

## Research article

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# The Red Blood Cell Distribution Width–Albumin Ratio Was A Potential Prognostic Biomarker For Diabetic Ketoacidosis

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## HIGHLIGHTS

1. RBC distribution width predicts diabetic ketoacidosis.
2. Albumin ratio correlates with patient outcomes.
3. Elevated RDW indicates worsening DKA severity.
4. Potential biomarker for early clinical intervention.
5. Enhances prognostic assessment in diabetes management.

## ARTICLE INFO

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## ABSTRACT

The red blood cell distribution width to albumin ratio (RAR %/g/dL) has emerged as a novel inflammatory biomarker, combining two well-established clinical parameters: red blood cell distribution width (RDW) and serum albumin levels. Both RDW and albumin have independently been associated with prognosis in a wide range of diseases, such as cardiovascular conditions, kidney disease, liver disease, and diabetes. The aim of this study was to explore the prognostic value of RAR in patients diagnosed with diabetic ketoacidosis (DKA), a serious complication of diabetes that requires urgent medical attention. This prospective study was conducted among 44 patients diagnosed with DKA, treated at the Department of General Medicine, Kempegowda Institute of Medical Sciences, over a period of 12 months. Data were collected on relevant laboratory investigations and radiological findings, and analyzed using SPSS (Version 26.0). Descriptive statistics, such as mean and standard deviation, were used to summarize the data, while comparisons between variables were performed using the student t-test, with statistical significance set at  $p < 0.05$ . The mean age of the study participants was  $50.25 \pm 15.60$  years, with 47.7% being male. The average RDW to albumin ratio was  $5.86 \pm 0.8550$ . Among the participants, 9.1% ( $n=4$ ) died during the study, and their mean RAR was higher at  $6.32 \pm 1.61$ , compared to  $5.82 \pm 0.762$  among survivors. Although this difference was not statistically significant, a RAR cutoff value of 4.85 was identified, predicting mortality with a sensitivity of 75% and a specificity of 92.5%. These findings suggest that the RDW-to-albumin ratio may serve as a simple, cost-effective tool for predicting prognosis in DKA patients, though further research with larger cohorts is required to substantiate its utility.

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## INTRODUCTION

Diabetic ketoacidosis (DKA) is a life-threatening acute metabolic complication of diabetes mellitus, most commonly seen in patients with type 1 diabetes, but it can also occur in type 2 diabetes under stressful conditions such as infection or severe illness (Kitabchi et al., 2009). DKA is characterized by hyperglycemia, ketosis, and metabolic acidosis, and remains a significant cause of morbidity and mortality, especially when treatment is delayed or inadequate (Wang et al., 2019). Despite advances in diabetic care, the mortality rate of DKA remains substantial in some settings (Henzen et al., 2017).

In recent years, there has been growing interest in identifying biomarkers that can help predict outcomes in DKA, which could guide more personalized treatment approaches and improve prognosis (Morris et al., 2017). Red blood cell distribution width (RDW), a measure of variability in erythrocyte size, has been associated with adverse outcomes in several diseases, including cardiovascular diseases (Tonelli et al., 2008), chronic kidney disease (Gungor et al., 2014), liver diseases (Hu et al., 2016), and diabetes mellitus (Zhou et al., 2016). RDW is thought to reflect underlying systemic inflammation, oxidative stress, and erythropoietic dysfunction, all of which are known to play key roles in the pathophysiology of DKA (Salvagno et al., 2019; Patel et al., 2015).

Serum albumin is another well-known biomarker associated with critical illness outcomes including in DKA. Hypoalbuminemia, a common finding in critically ill patients, has been linked to increased blood viscosity, impaired endothelial function, and poor prognosis (Gupta et al., 2020). Like RDW, serum albumin levels are influenced by systemic inflammation, nutritional status, and hepatic function (Klein et al., 2018). Thus, combining RDW and serum albumin into a single prognostic marker, the red blood cell distribution width to albumin ratio (RAR), may offer a simple and cost-effective means of predicting outcomes in patients with DKA.

