Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/q9q7gs26

STUDY ON THE ROLE OF HBA1C AS A PROGNOSTIC FACTOR IN TYPE 2 DIABETES PATIENTS WITH SEPSIS

Dr. Lavanya Kumaresan[1*], Dr. Diana Gunasekaran[2], Dr. Aishwarya Duraisingam[3]

[1*]Specialist and HOD, Department of General Medicine, ESIC Hospital, Tirunelveli, Ministry of Labour and Employment, Government of India, Tamil Nadu, India.
[2]Junior Resident, Department of General Medicine, Government Pudukkottai Medical College and Hospital, Pudukkottai, Tamil Nadu, India.
[3]Assistant Professor, Department of General Medicine, Tagore Medical College Hospital, Chennai, Tamil Nadu, India.

***Corresponding Author:** Dr. Lavanya Kumaresan
*Specialist and HOD, Department of General Medicine, ESIC Hospital, Tirunelveli, Ministry of Labour and Employment, Government of India, Tamil Nadu, India.

ABSTRACT

Background: Diabetes mellitus, particularly type 2, is associated with increased susceptibility to infections and poor outcomes in septic states due to impaired immune responses and organ dysfunction. HbA1c, reflecting long-term glycemic control, may offer prognostic insights in such patients. This study evaluates the utility of HbA1c as a predictor of mortality and hospital outcomes in type 2 diabetic patients admitted with sepsis.

Methods: This observational study was conducted at Madras Medical College and Rajiv Gandhi Government General Hospital over six months, including 100 type 2 diabetes mellitus patients with sepsis. Patients were evaluated using clinical examination and laboratory parameters, including HbA1c, CRP, blood glucose, APACHE II, and SOFA scores. Exclusion criteria included chronic kidney disease, type 1 diabetes, anemia, pregnancy, and immunosuppressive states. The primary outcome was 30-day mortality. Data analysis was performed using SPSS and Epi Info.

Results: The 30-day mortality rate was 29%. Mean HbA1c in non-survivors (10.55%) was significantly higher than in survivors (7.64%) ($p < 0.001$). Mortality was 93% in patients with HbA1c >9%. APACHE II, SOFA scores, CRP, leukocyte count, and vital parameters (heart rate, respiratory rate, temperature, and blood pressure) significantly correlated with mortality. Admission blood glucose, serum sodium, potassium, bicarbonate, bilirubin, and platelet count did not show significant correlation with mortality.

Conclusion: HbA1c is a significant independent predictor of mortality in type 2 diabetes patients with sepsis, comparable in efficacy to APACHE II and SOFA scores. Chronic glycemic control plays a critical role in sepsis outcomes. HbA1c can aid in early identification of high-risk patients, allowing for prompt intervention and improved prognostication.

Keywords: HbA1c, Type 2 Diabetes Mellitus, Sepsis, Prognostic Marker, APACHE II, SOFA Score, Mortality, Glycemic Control.

INTRODUCTION

Diabetes mellitus is a heterogeneous group of metabolic disorders characterized by chronic hyperglycemia, resulting from defects in insulin secretion, insulin action, or both. This persistent elevation in blood glucose levels is associated with disturbances in the metabolism of carbohydrates, fats, and proteins.[1,2] Over time, the chronic metabolic imbalance leads to progressive damage, dysfunction, and failure of various organ systems, particularly the kidneys, eyes, peripheral nerves, blood vessels, and the cardiovascular system.[2]

It is a well-documented clinical observation that individuals with diabetes are more prone to infections, which tend to be more frequent and severe than in the general population. The increased susceptibility to infections is multifactorial, primarily attributed to the presence of diabetic complications such as micro- and macrovascular disease and a compromised immune system. Key contributors to the impaired host defense include reduced neutrophil function, altered cytokine production, and diminished cell-mediated immunity, all of which impair the body's ability to localize and control infections effectively.[1,3,4].

In acutely ill patients, such as those hospitalized with sepsis, plasma glucose levels are often elevated due to stress-induced hyperglycemia, variations in drug therapy, and fluctuations related to meal timing or fasting. These acute changes can make it difficult to assess a patient's underlying glycemic control. In contrast, HbA1c (Glycated Hemoglobin**)** provides a more stable and reliable measure, reflecting the average blood glucose concentration over the preceding 8 to 12 weeks. HbA1c is produced via a non-enzymatic reaction between glucose and hemoglobin and is less influenced by short-term physiological variations.[1,2]

Recent evidence suggests that HbA1c may have prognostic significance in patients with type 2 diabetes who develop sepsis. A few studies have shown that elevated HbA1c levels are associated with increased mortality in this patient population[1]. This raises the possibility that long-term glycemic control, as indicated by HbA1c, may influence outcomes in critically ill diabetic patients.

