ECRONICON OPEN ACCESS

EC DIABETES AND METABOLIC RESEARCH

Research Article

Assessment of the Relationship between the Hematological Parameters Activity and Type 2 Diabetic Ketoacidosis in Intensive Care Unit

Muhammet Emin Naldan[1]*, Duygu Kara[2], Havva Tuğba Kiper Yilmaz[3], Faruk Yildiz[3], Kenan Çadirci[3] and Ayşe Çarlioğu[3]

[1]Anesthesia and Reanimation Department, Erzurum Region Training and Research Hospital, Erzurum, Turkey

[2]Anesthesia and Reanimation Department, Adnan Menderes University, Aydin, Turkey

[3]Internal Medicine Department, Erzurum Region Training and Research Hospital, Erzurum, Turkey

***Corresponding Author:** Muhammet Emin Naldan, Anesthesia and Reanimation Department, Erzurum Region Training and Research Hospital, Erzurum, Turkey.

Received: July 24, 2020; **Published:** September 30, 2020

Abstract

Objective: In the intensive care unit, we investigated the relationship between MPV (mean platelet volume), RDW (red cell width distribution), NLR (Neutrophil to lymphocyte ratio), PLR (platelet to lymphocyte ratio) markers to identify chronic inflammation between patients diagnosed with DKA, patients diagnosed with diabetes, and healthy volunteers.

Methods: Sixty-five patients with DM diagnosis were included in the study. Of these, 32 had DKA, 33 did not have any diabetes complications. Forty five completely healthy persons were included in the study. Healthy volunteers Group 1, Diabetes alone Group 2, DKA-recognized domains were defined as Group 3. The MPV, RDW, PLO, NLO values were obtained by performing a hemogram examination.

Results: The mean MPV of Group 1 was 6.6 ± 0.9 fl, Group 2 was 7.7 ± 0.7 and Group 3 was 8.6 ± 1.6. There was a significant difference between groups in terms of MPV ($p < 0.001$). Positive correlation between serum NLR and RDW, PCT, PLR, MPV, age, AST, ALT, Basophil, MCHC, MCV, Hgb, Wbc, Plt, Neutrophil values; There was a negative correlation between albumin, SPO2, HCO3, pH and GCS values. MPV values correlated with HCO3, GKS, RDW, SPO2, NLR and pH values.

Conclusion: Elevated levels of NLR, PLR, MPV and RDW in patients with DKA lying in intensive care unit ere potential showed the presence of the inflation and mortalities were increased in these patients.

Keywords: *Diabetic Ketoacidosis; Hematological Parameters; ICU*

Introduction

Most of the Type 2 diabetes mellitus patients are admitted with DKA to the intensive care unit as they require intensive treatment. Diabetic Ketoacidosis (DKA) is a rare and fatal hyperglycemic crisis that occurs in patients with both Type 1 and 2 diabetes mellitus. It is characterized by uncontrolled hyperglycaemia, high concentration of ketone bodies, acidosis. Due to the delays in the diagnosis of DKA, the risk of advanced complications increases [1]. If DKA is not treated properly, it can be life-threatening. Because of its increasing incidence and economical impact, effective definition, management and prevention is strongly recommended.

Several methods have been studied in clinical trials, such as looking at the amount of ketone and için APACHE 2 II score for predicting DKA [2,3]. However, tests that are practical, easy to apply, cost effective and prognostic enough are not yet found. In our study, we planned

our study based on hemogram examination as an inexpensive method that has a permanent place in routine use. Predictive data were obtained for DKA.

In literature we have not seen any study about the relationship between the NLR, PLR, RDW and MPV and type 2 diabetic ketoacidosis patients in intensive care unit.

Materials and Methods

Following ethical approval from the Erzurum Regional Training and Research Hospital Ethical Committee, files of all diabetic ketoacidosis patients aged mean 56, 56 year and who had been hospitalized in Anesthesiology and Reanimation ICU in the previous 7 years, were analyzed retrospectively.

