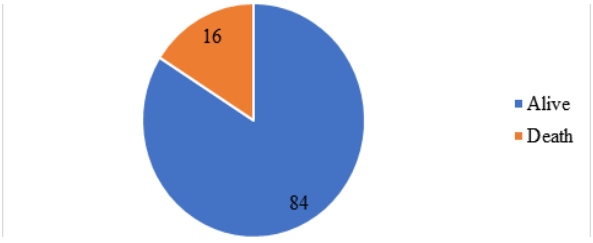
Neurological evaluation using the Glasgow Coma Scale showed that 78% of patients had mild or normal neurological status (GCS 13–15), whereas 13% had severe neurological impairment (GCS ≤8). The mean GCS score was 13.09 ± 2.56.

Assessment of organ dysfunction using the SOFA score revealed that 58% of patients had mild organ dysfunction (SOFA 2–4), 26% had moderate dysfunction (SOFA 5–8), and 16% had severe organ dysfunction (SOFA ≥9). The mean SOFA score was 5.36 ± 3.16.

The mean duration of hospital stay was 7.36 ± 3.19 days. Most patients (44%) had hospital stays of 5–7 days, whereas 37% required hospitalization for more than 7 days. ICU admission was required in 58% of patients, indicating a high burden of severe illness.

The overall 30-day mortality rate was 16%, while 84% of patients survived during follow-up.

Figure 2: 30-Day Mortality (n = 100)



Correlation analysis demonstrated a significant negative correlation between HbA1c and GCS score (r = -0.240, p = 0.016), suggesting that poorer long-term glycemic control was associated with worse neurological status. HbA1c showed a positive correlation with SOFA score (r = 0.182), although this association did not reach statistical significance (p = 0.070).

Comparison between survivors and non-survivors demonstrated significantly higher CRP levels among non-survivors (395.50 ± 52.54 mg/L vs 97.55 ± 22.94 mg/L, p <0.001), indicating severe systemic inflammation in fatal cases. Admission blood glucose levels were similar between the two groups and showed no statistically significant difference (p = 0.950).

Non-survivors had significantly higher SOFA scores compared to survivors (12.25 ± 1.34 vs 4.24 ± 1.37, p <0.001), confirming that organ dysfunction was strongly associated with mortality.

Hematological parameters revealed significantly higher WBC counts (21,380 ± 4,450/µL vs 18,114 ± 3,915/µL, p = 0.030) and significantly lower platelet counts (112,188 ± 64,164/µL vs 194,821 ± 66,516/µL, p = 0.002) among non-survivors. Hemoglobin levels were comparable between groups.

Renal dysfunction was significantly more severe among non-survivors, with mean creatinine levels of 2.53 ± 0.85 mg/dL compared to 1.63 ± 0.34 mg/dL among survivors (p = 0.001).

Similarly, liver function abnormalities were significantly greater among non-survivors. Mean ALT, AST, and bilirubin levels were all significantly elevated in patients who died compared to survivors (p <0.01 for all comparisons), indicating substantial hepatic involvement in severe sepsis.

Potassium levels did not differ significantly between survivors and non-survivors (p = 0.780).

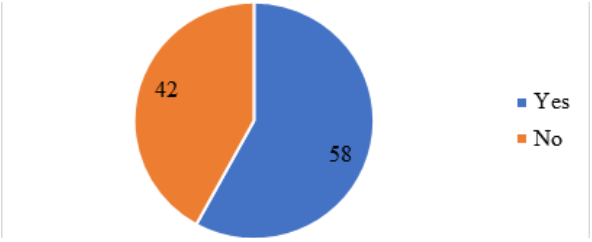
Table 4. Comparison of Clinical and Laboratory Parameters Between Survivors and Non-Survivors

Parameter	Alive (Mean ± SD)	Death (Mean ± SD)	p-value
HbA1c (%)	9.13 ± 2.12	10.66 ± 2.09	0.009*
CRP (mg/L)	97.55 ± 22.94	395.50 ± 52.54	<0.001*
Admission blood sugar (mg/dL)	253.73 ± 89.63	252.81 ± 84.16	0.950
SOFA score	4.24 ± 1.37	12.25 ± 1.34	<0.001*
Hemoglobin (g/dL)	12.69 ± 1.18	12.41 ± 1.30	0.420
WBC count (/µL)	18,114 ± 3,915	21,380 ± 4,450	0.030*
Platelets (/µL)	194,821 ± 66,516	112,188 ± 64,164	0.002*
Creatinine (mg/dL)	1.63 ± 0.34	2.53 ± 0.85	0.001*
ALT (U/L)	65.77 ± 28.86	110.56 ± 53.54	0.004*
AST (U/L)	75.85 ± 32.78	119.00 ± 48.12	0.003*
Total bilirubin (mg/dL)	1.33 ± 0.35	2.21 ± 0.59	0.001*
Potassium (mEq/L)	4.20 ± 0.60	4.24 ± 0.47	0.780