AIMS AND OBJECTIVES

The primary objective of this study is to evaluate the predictive value of HbA1c in determining hospital mortality and length of stay among patients with type 2 diabetes mellitus admitted with sepsis[1]. In addition, the secondary objective is to examine the correlation between HbA1c and other clinical and laboratory parameters such as admission blood glucose levels, CRP (C-Reactive Protein), APACHE II score, and SOFA score in order to assess the overall efficacy of HbA1c as a prognostic marker in this patient population.

MATERIALS AND METHODS

Study Design

This observational study was conducted over a period of six months at Madras Medical College and Rajiv Gandhi Government General Hospital, Chennai**.** A total of 100 patients with type 2 diabetes mellitus admitted with sepsis were enrolled based on predefined inclusion and exclusion criteria. The study aimed to assess the prognostic significance of HbA1c in predicting hospital outcomes such as mortality and length of stay in this patient population.

Inclusion and Exclusion Criteria

The study included adult patients aged over 18 years who had either a previously established or newly diagnosed case of type 2 diabetes mellitus and were admitted to the medical wards with sepsis**.** Patients were excluded if they had chronic renal failure, end-stage malignant disease, were receiving immunosuppressive therapy, had type 1 diabetes mellitus, were pregnant, had decompensated liver disease, or had any form of anaemia. These criteria were set to eliminate confounding variables that could influence the assessment of HbA1c as a prognostic marker.

Data Collection Procedure

Patients who met the inclusion criteria and none of the exclusion criteria were enrolled in the study and subjected to a structured data collection process. On admission, a detailed clinical history was obtained using a pre-designed questionnaire, followed by a thorough clinical examination. Relevant investigations, including HbA1c**,** admission blood glucose**,** CRP**,** APACHE II score**,** and SOFA score**,** were performed on the day of admission. The patients were then followed up for a period of 30 days to assess their clinical outcomes, including mortality and duration of hospital stay. This methodology facilitated the evaluation of correlations between HbA1c and other prognostic indicators in diabetic patients with sepsis.

Statistical Analysis

All collected data were compiled and analyzed using statistical software tools SPSS and Epi Info. Descriptive statistics were used to summarize baseline characteristics of the study population. Continuous variables such as HbA1c, blood glucose, CRP, APACHE II and SOFA scores were expressed as mean ± standard deviation. Comparative analysis between survivors and non-survivors was performed using appropriate statistical tests, and p-values <0.05 were considered statistically significant. Correlation analyses were conducted to assess the relationship between HbA1c and other prognostic indicators, thereby evaluating its predictive value in determining hospital outcomes in type 2 diabetes patients with sepsis.

RESULTS

Category	Survivors (n=71)	Non-Survivors (n=29)	Total (n=100)	Mortality Rate
Age (Mean ± SD)	48 ± 9.58	67 ± 9.32	—	Significant (p<0.001)
Male	41	12	53	22.64%
Female	30	17	47	36.17%

Table 1: Demographic Profile and Mortality Distribution

Table 1 observes age was a significant risk factor, with mortality increasing in patients over 60 years. Female patients had a slightly higher mortality rate than males.

HbA1c (%) Range	Survivors	Non-Survivors	Total	Mortality Rate
< 9	69	4	73	5%
> 9	2	25	27	93%

Table 2: Correlation between HbA1c Levels and Mortality

Table 2 shows that HbA1c levels have a strong correlation with 30-day mortality. Patients with HbA1c >9% had a markedly higher mortality rate, suggesting poor glycemic control as a predictor of adverse outcomes.

Parameter	Survivors (Mean ± SD)	Non-Survivors (Mean ± SD)	p-value
APACHE II Score	13.23 ± 4.03	30.66 ± 2.82	<0.001**
SOFA Score	4.11 ± 1.10	12.69 ± 2.38	<0.001**
CRP (mg/L)	97.25 ± 59.82	401.03 ± 134.75	0.03*
TLC (cells/mm³)	14440 ± 3308	19932 ± 6218	0.04*

Table 3: Clinical Scores and Inflammatory Markers

Both APACHE II and SOFA scores showed a significant association with mortality in Table 3. Elevated CRP and leukocyte counts were also significantly higher in non-survivors.

