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PJBS

ISSN 1028-8880

Pakistan Journal of Biological Sciences

ANSInet
Asian Network for Scientific Information
308 Lasani Town, Sargodha Road, Faisalabad - Pakistan

OPEN ACCESS Pakistan Journal of Biological Sciences

ISSN 1028-8880
DOI: 10.3923/pjbs.2023.279.286

Research Article
Impact of Uncontrolled Diabetes Mellitus on Blood Cells Indices and Plasma Components in Patients Without Nephropathy

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Abstract

Background and Objective: Diabetes mellitus (DM) the most prevalent consequences are diabetic retinopathy, neuropathy, cardiovascular illnesses, erectile dysfunctions, stroke and cardiovascular difficulties. The main goal of this study was to evaluate the impact of uncontrolled diabetes mellitus on blood cells' indices and plasma components. **Materials and Methods:** This is a prospective cross-sectional study. The research was carried out at the King Fahad Medical Center in Riyadh, in duration from February, 2023 to May, 2023, in the interest of healthcare consumers attending the hematology laboratory for routine investigations. Sixty samples were collected and complete blood count, lipid profile, HbA1c and blood glucose for blood samples. **Results:** In this study, females accounted for 53.3% of the participants, while males accounted for 46.7%. In terms of age distribution, more than 55 years old accounted for 50% of the study's participants. A significant correlation has been found between HbA1c and red blood cell Mean Cell Volume (MCV) and there was a significant association between the high level of HbA1c and the red blood count. However, there was no significant correlation between plasma components and HbA1c. **Conclusion:** There is a remarkable effect of uncontrolled diabetes mellitus and RBCs count and erythrocyte MCV.

Key words: Diabetes mellitus, HbA1c, Mean Cell Volume (MCV), platelets, WBCs, plasma components

Citation: Waggiallah, H.A., H.E. Khair, R.S. Suliman, H. Al Shmrany and E.E. Elkhider *et al*., 2023. Impact of uncontrolled diabetes mellitus on blood cells indices and plasma components in patients without nephropathy. Pak. J. Biol. Sci., 26: 279-286.

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Competing Interest: The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

According to the World Health Organization, a fasting blood glucose level of below 6.1 mg dL^{-1} is considered normal and 6.1-7 indicates diminished HbA1c (%) (glycated hemoglobin (%)) is a more reliable and essential method of categorizing different 'shades' of diabetes. It is a straightforward assessment of glucose's connection to adult hemoglobin HbA when it is below 6%, it is normal, if the range is 6-7, it indicates pre-diabetes or an extreme situation, while if it is greater than 7%, it indicates diabetes. Despite of diabetes is widely recognized as an important predictor for CVD, the damage done to erythrocytes has received little attention, with the exception of a few isolated studies[1]. Erythrocytes, also known as Red Blood Cells (RBCs), are the cells that consume the greatest amount of glucose erythrocyte shape, metabolism and function are all affected by chronic hyperglycemia affecting hemorheology and microcirculation[2].

The MCV refers to erythrocyte volume and is commonly measured indirectly. Indicate increased MCV instability, which is typically produced by erythrocyte maturation or degradation disturbances. The MCV and RDW increase imply variability in erythrocyte size. The MCV and the RDW were both associated with HbA1c and the presence of diabetic retinopathy[3]. The MCV has additionally been identified as a possible risk indicator for the development of peripheral artery disease and to be connected to disease severity, thus, it can be used to predict diabetic macrovascular consequences[4].

People with diabetes have elevated atheromatous plaque stress as well as thrombotic diathesis, which is triggered in part by alterations in the coagulation system, such as elevated fibrinogen levels in the plasma, higher intravascular thrombin generation and reduced fibrinolytic capability[5]. Diabetes mellitus is characterized by hyperglycemia, which is associated with macrovascular disease even in the pre-diabetic phase. Hyperglycemia, particularly postprandial hyperglycemia, contributes an essential function in the development of cardiovascular disease illness associated with diabetes, as well as the DM prothrombotic condition[6].