We have three groups; first group hasn't any diabetic symptom it was control group. Second group has tip 1 DM but was not diabetic ketoacidosis. Third group was Diabetic Ketoacidosis (DKA) in DKA group laboratory findings were collected during when patients were in intensive care unit. A total of 110 patients (44 male, 66 female; mean age 52.07 ± 17.74); 45 patients control group (19 male, 26 female), 33 patients Tip 2 DM group (12 male, 21 female) and 32 patients DKA group (13 male, 19 female) were selected to the study.

Biochemical parameters

The following parameters were analyzed with a Siemens ADVIA 2400 instrument (Tarrytown, NY, USA): fasting glucose (70 - 105 mg/dL), urea (10 - 50 mg/dL), creatinine (0.50 - 1.2 mg/dL), uric acid (3.4 - 7.0 mg/dL), aspartate transaminase (AST, 0 - 38 U/L), alanine aminotransferase (ALT, 0 - 41 U/L), total cholesterol (110 - 200 mg/dL), high density lipoprotein (HDL) cholesterol (35 - 65 mg/dL), LDL cholesterol (60 - 130 mg/dL), triglycerides (< 150 mg/dL).

The statistical analysis was performed using SPSS version19,0 (IBM SPSS, Chicago, USA). Comparisons between groups were done using Student's t-test or Mann-Whitney U test for continuous data. One-tailed Pearson's correlation test or Spearman correlation test were done to find the correlation between various variables. Logistic regression analysis was done whenever appropriate. Chi-square test, chi-square with yates correction and fisher's exact test, wherever applicable, were done to test the association between two findings. ROC curve analysis assessed the cut-off MPV with the best diagnostic accuracy for detecting DTC. $P < 0.05$ was considered statistically significant.

We used an automated blood cell counter. A complete blood count (CBC) and biochemical analyses were obtained from hospital records at the clinic. We investigated NLR, RDW, MPV, WBC, HbA1c, PCT, PDW, MCHC, BUN, KREATİNİN, GKS, Arterial Blood Gases, Crp, FBG (Fasting Blood Glucose), AST, ALT, GGT, ALP, GGT, BMI. Body mass index (BMI) was calculated by using Quetlet index with weigh/height^2 formula.

NLR was noted as a simple ratio between the absolute neutrophil and the absolute lymphocyte counts. WBC, PCT, MCHC, NLR, MPV, PLR and RDW were derived from the CBC (Complete Blood Cell).

Results

Binary logistic regression analysis was also performed to define the variables associated with diagnosis of diabetes in whole group (Table 1) and impaired glucose regulation (HbA1c ≥ 7%) in diabetic patients.

Values are given as mean ± SD; $p < 0.05$ is significant. WBC: white blood cell count; RBC: red blood cell count; HGB: hemoglobin; HCT: hematocrit; MCV: mean cell volume; MCH: mean cell hemoglobin; MCHC: mean cell hemoglobin concentration; RDW: red cell distri-

	Control group (n = 45)	Type 2 DM group (n = 33)	DKA group (n = 31)
WBC (×10³ mm⁻³)	8,06 ± 3,25	8,11 ± 2,35	15,62 ± 6,82
HGB (g/dL)	14,58 ± 1,54	14,44 ± 1,42	13,42 ± 2,71
HCT (%)	44,09 ± 3,97	46,37 ± 5,04	39,96 ± 7,48
MCV (fL)	84,99 ± 4,84	85,46 ± 4,41	88,02 ± 6,55
MCHC (g/dL)	12,89 ± 0,77	32,85 ± 0,07	33,22 ± 2,31
RDW (%)	9,94 ± 3,85	14,26 ± 0,51	15,22 ± 3,47
PLT (×10³ mm⁻³)	274,46 ± 55,52	297,00 ± 82,14	287,86 ± 121,70
MPV (fL)	6,66 ± 1,01*	7,76 ± 0,75*	8,74 ± 1,77*
PCT (%)	0,15 ±	0,21 ± ,014	0,22 ± ,096
PDW (%)	19,35 ± 1,14	18,31 ± 0,55	17,97 ± 1,36
Lym# (×10³ mm⁻³)	2,41 ± 0,65	2,73 ± 0,04	4,62 ± 3,40
Neu# (×10³ mm⁻³)	3,47 ± 1,83	4,56 ± 1,18	12,27 ± 6,46
NLR	1,73 ± 0,78	1,67 ± 0,46	3,34 ± 2,97
PLR	119,15 ± 47,71	130,38 ± 20,93	97,86 ± 79,95
CRP (mg/L)	1,70 ± 1,76	1,73 ± 3,64	29,36 ± 81,99
GKS	15 ± 0	15 ± 0	9,72 ± 4,71
AGE	46,93 ± 20,71	54,73 ± 11,05	56,56 ±
BMI	24,64 ± 3,26	31,34 ± 4,51	25,78 ± 3,69
HbA1C	6,12 ± 1,38**	8,75 ± 1,97**	10,44 ± 2,68**