Parameter	Survivors (Mean ± SD)	Non-Survivors (Mean ± SD)	p-value
Rectal Temperature (°F)	99.34 ± 1.40	102.13 ± 1.85	<0.001**
Heart Rate (bpm)	116.52 ± 16.50	135.93 ± 26.92	<0.001**
Respiratory Rate	24.61 ± 3.35	30.00 ± 3.86	<0.001**
Systolic BP (mmHg)	109.72 ± 23.11	80.00 ± 23.60	<0.001**
Diastolic BP (mmHg)	74.08 ± 14.88	56.55 ± 15.87	<0.001**

Table 4: Vital Signs on Admission

Table 4 shows that higher temperature, heart rate, respiratory rate and lower blood pressure were significantly associated with increased mortality.

Parameter	Survivors (Mean ± SD)	Non-Survivors (Mean ± SD)	p-value
pH	7.319 ± 0.0655	7.286 ± 0.0711	0.026*
PaO_2 (mmHg)	84.87 ± 6.37	80.24 ± 13.89	0.094
$PaCO_2$ (mmHg)	53.30 ± 11.10	63.62 ± 10.64	<0.001**
Serum Bicarbonate (mmol/L)	21.92 ± 2.70	21.14 ± 2.22	0.173
FiO_2 (%)	24.89 ± 11.64	83.86 ± 18.44	<0.001**

Table 5: Arterial Blood Gas and Biochemical Markers

In Table 5, low pH and high $PaCO_2$ were significantly associated with mortality. FiO_2 requirement was substantially higher in non-survivors, reflecting worse respiratory compromise.

Parameter	Survivors (Mean ± SD)	Non-Survivors (Mean ± SD)	p-value
Serum Creatinine (mg/dL)	2.156 ± 1.94	2.876 ± 0.95	0.015*
Serum Sodium (mEq/L)	132.18 ± 3.12	132.17 ± 4.55	0.989
Serum Potassium (mEq/L)	3.672 ± 0.57	3.603 ± 1.09	0.682
Serum Bilirubin (mg/dL)	2.382 ± 1.29	2.903 ± 1.14	0.061

Table 6: Renal and Hepatic Function Tests

Serum creatinine levels showed significant correlation with mortality, whereas sodium, potassium, and bilirubin did not show statistically significant differences in Table 6.

Parameter	Survivors (Mean ± SD)	Non-Survivors (Mean ± SD)	p-value
GCS	15.00 ± 0.00	11.79 ± 1.93	<0.001**
Hematocrit (%)	38.44 ± 3.88	37.17 ± 5.20	0.185
Platelet Count (/mm^3)	227881 ± 110028	228089 ± 178153	0.994
Urine Output (mL)	1305.63 ± 459.16	781.03 ± 230.07	<0.001**

Table 7: Neurological Status, Hematology, and Output Measures

In Table 7 lower GCS (Glasgow Coma Scale) scores and reduced urine output were significantly associated with higher mortality, indicating poor neurological and renal perfusion status in non-survivors.

DISCUSSION

The prognostic role of HbA1c in patients with T2DM (Type 2 Diabetes Mellitus) presenting with sepsis has become an area of growing clinical interest. Our study findings are consistent with emerging data suggesting that elevated HbA1c levels may be associated with adverse outcomes in septic diabetic patients.

Kim et al. observed that HbA1c ≥6.5% at ICU admission was independently associated with worsening organ dysfunction and higher ICU mortality in septic patients, even in those without a prior diagnosis of diabetes [5]. This implies that chronic hyperglycemia, as reflected by higher HbA1c, may intensify the pathophysiological burden of sepsis.

Supporting this, a systematic review and meta-analysis by Jiang and Cheng confirmed that diabetes mellitus is significantly associated with increased mortality in septic patients.[6] The study also

emphasized that poor glycemic control-indicated by elevated HbA1c-contributes to immune dysfunction and inflammation, worsening sepsis outcomes.