White Blood Cell (WBC) count is linked to an increased risk of cardiovascular mortality in T2DM patients[7]. Increased Plasminogen Activator Inhibitor-1 (PAI-1) and white blood cell counts, as well as cytokine measures, can be used to detect inflammatory immunological responses. Due to the statistical correlation between insulin sensitivity and WBCs, it has been suggested that dysfunction could have a significant role in the progression of type 2 diabetes[8].

Hyperglycemia enhances platelet activation both directly and via increasing platelet protein glycation. Both insulin resistance and insulin deficiency[9] elevate platelet responsiveness and hyperglycemia may boost platelet reactivity by generating nonenzymatic glycation of proteins on the platelet's surface. This type of glycation reduces membrane fluidity and enhances platelet activation[10]. The osmotic action of glucose is a second method by which hyperglycemia might increase platelet reactivity[11]. Protein kinase C activation is a third mechanism by which hyperglycemia can raise platelet sensitivity. Protein kinase C has an important role in activated platelets[12].

Higher WBC levels have been linked to the progression of diabetes complications[11]. The WBCs can also be produced by inflammatory responses, angiotensin II and glycemic end-products associated with hyperglycemia and they can activate proteins like interleukin 1 and Tumor Necrosis Factor (TNF) that are related to severe diabetes pathophysiology and health problems[13]. The goal of the current research was to find out if there was any correlation between CBC and diabetes.

MATERIALS AND METHODS

This prospective cross-sectional study was undertaken for patients at the Clinical Center in Riyadh from November, 2022 to February, 2023. The participants included in this study were patients attending hematology laboratory for routine investigations, 60 samples were collected and complete blood count, lipid profile, HbA1c and blood glucose for blood samples.

Inclusion criteria: Patients without nephropathy only were included in this study.

Blood counter principle and technique: The method was created primarily for rapidly counting blood cells by monitoring variations in electrical conductance when cells suspended in a conductive fluid passed through a tiny opening current, over 98% of automated cell counters use this type of technology, known as the Coulter Principle[14].

HbA1c principle and technique: The hemoglobinA1c (glycated hemoglobin) examination measures an individual's sugar management. The test represents a percentage of the average blood sugar level over the previous 90 days. Diabetes can also be determined using this test[15].

Lipid profile principle and technique: Lipid profile (calculated LDL, total cholesterol, HDL cholesterol and triglycerides). The Ortho Vitros Clinical Chemistry System 950IRC instrument (Johnson & Johnson Clinical Diagnostics, Rochester, New York) is used to perform these assays and use a colorimetric reaction to determine lipid levels quantitatively. Total cholesterol, HDL cholesterol, LDL cholesterol and

triglycerides are the four basic characteristics of the test. It typically occurs on fasting blood samples. Fasting is defined as a 12-14 hrs nocturnal eating limitation with an allowance of water and medicine[16].

Statistical analysis: The Statistical Program for Social Studies (SPSS version 21.0) was used to manage the data. The Pearson Chi-square Test and T-Test for statistical significance (p-value), as well as the Z Test for two percentages at a 95% confidence level, were used to test for significant variations in Kidd interactions found in this research, with the outcome disclosing statistical relevance at $p<0.05$.

Ethical approval: The Institutional Ethics and Research Commission of Prince Sattam Bin Abdulaziz University awarded ethical permission. Participation was voluntary and verbal consent was acquired from each participant.

RESULTS

Socio-demographic characteristics of the study: Table 1 depicts the socio-demographic distribution of study participants as well as the gender distribution, with females accounting for 53.3% and males accounting for 46.7%. In terms of age distribution, the age group of more than 55 years accounted for 50% of the participants in the study.

Table 2 displayed the average measurements of blood cells and the substances in plasma that depicted the body's metabolic picture. Figure 1 depicts the HbA1c and RBC counts. A significant link was detected between them, with a p-value of 0.029. Figure 2 depicts the statistically significant link between HbA1c and MCV of red blood cells, with a p-value of 0.020.