Table 1: *Hemogram parameters.*

bution width; PLT: platelet count; MPV: mean platelet volume; PCT: platelet crit; PDW: platelet distribution width; Lym#: lymphocyte count; Mo#: monocyte count; Neu#: neutrophil count; Eo#: eosinophil count; Ba#: basophil count; Lym%: lymphocyte percentage; Mo%: monocyte percentage; Neu%: neutrophil percentage; Eo%: eosinophil percentage and Ba%: basophil percentage. 0.05 for HH patients compared with control.

* $p < 0.05$ for control compared with other groups.

**$p < 0.05$ for DKA compared with other groups.

The correlation between NLR, RDW, MPV, PLR, PCT, PDW and hematological, biochemical parameters were tested using bivariate correlation analysis.

Positive correlation between serum NLR and Rdw, Group, PCT, PLR, MPV, Age, AST, ALT, Basophil, MCHC, MCV, Hgb, Wbc, Plt, Neu were determined.

Negative correlation between serum NLR and Albumin, Hgb, SPO_2, HCO_3, pH, GKS were determined.

Positive correlation between serum Rdw and MPV, PLR, Group, Neu, Plt, Wbc, MCHC, Basophil, FBG, Creatinine were determined.

Negative correlation between serum Rdw and Pdw, Age, Albumin, SPO_2, HCO_3, pH, GKS were determined.

A ROC analysis was performed for all parameters and NLR. The NLR cut off value was 1.6 (AUC: 0.68; p < 0.01; 95% CI: 0.54 - 0.81; 71.9% sensitivity; 59% specificity) (Figure 1). All patients were categorized into two groups according to their NLR value: patients with NLR < 1.6 were assumed to be NLR negative, and all others were assumed to be NLR positive. The CRP cut off value was 0.51 (AUC: 0.84; p < 0.000; 95% CI: 0.75 - 0.94; 93% sensitivity; 60% specificity). The MPV cut off value was 0.7.5 (AUC: 0.78; p < 0.000; 95% CI: 0.67 - 0.88; 80% sensitivity; 54% specificity). The PLR cut off value was 92 (AUC; p < 0.000; 95% CI: 0.75 - 0.94; 62.5% sensitivity; 80% specificity). The RDW cut off value was 12.4 (AUC: 0.88; p < 0.000; 95% CI: 0.81 - 0.96; 90% sensitivity; 77% specificity).