From a pathophysiological perspective, chronic hyperglycemia impairs both innate and adaptive immune responses. Neutrophil chemotaxis, phagocytosis, and cytokine signaling become dysfunctional, reducing the body's ability to fight infection effectively.[7] Furthermore, persistent hyperglycemia leads to the accumulation of AGEs (Advanced Glycation End products), which promote oxidative stress and systemic inflammation.[8]

These inflammatory and immunometabolic disturbances often manifest clinically as multi-organ dysfunction. Severity scoring systems like the SOFA and APACHE II scales, which are widely used to assess the burden of illness in sepsis, have been shown to correlate positively with HbA1c levels. Higher HbA1c values are linked to increased SOFA and APACHE II scores, reflecting more severe disease.[9,10]

The ADA (American Diabetes Association) recommends routine HbA1c testing in hospitalized patients to assess chronic glycemic control.[11] In the ICU setting, measuring HbA1c can help differentiate between stress-induced hyperglycemia and poorly controlled diabetes, which may have different management pathways and prognostic implications.

In a cohort study by van Vught et al., diabetes itself was not found to independently worsen outcomes in sepsis. However, poor glycemic control and certain antidiabetic therapies were associated with altered host responses and increased sepsis severity.[12] This underscores the importance of long-term glucose regulation in modulating the host's resilience to infection and inflammation.

Thus, integrating HbA1c measurement into the early evaluation of septic patients with T2DM could help guide clinical decision-making, risk stratification, and potential interventions aimed at improving glycemic control and sepsis outcomes.

LIMITATIONS

This study was limited by its single-center design, small sample size, and short in-hospital follow-up, which may affect the generalizability and strength of the findings. As an observational study, it cannot establish causality between elevated HbA1c and poor sepsis outcomes. Potential confounding factors such as variations in diabetes management and comorbidities were not fully controlled. Furthermore, HbA1c reflects long-term glycemic control but does not capture acute glucose fluctuations during sepsis. Larger multicenter studies with extended follow-up are needed to validate the prognostic value of HbA1c in this setting.

CONCLUSION

In our study, HbA1c, APACHE II score, SOFA score, C-reactive protein (CRP), and total leukocyte count showed a significant correlation with both 30-day mortality and length of hospital stay in patients with type 2 diabetes and sepsis. However, admission plasma glucose levels did not demonstrate any significant association with either mortality or duration of hospitalization. Furthermore, HbA1c levels were positively correlated with CRP, APACHE II score, and SOFA score, but not with admission plasma glucose. These findings suggest that HbA1c is comparable in prognostic efficacy to both the APACHE II and SOFA scores and may serve as a useful marker for risk stratification in diabetic patients with sepsis.

REFERENCES

[1] Gornik I, Gornik O, Gašparović V. HbA1c is outcome predictor in diabetic patients with sepsis. Diabetes Research and Clinical Practice 2007;77(1):120-5.
[2] Seshiah V. A handbook on diabetes mellitus. All India Publishers & Distributors 2018.
[3] Bessman AN, Sapico FL. Infections in the diabetic patient: the role of immune dysfunction and pathogen virulence factors. Journal of Diabetes and its Complications 1992;6(4):258-62.
[4] Turina M, Fry DE, Polk HC. Acute hyperglycemia and the innate immune system: clinical, cellular, and molecular aspects. Critical Care Medicine 2005;33(7):1624-33.
[5] Kim YJ, Park JS, Kim WY, et al. The value of glycated hemoglobin as predictor of organ

dysfunction in patients with sepsis. PLoS One 2019;14(5):e0216397.
[6] Jiang L, Cheng M. Impact of diabetes mellitus on outcomes of patients with sepsis: an updated systematic review and meta-analysis. Diabetol Metab Syndr 2022;14(1):39.
[7] Cavaillon JM, Adib-Conquy M. Bench-to-bedside review: endotoxin tolerance as a model of leukocyte reprogramming in sepsis. Crit Care 2006;10(5):233.
[8] Marik PE, Bellomo R. Stress hyperglycemia: an essential survival response! Crit Care 2013;17(2):305.
[9] Vincent JL, Moreno R, Takala J, et al. The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure. Intensive Care Med 1996;22(7):707–10.
[10] Knaus WA, Draper EA, Wagner DP, et al. APACHE II: a severity of disease classification system. Crit Care Med 1985;13(10):818-29.
[11] American Diabetes Association. Standards of Medical Care in Diabetes-2021. Diabetes Care 2021;44(Suppl 1):S1-232.
[12] van Vught LA, Scicluna BP, Wiewel MA, et al. Association of diabetes and diabetes treatment with the host response in critically ill sepsis patients. Crit Care 2016;20(1):252.