Table 1: Socio-demographic characteristics of the study participants (n = 60)

Variables	Number of respondents	Proportion (%)
Gender		
Male	28	46.7
Female	32	53.3
Age group		
16-28 years	14	23.3
42-54 years	16	26.7
>55 years	30	50.0
Age in years	Mean±SD	Range
	51.4±19.7	16-60

Table 2: Measures for central tendency for chemical, clinical, metabolic and erythropoietic markers

Markers	Mean±SD	Median	Range
Sodium	140.5±2.4	139.5	139.0-144.0
Potassium	4.6±0.5	4.7	4.1-5.1
Chloride	105.5±3.3	104.5	103.0-110.0
Bi-carbonate	24.0±1.8	24.0	22.0-26.0
Anion	15.5±2.5	16.0	12.0-18.0
Urea	7.7±2.8	8.8	3.6-9.6
Creatinine	89.1±38.6	76.0	41.0-173.0
Glucose	10.5±5.3	8.6	6.0-25.3
HbA1c	8.7±1.9	8.2	6.3-15.1
White blood cell	7.9±2.1	7.8	4.9-14.6
RBCs	5.1±0.5	5.2	4.2-6.1
Hb	133.7±18.9	132.5	95.0-176.0
Hematocrit	0.4±0.1	0.4	0.3-0.5
MCV	81.1±8.6	83.4	63.0-94.9
MCH	26.2±3.4	26.9	19.0-31.2
MCHC	311.5±54.2	322.0	34.1-352.0
RDW	14.5±2.4	14.1	11.9-20.0
Platelets	303.0±83.8	299.4	169.0-513.0
MPV	10.4±2.2	10.7	0.0-12.6
NEUT (%)	58.1±11.5	52.8	44.3-76.7
LYMPHS (%)	29.4±8.8	31.0	15.6-41.2
Monocytes (%)	8.8±2.5	8.5	5.2-13.8
Eosinophils (%)	2.8±1.8	3.4	0.0-5.1
Basophilic (%)	0.9±0.5	0.9	0.2-1.6
NRBC count	0.0±0.0	0.0	0.0-0.1
NRBC Abs	0.0±0.0	0.0	0.0-0.0
Neutrophils Abs	4.8±2.4	4.1	2.4-10.5
Lymphocytes Abs	2.0±0.7	1.9	0.6-3.0
Monocytes Abs	0.7±0.2	0.6	0.5-1.0
Eosinophils Abs	0.2±0.2	0.2	0.0-0.5
Basophilic Abs	0.1±0.0	0.1	0.0-0.1

HbA1c: Hemoglobin A1c, Hb: Hemoglobin, MCV: Mean Cell Volume, MCH: Mean Cell Hemoglobin, MCHC: Mean Cell Hemoglobin Concentration, RDW: Red Cell Distribution Width, MPV: Mean Platelet Volume and NRBC: Nucleated Red Blood Cell