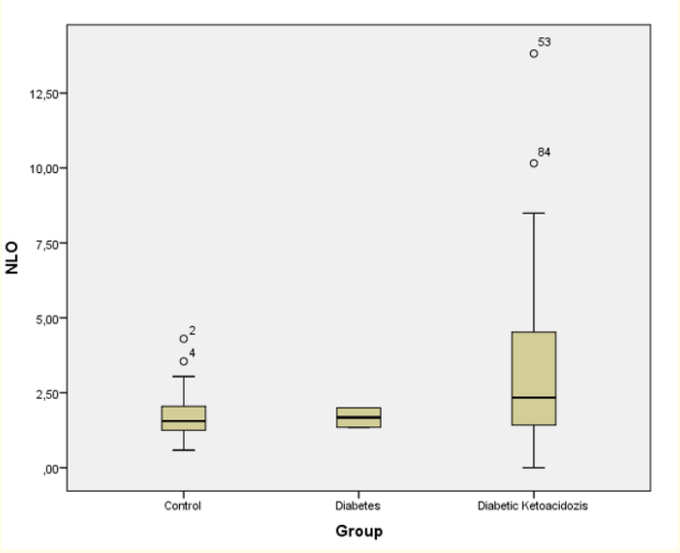

Figure 1

Diabetes and uncontrolled hyperglycemia are known to play a significant role in the development of cardiovascular disease (CVD) since Framingham study [1,4]. Elevated white blood cell count (WBC) is a classical inflammatory marker and is associated with several cardiovascular disease risk factors and diabetes [5-9]. We noticed our DKA patients have higher PLR, WBC, PCT, MCHC, NLR, MPV, RDW, MCHC, CRP.

In patients with DKA, Mpv was found to be high independent of Age, BMI, Genus, Crp.

Results

MPV values were significantly higher in DKA (Figure 2).

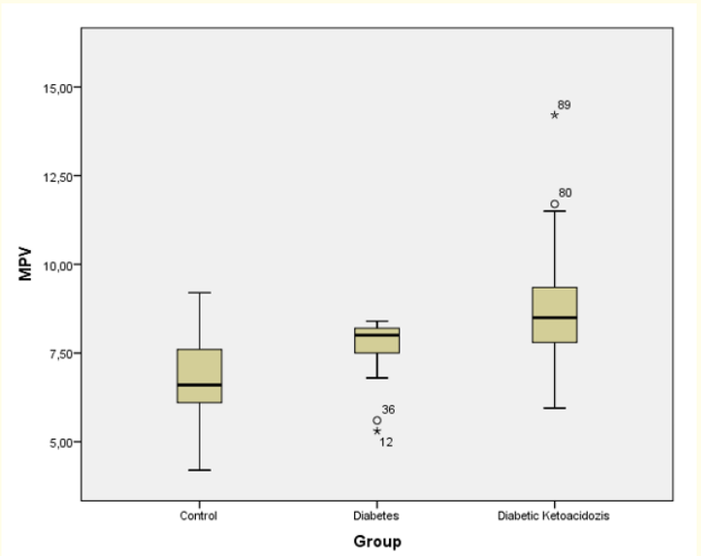

Figure 2

HbA1C values were significantly higher in DKA.

The NLR ratio was significantly higher in DKA.

CRP was significantly higher in DKA.

WBC values were significantly higher in DKA.

Creatinine values were significantly higher in DKA.

RDW value was significantly higher in DKA.

There is no difference between the groups in terms of PLR.

The Hb value was significantly lower in DKA.

GKS was significantly lower in DKA.

PH, SPO_2, HCO_3 values were significantly poor in DKA.

Albumin values were significantly lower in DKA.

There was a significant negative correlation between NLR and GCS when the correlation was made.

There is a significant negative correlation between NLR and pH, HCO_3, SPO_2 in correlation.

When multiple logistic regression was performed, MPV values were significantly higher in age, BMI, CRP and gender in DKA than

- For MPV > 7.5, DKA senses sensitivity to 80% specificity 54%.
- The DKA for NLR > 1.6 specifies a sensitivity of 71% to a specificity of 59%.
- For RDW > 12.4, DKA senses sensitivity 90% specificity 77%.

Variables	NLR		RDW		MPV		PLR		PCT		PDW	
	r	p	r	p	r	p	r	p	r	p	r	p
NLR	-	-	0,34 0.402	0.005	0,27	0.027	0.40	0.001	0.53	0.001	-0.31	0.059
Rdw	0.34	0.005	-	-	0.49	0.000	0.133	0.287	0.301	0.079	-0.314	0.030
MPV	0.275	0.027	0.493	0.000	-	-	-0.141	0.263	-0.334	0.053	-0.120	0.424
PLR	0.407	0.001	0.133	0.287	-0.141	0.263	-	-	0.465	0.005	-0.121	0.481
PCT	0.538	0.001	0.301	0.079	-0.334	0.053	0.465	0.005	-	-	-0.391	0.022
PDW	-0.318	0.059	-0.314	0.030	-0.120	0.424	-0.121	0.481	-0.391	0.022	-	-
Age	0.250	0.043	-0.163	0.153	0.106	0.277	0.090	0.474	-0.184	0.291	-0.273	0.061
Group	0.351	0.004	0.581	0.000	0.583	0.000	-0.162	0.195	0.120	0.493	-0.449	0.001
Neu	0.680	0.000	0.467	0.000	0.481	0.000	-0.099	0.429	0.452	0.006	-0.313	0.030
Plt	0.377	0.002	0.106	0.357	-0.319	0.001	0.456	0.000	0.893	0.000	-0.331	0.022