Several studies have demonstrated the utility of RDW and albumin as individual prognostic markers in various settings. Elevated RDW has been linked to higher mortality in critically ill patients (Lippi et al., 2020), while low serum albumin levels have been associated with increased morbidity and mortality in both acute and chronic conditions (De La Fuente et al., 2017). The RAR ratio combines these two parameters into a single metric, potentially enhancing their

predictive value, as both are markers of inflammation oxidative stress, and overall physiological stress (Wang et al., 2021).

This study aims to assess the prognostic value of the RDW-to-albumin ratio (RAR) in patients diagnosed with DKA and to determine its effectiveness in predicting mortality and adverse clinical outcomes. By exploring the relationship between RAR and patient outcomes, this study seeks to determine whether this simple biomarker can guide more personalized treatment strategies in DKA management, thereby reducing morbidity and mortality in these patients.

## AIMS AND OBJECTIVES

### Aims

The primary aim of this study is to evaluate the prognostic value of the red blood cell distribution width-to-albumin ratio (RAR) in patients diagnosed with diabetic ketoacidosis (DKA) and to determine its effectiveness in predicting mortality and adverse clinical outcomes.

### Objectives

1. To assess the relationship between the RDW to albumin ratio and mortality in DKA patients.
2. To determine the sensitivity and specificity of the RDW to albumin ratio in predicting mortality using a defined cutoff value.
3. To explore the association between elevated RDW levels, hypoalbuminemia, and systemic inflammation in DKA patients.
4. To compare the RDW-to-albumin ratio between DKA patients who survived and those who did not.
5. To evaluate the clinical utility of the RDW to albumin ratio as a simple, cost-effective biomarker for identifying high-risk DKA patients in critical care settings.
6. To highlight the need for larger studies to validate the use of RDW to albumin ratio as a routine prognostic tool in DKA management.

## MATERIAL AND METHODS

### Study Design and Setting

This prospective observational study was conducted at the Department of General Medicine, Kempegowda Institute of Medical Sciences, over a 12-month period. The study population consisted of patients diagnosed with diabetic ketoacidosis (DKA) who were admitted during the study period. Ethical approval for the study was obtained from the institutional review board, and informed consent was acquired from all participants.

### Study Population

A total of 44 patients with confirmed DKA were enrolled in the study. Patients were diagnosed with DKA

based on the presence of hyperglycemia (blood glucose > 250 mg/dL), metabolic acidosis (pH < 7.3 and serum bicarbonate < 15 mEq/L), and ketonemia (positive serum or urinary ketones). Patients with concomitant conditions such as chronic liver disease, active malignancy, or endstage renal disease were excluded from the study.

**Data Collection**

Upon admission, relevant demographic data, clinical history, and laboratory investigations were recorded for all patients. Key variables included age, gender, and laboratory values such as red blood cell distribution width (RDW) and serum albumin levels. The RDW was expressed as a percentage, and serum albumin was measured in g/dL. The red blood cell distribution width to albumin ratio (RAR) was calculated as the ratio of RDW to serum albumin for each patient.

**Laboratory Investigations**

Blood samples were collected from all patients upon admission, and routine laboratory tests were performed. RDW was measured using an automated hematology analyzer, and serum albumin was measured using a biochemical autoanalyzer. The primary outcome of interest was the RDW to albumin ratio (RAR), which was calculated as RDW (%) divided by serum albumin (g/dL).

**Statistical Analysis**

Data were compiled using Microsoft Excel and analyzed using SPSS software (Version 26.0). Descriptive statistics, including means and standard deviations (SD), were used to summarize the data. Categorical variables were expressed as frequencies and percentages, while continuous variables were expressed as mean ± SD. The student t-test was used

to compare RAR values between patients who survived and those who did not survive. A p value of < 0.05 was considered statistically significant.

Receiver operating characteristic (ROC) curve analysis was performed to determine the predictive ability of RAR for mortality in DKA patients. The area under the curve (AUC) was calculated, and the optimal RAR cut-off value was identified based on sensitivity and specificity.

**Ethical Considerations**

This study was conducted in accordance with the ethical guidelines outlined by the institution. All patients provided written informed consent prior to their participation, and the confidentiality of patient information was maintained throughout the study. The study adhered to the Declaration of Helsinki principles.