*Statistically significant (p <0.05)

The relationship between HbA1c and ICU admission showed that patients requiring ICU care had slightly higher HbA1c levels (9.63 ± 2.26%) compared to those not admitted to ICU (9.02 ± 2.02%), although the difference was not statistically significant (p = 0.164).

Figure 3: ICU Admission (n = 100)



In contrast, HbA1c showed a significant association with mortality. Patients who died had significantly higher mean HbA1c levels compared to survivors (10.66 ± 2.09% vs 9.13 ± 2.12%, p = 0.009), suggesting that poor long-term glycemic control was associated with increased mortality among septic diabetic patients.

Figure 4: Comparison of HbA1c Levels According to ICU Admission (n = 100)

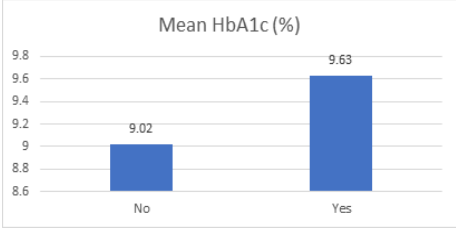


Figure 5: Comparison of HbA1c Levels with 30-Day Mortality (n = 100)

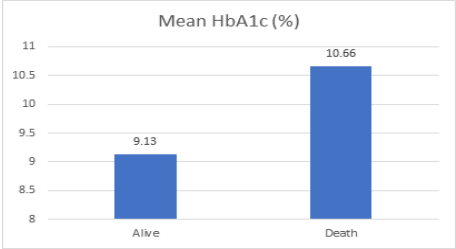


Table 5. Correlation of HbA1c with Prognostic Parameters

Variable	Result	p-value
Correlation of HbA1c with GCS	r = -0.240	0.016*
Correlation of HbA1c with SOFA	r = 0.182	0.070

DISCUSSION

Sepsis remains a major cause of morbidity and mortality worldwide, particularly among patients with type 2 diabetes mellitus (T2DM), where chronic hyperglycemia, impaired immune function, and endothelial dysfunction contribute to increased susceptibility and worse outcomes. HbA1c, a marker of long-term glycemic control, has emerged as a potential prognostic indicator in septic patients, reflecting chronic metabolic status and immune dysregulation. The present study evaluated the prognostic significance of HbA1c in diabetic patients with sepsis and compared the findings with existing literature.

Demographic Profile

In the present study, the majority of patients belonged to the 51–60 years age group (24%), followed by 41–50 years (22%), indicating that sepsis predominantly affected middle-aged and elderly diabetic individuals. A female predominance was observed (61%), whereas males constituted 39% of the study population. These findings are consistent with previous studies reporting higher prevalence of sepsis among older adults. Panduranga G et al[21], Juhász I et al[26], Anandakumar S et al[27], and Haji IM et al[28] all demonstrated that septic diabetic patients were predominantly elderly. Similarly, Lee YS et al[29] reported a median age of 77 years, highlighting advanced age as an important risk factor for severe sepsis. However, unlike most earlier studies demonstrating male predominance, our study showed female predominance. Studies by Panduranga G et al[21], Guo F et al[30], and Prasanta Dihingia et al[31] reported male predominance ranging between 54% and 70%. A comparable female predominance was reported only by Kaman GK et al[32].

Diabetes Characteristics and HbA1c Profile

The mean duration of diabetes in our study was 8.91 ± 7.27 years, with most patients having diabetes duration between 1–5 years (28%) and 6–10 years (25%). Similar observations were reported by Anandakumar S et al[27], who demonstrated a mean diabetes duration of 10.2 ± 3.75 years. The present study demonstrated poor long-term glycemic control, with a mean HbA1c of 9.63 ± 2.03%. More than half of the patients (55%) had HbA1c between 7–8.9%, while 44% had HbA1c ≥9%. These findings indicate substantially poorer glycemic control compared with many previous studies. Anandakumar S et al[27] reported a lower mean HbA1c of 8.13 ± 2.25%, while Juhász I et al[26] observed mean HbA1c values around 7.3–7.5%. Prasanta Dihingia et al[31] reported a mean HbA1c of 8.3% and demonstrated that patients with HbA1c <7% had fewer complications. Similarly, Kaman GK et al[32] reported a median HbA1c of 9.03%, which closely resembles our findings. Lee YS et al[29] also demonstrated significantly higher HbA1c levels in severe sepsis compared to non-severe cases, supporting the association between chronic hyperglycemia and adverse outcomes. Overall, our findings reinforce the importance of poor glycemic control as a contributor to increased susceptibility and severity of sepsis.