CRP	0.086	0.634	-0.031	0.862	0.269	0.034	-0.227	0.205	-0.200	0.265	-0.032	0.864
GKS	-0.417	0.000	-0.428	0.000	-0.550	0.000	0.045	0.718	0.158	0.366	0.212	0.147
pH	-0.382	0.014	-0.653	0.000	-0.749	0.000	0.133	0.408	-0.209	0.237	0.446	0.002
HCO3	-0.410	0.001	-0.486	0.000	-0.482	0.000	0.124	0.320	-0.110	0.531	0.385	0.007
SPO2	-0.154	0.220	-0.338	0.003	-0.276	0.004	0.277	0.025	-0.173	0.329	0.217	0.143
WBC	0.603	0.000	0.642	0.000	0.307	0.001	-0.013	0.918	0.364	0.034	-0.143	0.337
HGB	-0.275	0.026	-0.200	0.080	-0.191	0.049	0.045	0.722	-0.078	0.655	0.225	0.124
MCV	0.434	0.000	-0.006	0.961	0.064	0.516	0.123	0.326	0.242	0.160	-0.178	0.226
MCHC	0.180	0.300	0.740	0.000	0.607	0.000	-0.407	0.015	0.023	0.899	-0.482	0.001
Basophil	0.568	0.000	0.187	0.209	-0.135	0.455	0.441	0.009	0.511	0.002	-0.128	0.478
FBG	0.233	0.062	0.374	0.001	0.460	0.000	-.210	0.093	-0.063	0.721	-0.290	0.053
Creatinine	-0.095	0.580	0.303	0.043	0.330	0.004	-0.243	0.153	-0.068	0.702	-0.117	0.451
Albumin	-0.241	0.169	-0.214	0.198	-0.360	0.007	-0.023	0.898	0.039	0.834	0.029	0.863
AST	0.156	0.371	0.070	0.646	0.241	0.039	-0.052	0.768	-0.050	0.778	0.016	0.920
ALT	0.192	0.269	0.073	0.632	0.259	0.025	-0.013	0.922	-0.059	0.742	-0.040	0.796

Table 2: *Bivariate correlation between hemogram parameters and other variables in DKA.*
p < 0.05 was accepted as statistically significant.

Variables	Cut-off value	AUC	95% Confidence Interval	Sensitivity	Specificity	P value
NLR	1.6	0.68	0.54 - 0.81	71.9	59	0.012
CRP	0.51	0,84	0.75 - 0.94	93	60	0.000
MPV	7.5	0.78	0.67 - 0.88	80	54	0.000
RDW	12.4	0.88	0.81 - 0.96	90	77	0.000

Table 3: *Receiver operating characteristic (ROC) analysis for the presence of DKA.*
p < 0.05 was accepted as statistically significant.

Variables	MPV		NLO		PLO		RDW	
	Beta	P	Beta	p	Beta	p	Beta	p
Mpv	1.377	0.003						
Age	-0.017	0.441	0.024	0.340	0.037	0.142	-0.009	0.729
BMI	0.104	0.478	0.226	0.223	0.125	0.363	0.137	0.314
Crp	0.317	0.048	0.409	0.045	0.422	0.086	0.409	0.065
Gender	-0.198	0.843	-0.233	0.810	-0.630	0.469	0.279	0.777

Table 4: *Regression analysis.*

Discussion

Patients in the ICU are at significantly increased risk of death and risk stratification is of paramount importance that it can better inform clinicians.