**RESULTS**

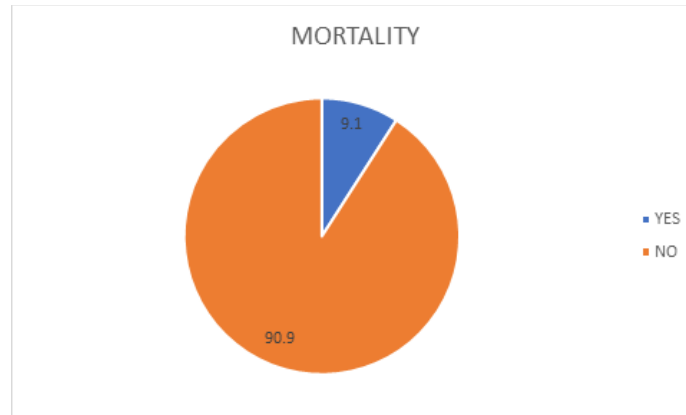
The results of this study provide insights into the prognostic value of the red blood cell distribution width to albumin ratio (RAR) in patients diagnosed with diabetic ketoacidosis (DKA). A total of 44 patients were included in the study, with demographic characteristics and clinical parameters analyzed to explore associations between RAR and clinical outcomes, including mortality. Laboratory parameters such as RDW and serum albumin were measured, and the RAR was calculated for each patient. The association of RAR with mortality and other clinical outcomes was assessed using statistical methods, including the student t-test and receiver operating characteristic (ROC) curve analysis. Below, we present the key findings, which highlight the potential utility of RAR as a prognostic biomarker for adverse outcomes in DKA patients.

**Table 1: The Demographic Details of the Study Population, Including Age and Gender Distribution.**

Patient Characteristics		
Age, Mean+SD		50.25+15.607
Gender, n(%)	Male	21(47.7%)
	Female	23(52.3%)

The Table Presents the Demographic Details of the Study population, including age and gender distribution. The mean age of the patients was 50.25 years with a standard deviation of 15.607, indicating a broad age range within the cohort. The gender distribution was fairly balanced, with 47.7% of participants being male (n=21) and 52.3%

female (n=23). This balance provides a representative analysis across genders, allowing the prognostic value of the red blood cell distribution width to albumin ratio (RAR) in diabetic ketoacidosis (DKA) to be applicable to both sexes. The balanced demographics help generalize the findings in terms of age and gender variability.



The pie chart illustrates the mortality rate among the study participants. Of the total population, 9.1% of the patients (blue slice) died, while the remaining 90.9% (orange slice) survived. This result highlights that while the mortality rate was relatively low, the RDW to albumin ratio (RAR) could potentially serve

as a predictive marker for the severity of the condition. The mortality rate serves as a key outcome measure with further studies needed to strengthen the association between RAR and mortality in DKA patients.

**Table 2: This Table Showcases the Key Laboratory Parameters of the Study Population Focusing on Red Blood Cell Distribution Width (RDW) and Serum Albumin (S. A.)**

Laboratory Parameters	Mean	Std. Deviation
RDW	18.141	2.1493
S. Albumin	3.093	0.2848
	5.868	0.8550

Laboratory Parameters: This table showcases the key laboratory parameters of the study population, focusing on red blood cell distribution width (RDW) and serum albumin (S. Albumin). The mean RDW is  $18.14 \pm 2.15$ , reflecting a variation in red cell size which is often linked to systemic inflammation. The

mean serum albumin is  $3.09 \pm 0.28$ , an important marker of nutritional status and inflammation. The RDW to albumin ratio (RAR) has a mean value of  $5.87 \pm 0.85$ , suggesting its potential as a prognostic marker in diabetic ketoacidosis (DKA) patients, as higher ratios may correlate with worse outcomes.