Severity of Illness

In the present study, the mean SOFA score was 5.36 ± 3.16, with 58% of patients having mild organ dysfunction, 26% moderate dysfunction, and 16% severe dysfunction. This suggests that most patients presented with mild-to-moderate disease severity. Comparable findings were reported by Panduranga G et al[21], where most patients had low SOFA scores. However, they demonstrated significantly higher mortality with increasing SOFA scores (p = 0.001). Studies by Lee YS et al[29] and Mahmoodpoor A et al[34] reported higher mean SOFA scores around 9–9.7, indicating more critically ill populations. Haji IM et al[28] similarly reported markedly elevated SOFA scores among non-survivors. Kumar DS et al[33] demonstrated significantly higher SOFA scores among patients with elevated HbA1c levels, further supporting the relationship between poor glycemic control and greater organ dysfunction.

Clinical Outcomes

In our study, 58% of patients required ICU admission and the overall 30-day mortality rate was 16%. These findings indicate a considerable burden of severe illness, although mortality was lower than in several previous studies. Panduranga G et al[21] and Haji IM et al[28] reported mortality rates around 33%, whereas Lee YS et al[29] reported ICU mortality approaching 48% in patients with progressive organ dysfunction. Kaman GK et al[32] also demonstrated higher complication rates including shock, acute kidney injury, ARDS, and multiorgan dysfunction. In contrast, Mahmoodpoor A et al[34] reported lower ICU mortality (9.2%), suggesting variability in outcomes depending on disease severity and management protocols. The mean duration of hospital stay in our study (7.36 ± 3.19 days) was comparable to that reported by Kaman GK et al[32].

Correlation of HbA1c with Severity

A significant negative correlation was observed between HbA1c and GCS score (r = -0.240, p = 0.016), indicating that higher HbA1c levels were associated with poorer neurological status at presentation. HbA1c also showed a positive correlation with SOFA score, although this did not achieve statistical significance. These findings partially align with existing literature. Lee YS et al[29] reported that elevated HbA1c independently predicted progression of organ dysfunction. Similarly, Balintescu A et al[25] demonstrated increased sepsis risk among patients with HbA1c >9.7%. However, Juhász I et al[26] reported no consistent relationship between HbA1c and severity indices, which is comparable to our finding of a non-significant correlation with SOFA score.

HbA1c and Clinical Outcomes

In our study, mean HbA1c levels were significantly higher among non-survivors than survivors (10.66 ± 2.09% vs 9.13 ± 2.12%, p = 0.009), demonstrating that poor long-term glycemic control was associated with increased mortality. However, HbA1c did not significantly predict ICU admission. These observations are consistent with previous literature. Guo F et al30 demonstrated significantly higher 30-day mortality among patients with elevated HbA1c, while Lee YS et al[29] identified HbA1c ≥6.5% as an independent predictor of ICU mortality. Haji IM et al[28] and Mahmoodpoor A et al[34] also reported significantly higher HbA1c levels among non-survivors. Kumar DS et al[33] similarly demonstrated increased ICU and 28-day mortality among patients with elevated HbA1c. Lupu L et al[23] reported increased crude mortality with higher HbA1c states, although HbA1c did not remain independently predictive after multivariate adjustment. Overall, the findings of the present study support the growing evidence that elevated HbA1c is associated with worse outcomes in septic diabetic patients, particularly increased mortality. Chronic glycemic control therefore appears to play an important role in influencing prognosis during sepsis.

CONCLUSION

The present study demonstrates that elevated HbA1c levels are associated with increased mortality and poorer neurological status in diabetic patients with sepsis, highlighting the prognostic significance of poor long-term glycemic control. Higher SOFA scores, inflammatory markers, and organ dysfunction were also strongly associated with adverse outcomes. These findings suggest that HbA1c may serve as a useful adjunctive marker for early risk stratification and prognostic assessment in septic diabetic patients. Further large-scale multicentric studies are required to validate these findings.

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