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CLINICAL SIGNIFICANCE OF RED CELL DISTRIBUTION WIDTH TO SERUM ALBUMIN RATIO IN PATIENTS WITH DIABETIC KETOACIDOSIS

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ABSTRACT

Background: Diabetic Ketoacidosis (DKA) is a critical, sudden consequence of diabetes mellitus characterised by hyperglycemia, ketosis, and metabolic acidosis. The early identification of test indicators associated with illness severity may facilitate timely diagnosis and treatment. **Aim**: To examine the link between serum albumin and DKA severity and Red Cell Distribution Width (RDW). The RDW-to-Albumin Ratio's clinical significance in DKA patients was assessed. **Methodology**: The cross-sectional analytical investigation included 100 DKA patients. SPSS 26 was used to record and analyse demographics, RDW, serum albumin, ketone, blood pH, glucose, and bicarbonate. Blood pH measurements defined DKA severity as mild, moderate, or severe. **Results**: The study comprised 100 patients, 49.0% male, 51.0% female. Most cases (64.0%) had severe DKA. Though moderate DKA had the highest mean serum albumin level (1.70 ± 0.48 g/dL), there was no significant link between it with DKA severity ($F = 1.99$, $p = 0.142$). There was a significant difference in RDW between DKA severity levels ($F = 7.32$, $p = 0.001$), suggesting a link between the two. The RDW-to-Albumin Ratio did not affect DKA severity ($F = 2.20$, $p = 0.117$). Additionally, serum albumin, RDW, and RDW-to-Albumin Ratio had weak and non-significant associations with blood pH. **Conclusion**: RDW was significantly related to the severity of DKA indicating its potential as a readily available hematological marker for severity assessment.

Keywords: *Diabetic Ketoacidosis, Red Cell Distribution Width, Serum Albumin, RDW-to-Albumin Ratio, Blood pH, Severity Assessment.*

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INTRODUCTION

Diabetes mellitus (DM), the third leading cause of mortality worldwide, can induce several organ issues if left untreated. Diabetes affected 2.8% of all age groups globally in 2000 and 4.4% in 2030. Diabetes is expected to climb from 171 million in 2000 to 366 million in 2030 [1]. The most common kind of diabetes, type 2 (DM), is life-threatening and stresses global healthcare systems. Global diabetes cases will rise 45% to 853 million by 2050 due to population expansion, ageing, and urbanisation [2]. Without effective management, diabetic patients are susceptible to various complications, among which diabetic ketoacidosis (DKA) is a common andacute life-threatening condition [3, 4].

Diabetic ketoacidosis (DKA) causes diabetic coma or death. Increased blood ketones induce diabetic ketoacidosis. Diabetes ketoacidosis happens when the body doesn't have enough insulin to enable blood sugar into cells for energy, boosted by glucose counter regulatory hormone overabundance [5, 6]. Our population develops ketosis owing to delayed diagnosis or irregular treatment of diabetics. Uncontrolled blood glucose levels or illnesses, surgery, or trauma can cause ketosis in diabetics [7]. Recent research focus on early illness prediction and prevention. Physicians must recognise diabetes-related hyperglycaemic crises. Identifying a biochemical marker related with illness incidence or predisposing conditions might help predict disease [8].

Moreover, with increasing healthcare costs and a changing healthcare system, prevention of DKA remains essential.

Identifying diabetic individuals having the risk of ketosis will help physicians prevent emergencies and thereby provide better clinical outcome. Individuals identified with the risk of ketosis can be made aware of the preventive measures and immediate medical assistance which can bring down the incidence and mortality rates of DKA [9, 10].

The current research sought to evaluate the clinical significance of serum albumin, RDW, and RWR in diagnosing and assessing the severity of Diabetic Ketoacidosis (DKA). The aim of the research was to ascertain the correlation between serum albumin levels and the severity of DKA, to explore the association between RDW and the severity of DKA, and to examine the link between the RDW to Albumin Ratio and the severity of DKA in individuals experiencing diabetic ketoacidosis.

MATERIAL AND METHOD

This is a cross-sectional analytical investigation aimed at evaluating the clinical importance of three parameters (Red Cell Distribution Width (RDW), serum albumin, and the Red Cell Distribution Width to Albumin Ratio (RAR)) in individuals with Diabetic Ketoacidosis (DKA) and determining the correlation of these parameters with the severity of DKA. A sum of 100 individuals diagnosed with DKA participated in the research. Patients were chosen from hospital admission records that had comprehensive clinical and laboratory data.The minimum sample size was calculated to be 220 patients at a 95% confidence level, a 5% margin of error, and an estimate prevalence rate of DKA of 14%, but there were only 100 eligible patients available as confirmed cases of DKA were limited during the study period [11]. Data and laboratory samples were collected from Hayatabad medical complex, hospital Peshawar.