This is the first study to determine NLR, PLR, RDW and MPV levels in patients with type 2 diabetic ketoacidosis at the Intensive Care Unit with a healthy control group. And so, in this study we aimed to show the correlation between the NLR, PLR, RDW and MPV and intensive care unit patients admitted with DKA table and also investigated whether one of these parameters can be used for a diagnosis of Type 2 DKA.

High-out of NLR, PLR, RDW, and MPV levels in patients with DKA at the Intensive Care Unit is the presence of a potential inflammation and increased in mortality in these patients.

Inflammation is closely associated with both secretory function of beta cell and insulin resistance [5,6]. Circulating inflammatory molecules can decrease beta cell functions directly by secretory dysfunction or uncontrolled apoptosis [5,7]. As a result glucotoxicity and lipotoxicity occurs and causes enhanced inflammatory process and a vicious cycle [7].

In recent years, there has been renewed interest in hematological parameters such as white blood count (WBC), mean platelet volume (MPV), platelet distribution width (PDW), platelet crit (PCT), platelet count, platelet to lymphocyte ratio (PLR) and neutrophil to lymphocyte ratio (NLR) and are designated as predictors of endothelial dysfunction and inflammation. Elevated WBC is a classical inflammatory marker and reveals association of inflammation with impaired glucose metabolism, insulin resistance and DM [8,9]. The association of increased MPV, PDW, PCT and platelet count with diseases related to endothelial dysfunction and inflammation as metabolic syndrome, diabetes, coronary artery disease and malignancy have been shown [10,11]. In the last decades, PLR and NLR were introduced as potential markers to determine inflammation in cardiac and noncardiac disorders [11,12].

Shao-Gang Ma., *et al*. showed that the platelet parameters were significantly elevated in patients with Type 1 DKA compared with the parameters in non-DKA and control subjects [1]. Zhang., *et al*. showed that higher mean platelet volume (MPV) and platelet distribution width are associated with increased risk of death, whereas the decrease in platelet crit is associated with increased mortality risk [13].

Many investigators have suggested that MPV reflects disease activity, inflammatory load, and/or systemic inflammation in many diseases such as hypertension, myocardial infarction, rheumatoid arthritis, FMF and acute pancreatitis [14,15]. Patients with type 2 diabetes mellitus (T2DM) have an increased risk of coagulation abnormalities and thromboembolic events. Platelets have a key role and increased adhesion, activation, and aggregation of platelets due to dysregulation of several signaling pathways and metabolic disturbances including insulin resistance hyperglycemia, and dyslipidemia have been noted in diabetic patients [16,17]. Systematic inflammation, oxidative stress, impaired calcium metabolism, decreased bio availability of nitric oxide, increased phosphorylation and glycosylation of cellular proteins are responsible for increased platelet activation and increased release of prothrombotic and proinflammatory agents in diabetes [18]. Larger platelets which can be demonstrated by increased MPV are more active because of elevated prothrombic contents, such as thromboxane A2, thromboxane B2, platelet factor 4, serotonin, and platelet-derived growth factor [19]. The platelet parameters can be determined by a routine blood counting system. Association of increased MPV with prediabetes, diabetes and vascular diabetic complications are stated in the literature [20-22]. Moreover, association of MPV and impaired glucose regulation in diabetic patients also reported [23]. As with MPV, increased PDW is also reported to be associated with diabetes and vascular complications [20,24-26]. Performed studies did not report a relation between increased PCT, diabetes and related complications [20,26,27]. Conflicting results have been reported for the relation of platelet count and diabetes. Several studies reported no relation [20,23,24] while some reported positive association [21,28] between diabetes and platelet count. In this study, the platelet parameters were significantly elevated in patients with DKA compared with the parameters in non-DKA and control subjects. Discriminant analysis using PDW and MPV could distinguish the majority of patients with DKA. Statistical evaluation revealed that the PDW can be a risk marker for DKA.

In this study, we found that PLR and MPV levels are higher in patients with DKA and, furthermore, MPV was also correlated with CRP. However, the link between MPV and CRP is still weaker than the link between MPV and NLR.

The ROC analysis showed that the five variables (RDW, CRP, PLO, NLO, MPV) can predict the presence of DKA. DKA is an acute complication of bad controlled or freshly diagnosed type 2 diabetes. It has been noted that the pathophysiology of DKA is associated with an elevated level of oxidative stress [29,30]. And active systemic inflammatory processes [31].