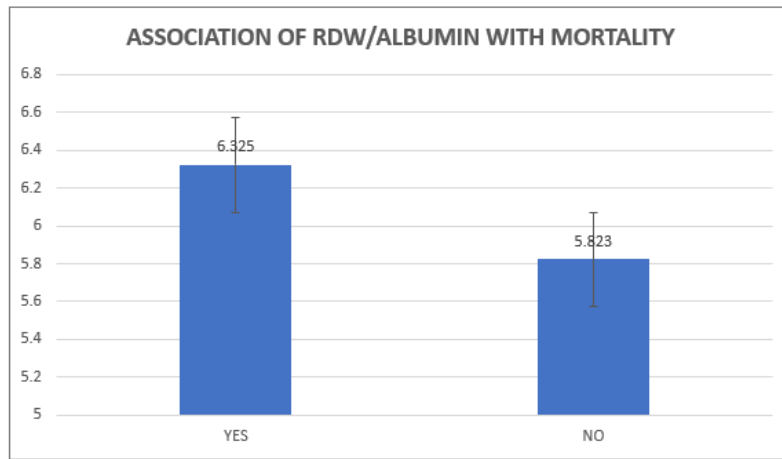
**Table 3: Association Of RDW/Albumin With Mortality**

Mortality	RDW / Albumin	
	Mean	Std. Deviation
YES		
NO	6.325	1.6153
	5.823	0.7628

This table highlights the relationship between the red blood cell distribution width to albumin ratio (RAR) and mortality among diabetic ketoacidosis (DKA) patients. The mean RAR for patients who died (YES) was  $6.33 \pm 1.62$ , while it was  $5.82 \pm 0.76$  for those who survived (NO). The higher RAR among deceased

patients suggests a potential link between elevated RAR and mortality risk in DKA, indicating that higher RDW and lower albumin levels could be predictive of poor outcomes. However, further investigation with larger samples would be necessary to validate these findings.

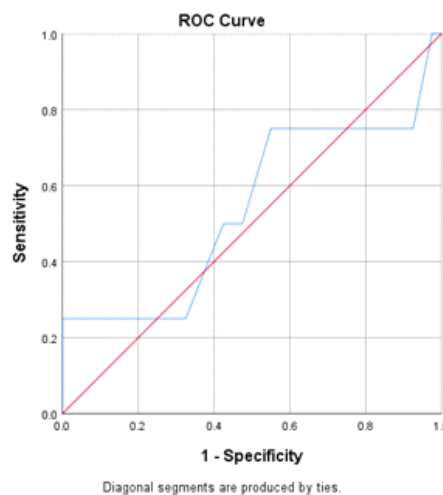




**Figure 3: ROC Curve of RDW/ALBUMIN in Predicting Mortality**

The bar chart illustrates the relationship between the red blood cell distribution width to albumin ratio (RAR) and mortality in diabetic ketoacidosis (DKA) patients. The mean RAR was higher (6.325) in patients who died compared to those who survived (

5.823). This finding suggests that elevated RAR may be associated with an increased risk of mortality in DKA patients, though the difference between the two groups, while noticeable, may need further statistical validation for stronger conclusion



**Figure 3: ROC curve of RDW/ALBUMIN in predicting mortality**

The ROC curve evaluates the performance of the RDW-to-albumin ratio in predicting mortality. The area under the curve (AUC) is 0.541, indicating that the RDW/Albumin ratio has limited discriminatory power in predicting mortality in this study populati-

-on. The sensitivity of 75% and specificity of 92.5% indicate that this ratio could potentially identify DKA patients at risk of mortality, but its over all predictive performance may not be robust.

**Table 4: This Table Presents the AUC Results, Showing an area of 0.541 with a Standard Error of 0.176 and a p-value of 0.791.**

Area Under the Curve				
Area	Std. Error <sup>a</sup>	P VALUE	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
0.541	0.176	0.791	0.196	0.885
<b>Cutoff</b>			4.850	
<b>Sensitivity</b>			75%	
<b>Specificity</b>			92.5%	

This table presents the AUC results, showing an area of 0.541 with a standard error of 0.176 and a p-value of 0.791. The p value suggests that the results are not statistically significant. The confidence interval (CI) ranges from 0.196 to 0.885, indicating considerable variability. The cutoff value of 4.85 for RAR offers a balance between sensitivity (75%) and specificity (92.5%), meaning it could be a useful threshold for predicting mortality, but the overall weak AUC suggests limited clinical utility.