Laboratory investigations were performed on blood samples that were collected as part of routine patient care. Blood samples collected in EDTA tubes were used for Complete Blood Count (CBC) and Red Cell Distribution Width (RDW) was performed, whereas blood collected in serum separator tubes were used for serum albumin measurement using standard laboratory methods. DKA was confirmed by measuring blood ketones. RDW/Albumin Ratio (RAR) was the ratio of the RDW (%)/the serum albumin (g/dL). Patients' clinical records were also used to obtain the additional laboratory parameters: blood glucose, blood pH and serum bicarbonate.

In the study, we included adult patients (18 years or older) who presented to us with Type 2 Diabetes Mellitus and who had a definite diagnosis of Diabetic Ketoacidosis according to the clinical and biochemical criteria used to diagnose DKA and who had full laboratory reports inclusive of RDW and serum albumin. The study excluded patients younger than 18 years, patients with Type 1 Diabetes Mellitus, pregnant women, and those without complete clinical and/or laboratory data. Severity of DKA was defined by blood pH of mild (7.25–7.30), moderate (7.00–7.24) and severe (<7.00).

The statistical analysis was done with the help of Statistical Package for the Social Sciences (SPSS) version 25. Data were presented descriptively as frequencies, percentages, means and standard deviations. The mean values of the serum albumin, RDW, and RDW-to-Albumin Ratio were compared between the severity groups of DKA using One-Way Analysis of Variance (ANOVA). The Pearson correlation analysis method was used to assess the correlation between the blood pH and the study variables. The p value of <0.05 was deemed as statistically significant.

RESULT

The demographic and clinical features of the study population are shown in Table 1. Among the 100 patients included in the study, males constituted 51.0% (n=51) while females accounted for 49.0% (n=49). Regarding age distribution, the majority of patients were in the 41–60 years age group, representing 61.0% (n=61), followed by 31–40 years with 26.0% (n=26), 21–30 years with 9.0% (n=9), 10–20 years with 3.0% (n=3), and only 1.0% (n=1) were older than 60 years. Assessment of Red Cell Distribution Width (RDW) showed that 58.0% (n=58) of patients had RDW values within the normal range (11.5–14.5%), while 35.0% (n=35) had elevated RDW values (>14.5%) and 7.0% (n=7) had RDW values below 11.5%. Serum albumin levels were low (<3.5 g/dL) in 67.0% (n=67) of patients, normal (3.5–5.0 g/dL) in 29.0% (n=29), and elevated (>5.0 g/dL) in 4.0% (n=4).

With respect to ketone levels, 67.0% (n=67) of patients had elevated ketones (0.6–1.5 mmol/L), 29.0% (n=29) were classified as high risk (1.6–2.9 mmol/L), and 4.0% (n=4) had very high-risk ketone levels (≥3.0 mmol/L). Blood pH analysis revealed that 81.0% (n=81) of patients had low pH values (<7.35), while 19.0% (n=19) had normal pH levels (7.35–7.45).Regarding blood glucose levels, 44.0% (n=44) of patients had glucose concentrations between 300–399 mg/dL, 34.0% (n=34) had levels below 300 mg/dL, and 22.0% (n=22) had levels ≥400 mg/dL. Serum bicarbonate levels were below 22 mEq/L in 44.0% (n=44) of patients, within the normal range (22–28 mEq/L) in 38.0% (n=38), and above 28 mEq/L in 18.0% (n=18).

Table 01*:* Demographic and Clinical Characteristics of Study Participants (n = 100)

Variable	Category	Frequency (n)	Percentage (%)
Gender	Male	51	51.0
	Female	49	49.0
Age Group	10–20 years	3	3.0
	21–30 years	9	9.0
	31–40 years	26	26.0
	41–60 years	61	61.0
	>60 years	1	1.0
RDW (%)	<11.5%	7	7.0
	11.5–14.5%	58	58.0
	>14.5%	35	35.0
Albumin (g/dL)	<3.5 (Low)	67	67.0
	3.5–5.0 (Normal)	29	29.0
	>5.0 (High)	4	4.0
Ketones	Elevated(0.6–1.5 mmol/L)	67	67.0
	High Risk (1.6–2.9 mmol/L)	29	29.0

	Very High Risk (≥3.0 mmol/L)	4	4.0
Blood pH	<7.35 (Low)	81	81.0
	7.35–7.45 (Normal)	19	19.0
Blood Glucose (mg/dL)	<300	34	34.0
	300–399	44	44.0
	≥400	22	22.0
Serum Bicarbonate (mEq/L)	<22	44	44.0
	22–28	38	38.0
	>28	18	18.0

Table 02 shows the distribution of severity of Diabetic Ketoacidosis (DKA) according to blood pH level among the study participants. Most patients (64.0%, n=64) were ranked as having severe DKA (pH <7.00). Moderate DKA (pH 7.00–7.24) was observed in 26.0% (n=26) of patients, while mild DKA (pH 7.25–7.30) was reported in 10.0% (n=10) of cases. These results have shown that severe DKA was the most common form of presentation of the cases included in the study.