Patients in the ICU are at significantly increased risk of death, and risk stratification is of paramount importance that it can better inform clinicians.

This is the first study to determine NLR, PLR, RDW, and MPV levels in patients with type 2 diabetic ketoacidosis at the Intensive Care Unit with a healthy control group. And so, in this study we aimed to show the correlation between the NLR, PLR, RDW and MPV and intensive care unit patients admitted with DKA table and also investigated whether one of the parameters can be used for a diagnosis of Type 2 DKA.

High-out of NLR, PLR, RDW and MPV levels in patients with DKA at the Intensive Care Unit is the presence of a potential inflammation and increased in mortality in these patients.

Results of the present study reveal that inflammation and tendency to coagulation and thrombosis can be detected with easy accessible and inexpensive hematological indices. However, large scaled studies need to be conducted in order to evaluate it suitability and efficiency.

Conclusion

Elevated levels of NLR, PLR, MPV and RDW in patients with DKA lying in intensive care unit are potential showed the presence of the inflation and mortalities were increased in these patients. NLR, PLR, MPV and RDW values may be indicative of the presence of a potential inflammation in patients with DKA in intensive care unit, which may be indicative of subclinical inflammation. Significant correlation with parameters related to mortality increase such as GCS, HCO_3, SPO_2, pH emphasizes the importance of the following simple markers.

Conflicts of Interest

None declared.

Ethical Approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed Consent

Informed consent was obtained from all individual participants included in the study.

Bibliography

1. Ma SG., *et al.* "Assessment of the platelet parameters and serum butyrylcholinesterase activity in type 1 diabetes patients with ketoacidosis". *Platelets* 24.7 (2013): 544-548.

2. Safari S., *et al.* "Can APACHE II Score Predict Diabetic Ketoacidosis in Hyperglycemic Patients Presenting to Emergency Department?" *Anesthesia and Pain Medicine* 4.4 (2014): e21365.

3. Misra S and N Oliver. "Utility of ketone measurement in the prevention, diagnosis and management of diabetic ketoacidosis". *Diabetic Medicine* 32.1 (2015): 14-23.

4. Jindal S., *et al.* "Platelet indices in diabetes mellitus: indicators of diabetic microvascular complications". *Hematology* 16.2 (2011): 86-89.

5. Das A and S Mukhopadhyay. "The evil axis of obesity, inflammation and type-2 diabetes". *Endocrine, Metabolic and Immune Disorders - Drug Targets (Formerly Current Drug Targets-Immune, Endocrine and Metabolic Disorders)* 11.1 (2011): 23-31.

6. Akbas M., *et al.* "The emerging role of Sirtuin1,-3 and-4 in glucose and lipid metabolism and in diabetes mellitus". *Journal of Molecular and Genetic Medicine* 1 (2014): 1747-0862.

7. Agrawal NK and S Kant. "Targeting inflammation in diabetes: Newer therapeutic options". *World Journal of Diabetes* 5.5 (2014): 697.

8. Twig G., *et al.* "White blood cells count and incidence of type 2 diabetes in young men". *Diabetes care* (2012): 112298.

9. Vozarova B., *et al.* "High white blood cell count is associated with a worsening of insulin sensitivity and predicts the development of type 2 diabetes". *Diabetes* 51.2 (2002): 455-461.

10. Omu A., *et al.* "Butyrylcholinesterase activity in women with diabetes mellitus in pregnancy: correlation with antioxidant activity". *Journal of Obstetrics and Gynaecology* 30.2 (2010): 122-126.

11. Tavil Y., *et al.* "Coronary heart disease is associated with mean platelet volume in type 2 diabetic patients". *Platelets* 21.5 (2010): 368-372.

12. Turkmen K., *et al.* "Platelet-to-lymphocyte ratio better predicts inflammation than neutrophil-to-lymphocyte ratio in end-stage renal disease patients". *Hemodialysis International* 17.3 (2013): 391-396.