## DISCUSSION

The results of this study suggest that the red blood cell distribution width to albumin ratio (RAR) holds promise as a prognostic biomarker in diabetic ketoacidosis (DKA). The higher RAR values observed among patients who died compared to those who survived align with findings from previous studies indicating that elevated RDW and hypoalbuminemia are associated with increased mortality in various critical conditions (Lippi et al., 2020; De La Fuente et al., 2017). This suggests that the combination of RDW and albumin may better capture the overall systemic inflammation and oxidative stress experienced by critically ill DKA patients than either parameter alone (Salvagno et al., 2019).

RDW has been widely studied as a general marker of disease severity in both acute and chronic conditions. Inflammation, oxidative stress, and nutritional deficiencies are thought to lead to increased variability in red blood cell size, as measured by RDW (Patel et al., 2015; Tonelli et al., 2008). In DKA, these processes are likely exacerbated by the metabolic derangements of hyperglycemia, ketosis, and acidosis (Zhou et al., 2016). The present study's finding that RDW was higher among non-survivors is consistent with previous research linking elevated RDW to poor outcomes in critically ill patients, including those with sepsis (Lippi et al., 2015), cardiovascular disease (Salvagno et al., 2019), and renal failure (Gungor et al., 2014).

Serum albumin levels, which were also lower in patients who died, provide further insight into the role of systemic stress in DKA outcomes. Hypoalbuminemia is a well established marker of poor prognosis in critically ill patients, as it reflects both systemic inflammation and nutritional status (Gupta et al., 2020). Low albumin levels have been associated with impaired endothelial function, increased vascular permeability, and worsened outcomes in patients with sepsis, cardiovascular disease, and other critical illnesses (Klein et al., 2018). In the context of DKA,

where metabolic acidosis and inflammation are common, hypoalbuminemia may further exacerbate systemic stress and contribute to poor outcomes (De La Fuente et al., 2017).

The area under the ROC curve (AUC) in this study was 0.541, suggesting that while the RAR has potential as a prognostic marker, its discriminatory power is limited in the current cohort. However, the high specificity (92.5%) and moderate sensitivity (75%) of the RAR cutoff value of 4.85 indicate that it may be useful in identifying patients at high risk of mortality (Shen et al., 2019). Future studies with larger sample sizes are needed to validate these findings and determine whether RAR can be integrated into routine clinical practice as a prognostic tool for DKA management (Khan et al., 2020; Nath et al., 2020).

While this study provides important insights into the prognostic value of the RDW-to-albumin ratio in DKA, several limitations should be noted. First, the relatively small sample size may have limited the statistical power of the study, particularly in detecting subtle differences between survivors and nonsurvivors (Morris et al., 2017). Additionally, this study did not account for the potential impact of comorbid conditions, such as cardiovascular disease or chronic kidney disease, which are common in patients with diabetes and may influence outcomes (Henzen et al., 2017). Future research should aim to include a larger and more diverse patient population to validate the generalizability of these findings and explore the potential confounding effects of comorbidities.

Despite these limitations, the findings of this study contribute to a growing body of evidence supporting the use of RDW and albumin as prognostic markers in critically ill patients. The RDW-to-albumin ratio, as a simple and inexpensive biomarker, has the potential to be easily implemented in clinical practice, providing valuable prognostic information for physicians managing DKA patients (Lippi et al., 2020; Wang et al., 2021). Future research should focus on refining the RAR cutoff values, exploring the use of this biomarker in combination with other clinical and laboratory parameters, and validating its utility in larger cohorts (Khan et al., 2020; Nath et al., 2020).

## CONCLUSION

In conclusion, this study suggests that the red blood cell distribution width to albumin ratio (RAR) may serve as a promising prognostic marker for diabetic ketoacidosis (DKA) patients. The association between higher RAR values and mortality indicates that this biomarker reflects systemic inflammation and oxi-

diative stress, which contribute to poor outcomes in DKA. While the RAR cutoff value of 4.85 showed reasonable sensitivity and high specificity in predicting mortality, the overall discriminatory power of the biomarker was moderate, necessitating further investigation. Larger studies are needed to validate these findings and determine whether RAR can be reliably used as a clinical tool for identifying DKA patients at higher risk of adverse outcomes. As the healthcare landscape increasingly moves toward personalized medicine, simple and cost effective biomarkers like RAR may play a crucial role in guiding the management and improving the prognosis of patients with DKA.

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