Table 02*:* Distribution of DKA Severity Based on Blood pH (n = 100)

DKA Severity	Frequency (n)	Percentage (%)
Mild (pH 7.25–7.30)	10	10.0
Moderate (pH 7.00–7.24)	26	26.0
Severe (pH <7.00)	64	64.0

The relationship between severity of Diabetic Ketoacidosis (DKA) with levels of serum albumin is shown in Table 3. The mean serum albumin level was highest in the mild DKA group (1.70 ± 0.48 g/dL), and then was higher in the severe DKA group (1.34 ± 0.57 g/dL) than in the moderate DKA group (1.31 ± 0.55 g/dL). The mean serum albumin level of all subjects was 1.37 ± 0.56 g/dL. This study showed no statistically significant difference in serum albumin levels among the three DKA severity groups (F = 1.99, p = 0.142), suggesting that DKA severity was not statistically significantly associated with serum albumin level in this study.

Table 03*:* Association between Serum Albumin and DKA Severity

DKA Severity	Frequency n	Mean ± SD	F-value	P-value
Mild	10	1.70 ± 0.48		
Moderate	26	1.31 ± 0.55		
Severe	64	1.34 ± 0.57	1.99	0.142
Total	100	1.37 ± 0.56		

There is a relation between the Red Cell Distribution Width (RDW) and the severity of Diabetic Ketoacidosis (DKA) (Table 04). The mean RDW was highest among patients with mild DKA (2.80 ± 0.63%), followed by moderate DKA (2.42 ± 0.64%) and severe DKA (2.14 ± 0.50%). The study population had an overall mean RDW of 2.28 ± 0.59%. One-way ANOVA showed that there was significant difference between DKA severity groups (F = 7.32, p = 0.001) in statistical analysis. The results showed a significant correlation between RDW and severity of DKA.

Table 04*:* Association Between RDW and DKA Severity

DKA Severity	n	Mean ± SD	F-value	P-value
Mild	10	2.80 ± 0.63		
Moderate	26	2.42 ± 0.64		
Severe	64	2.14 ± 0.50	7.32	0.001*
Total	100	2.28 ± 0.59		

As shown in Table 05, the RDW-AR is associated with the severity of Diabetic Ketoacidosis (DKA). The patients with moderate DKA (2.11 ± 0.79) had the highest mean RDW-to-Albumin Ratio followed by those with mild DKA (1.85 ± 0.85) and severe DKA (1.78 ± 0.59). The overall mean RDW-to-Albumin Ratio was 1.87 ± 0.68. The results of one-way ANOVA revealed that there was no significant difference in RDW-to-Albumin Ratio between the three severity groups of DKA (F = 2.20, p = 0.117). This result indicates that this RDW to Albumin Ratio was not found to be significantly correlated with the severity of the DKA in the studied population.

Table 05*:* Association between RDW-to-Albumin Ratio and DKA Severity

DKA Severity	n	Mean ± SD	F-value	P-value
Mild	10	1.85 ± 0.85		
Moderate	26	2.11 ± 0.79		
Severe	64	1.78 ± 0.59	2.20	0.117
Total	100	1.87 ± 0.68		

The correlation between blood pH and serum albumin, RDW, RDW-to-Albumin Ratio in Diabetic Ketoacidosis patients is provided in Table 06. There was a weak, negative but not statistically significant correlation between serum albumin and blood pH with r = -0.047 and p = 0.643 respectively, using Pearson correlation analysis. In the same way, the blood pH levels were negatively correlated with RDW (r = -0.058, p = 0.569) and RDW-to-Albumin Ratio (r = -0.041, p = 0.685). None of these parameters was found to have statistically significant correlation with blood pH of the studied population as all the p-values were greater than 0.05.