13. Zhang Z., *et al.* "Platelet indices are novel predictors of hospital mortality in intensive care unit patients". *Journal of Critical Care* 29.5 (2014): 885.

14. Kaya A., *et al.* "Relation of neutrophil to lymphocyte ratio with the presence and severity of stable coronary artery disease". *Clinical and Applied Thrombosis/Hemostasis* 20.5 (2014): 473-477.

15. Akbas EM., *et al.* "Predictors of epicardial adipose tissue in patients with type 2 diabetes mellitus". *Diabetology and Metabolic Syndrome* 6.1 (2014): 55.

16. Kim JH., *et al.* "Response: clinical marker of platelet hyperreactivity in diabetes mellitus". *Diabetology and Metabolic Syndrome* 38.2 (2014): 160-161.

17. Suslova TE., *et al.* "Platelet hemostasis in patients with metabolic syndrome and type 2 diabetes mellitus: cGMP-and NO-dependent mechanisms in the insulin-mediated platelet aggregation". *Frontiers in Physiology* 5 (2015): 501.

18. El Haouari M and JA Rosado. "Platelet signalling abnormalities in patients with type 2 diabetes mellitus: a review". *Blood Cells, Molecules and Diseases* 41.1 (2008): 119-123.

19. Yuri Gasparyan A., *et al.* "Mean platelet volume: a link between thrombosis and inflammation?" *Current Pharmaceutical Design* 17.1 (2011): 47-58.

20. Jabeen F., *et al.* "Role of platelet indices, glycemic control and hs-CRP in pathogenesis of vascular complications in type-2 diabetic patients". *Pakistan Journal of Biological Sciences* 29.1 (2013): 152.

21. Lippi G., *et al.* "The mean platelet volume is significantly associated with higher glycated hemoglobin in a large population of unselected outpatients". *Primary Care Diabetes* 9.3 (2015): 226-230.

22. Zuberi B., *et al.* "Comparison of mean platelet volume in patients with diabetes mellitus, impaired fasting glucose and non-diabetic subjects". *Singapore Medical Journal* 49.2 (2008): 114.

23. Ozder A and HH Eker. "Investigation of mean platelet volume in patients with type 2 diabetes mellitus and in subjects with impaired fasting glucose: a cost-effective tool in primary health care?" *International Journal of Clinical and Experimental Medicine* 7.8 (2014): 2292.

24. Zaccardi F., *et al.* "Platelet mean volume, distribution width, and count in type 2 diabetes, impaired fasting glucose, and metabolic syndrome: a meta-analysis". *Diabetes/Metabolism Research and Reviews* 31.4 (2015): 402-410.

25. Xiao W., *et al.* "Relationship between platelet volume indices with macrovascular and peripheral neuropathy complications in type 2 diabetic patients". *Journal of Diabetes* 6.4 (2014): 298-303.

26. Erdoğan S., *et al.* "Liver enzymes, mean platelet volume, and red cell distribution width in gestational diabetes". *Turkish Journal Of Medical Sciences* 44.1 (2014): 121-125.

27. Citirik M., *et al.* "MPV may reflect subcinical platelet activation in diabetic patients with and without diabetic retinopathy". *Eye* 29.3 (2015): 376.

28. Akinsegun A., *et al.* "Mean platelet volume and platelet counts in type 2 diabetes: mellitus on treatment and non-diabetic mellitus controls in Lagos, Nigeria". *The Pan African Medical Journal* (2014): 18.

29. Abbott C., *et al.* "Relationship between serum butyrylcholinesterase activity, hypertriglyceridaemia and insulin sensitivity in diabetes mellitus". *Clinical Science* 85.1 (1993): 77-81.

30. Ma Sg., *et al.* "Increased serum levels of ischemia-modified albumin and C-reactive protein in type 1 diabetes patients with ketoacidosis". *Endocrine* 42.3 (2012): 570-576.

31. Stentz FB., *et al.* "Proinflammatory cytokines, markers of cardiovascular risks, oxidative stress, and lipid peroxidation in patients with hyperglycemic crises". *Diabetes* 53.8 (2004): 2079-2086.

Volume 4 Issue 10 October 2020