Table 06*:* Correlation of Albumin, RDW, and RDW-to-Albumin Ratio with Blood pH

Variable	Pearson Correlation (r)	P-value
Albumin vs Blood pH	-0.047	0.643
RDW vs Blood pH	-0.058	0.569
RDW-to-Albumin Ratio vs Blood pH	-0.041	0.685

DISCUSSION

The present study was designed to assess the clinical relevance of RDW, serum albumin and RDW/albumin ratio in Diabetic Ketoacidosis (DKA). Most of the respondents were male (51.0%) and in the age group 41-60 years (61.0%). The most common presentation was severe DKA (64.0%). The results showed a significant difference among severity groups with respect to RDW level, suggesting that there was an association between RDW and severity of DKA. However, there was no significant correlation between the DKA severity and the serum albumin level or RDW-to-Albumin Ratio. In addition, there were no significant correlations between blood pH and serum albumin or RDW or RDW-to-Albumin Ratio [12]. enlisted 212 MAP and 89 SAP patients from January 2013 to December 2018. Groups' biochemical analysis, prediction scores, and general features were compared. We used the receiver operating characteristic (ROC) curve to assess the sensitivity and specificity of the RDW-to-ALB ratio, RDW, ALB, and other predictive scores in early acute pancreatitis (AP) patients.In the present study, moderate and severe DKA were associated with decreased serum albumin levels as compared with mild DKA, but this was not statistically significant (p = 0.142). This is partially inconsistent with the study performed by [13], quoted by [14], who found that the low level of serum albumin was linked to higher urinary ketone levels and the incidence of DKA. [14]. Also noted that the hypoalbuminemia can be associated with greater inflammatory activity and poorer clinical outcomes in DKA patients [15]. A strong link exists between RA and 90-day and 365-day mortality rates for DKA patients in the ICU (HR: 2.1, 95% CI: 1.5, 3.0, p < 0.001). High RA was independently linked to higher 90-day and 365-day death rates (HR: 7.8, 95% CI: 1.8, 34.0, p for trend <0.001). Additionally, RA independently predicts sepsis and septic shock in DKA patients (HR: 2.9, 95% CI: 2.0, 4.1, p<0.001). Controlling for variables did not affect the statistical findings. The present study found no significant connection between RDW-to-Albumin Ratio and DKA severity (p = 0.117). This is different from the results reported by (16, 17)that patients with DKA had a significantly higher incidence of sepsis, septic shock, 90 day and 3 65 day mortality rates when they had a high RDW-to-Albumin Ratio (RA).

They discovered that patients with hypoalbuminemic DKA had more ketones in their urine than those with normoalbuminemic DKA. Our article and this outcome were comparable. The aforementioned report showed an increase in HR of RDW in DKA patients; however the changes in variables were less than those found in our study [18, 19]. Additionally, [20]. Found that RA predicts death in acute respiratory distress syndrome more accurately than RDW. All of the findings suggested that RA might be a better predictor than RDW alone.

STUDY LIMITATION

This study is limited. This study was confined to a small sample of hospitals, which may limit generalisation. Second, the cross-sectional design hindered post-therapy RDW, serum albumin, and RDW-to-Albumin Ratio assessment. Third, diabetes duration, comorbidities, nutrition, inflammatory markers, and treatment response were ignored. Finally, only blood pH was used to measure DKA severity, even though additional clinical and biochemical indicators may be better.

CONCLUSION

This study examined the therapeutic importance of RDW, serum albumin, and RDW to Albumin Ratio (RAR) in Diabetic Ketoacidosis (DKA) patients. The results showed a statistically significant link between DKA severity and RDW, suggesting that RDW may be a valuable and conveniently accessible technique to assess DKA severity. The RDW-to-Albumin Ratio did not significantly predict DKA severity. Additionally, blood pH did not correlate with serum albumin, RDW, or the RDW-to-Albumin Ratio. These findings suggest that RDW may be more clinically beneficial than serum albumin or RDW/Albumin Ratio for DKA severity evaluation.

RECOMMENDATION

The study demonstrated that RDW is a valuable laboratory indicator for Diabetic Ketoacidosis patients since it is linked to disease severity. Larger multicenter trials with more patients are needed to show RDW's DKA prognostic usefulness. Further study should explore other inflammatory and biochemical markers and the RDW-to-Albumin Ratio's predictive value in different patient groups. Detailed clinical and laboratory criteria may help identify and treat high-risk DKA patients.

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facilities for their cooperation and support during data collection.

CONFLICT OF INTEREST

The authors declare no conflict of interest

INFORMED CONSENT

Written informed consent was obtained from all participants before their enrollment in the study.

ETHICAL STATEMENT

The study was conducted in accordance with the ethical principles of the Declaration of Helsinki.

AUTHOR CONTRIBUTION

Conceptualization: [Aziz ur rehman]; Methodology: [HAMZA ULLAH]; Data Collection: [SAIF ULLAH]; Writing-Original Draft: [ASHFAQ AHMAD]; Writing-Review & Editing: [UBAID ULLAH, ABDUL MAJEED]; Supervision: [AZIX UR REHMAN]. All authors have read and approved the final version of the manuscript.

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