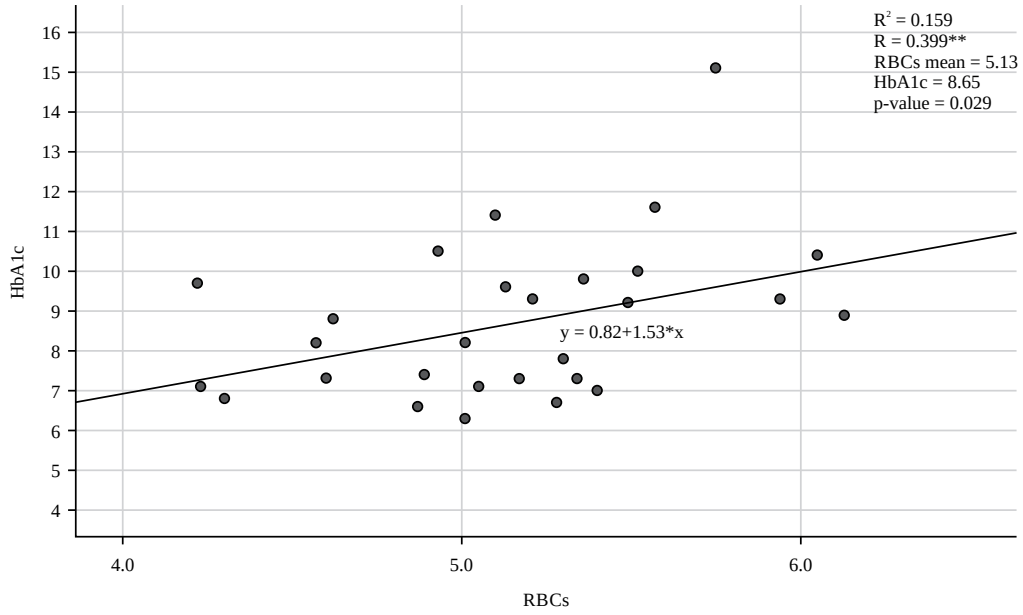

Fig. 1: Correlation between percentage HbA1c level with RBCs $\times 10^{12}$/L count

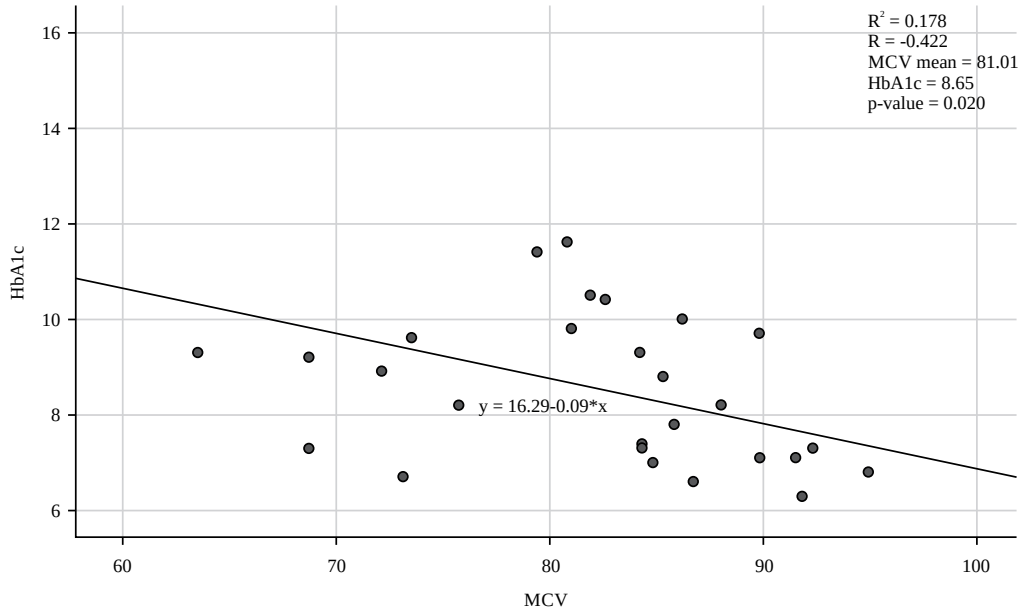

Fig. 2: Correlation between the percentage of HbA1c level with MCV/fL

Figure 3 depicted a significant and robust association between HbA1c and fasting blood glucose, with a p-value of 0.000.

Table 3 displayed the association between HbA1c and several blood chemical components relevant to kidney function tests, where a significant relationship is seen, indicating that the inclusion requirements were met. The HbA1c and CBC levels are shown in Table 4. It has been discovered a substantial association between HbA1c and red blood cell MCV, with a p-value of 0.020, as well as a significant relationship between HbA1c and RBC count, with a p-value of 0.029 and MCH (p-value 0.05).

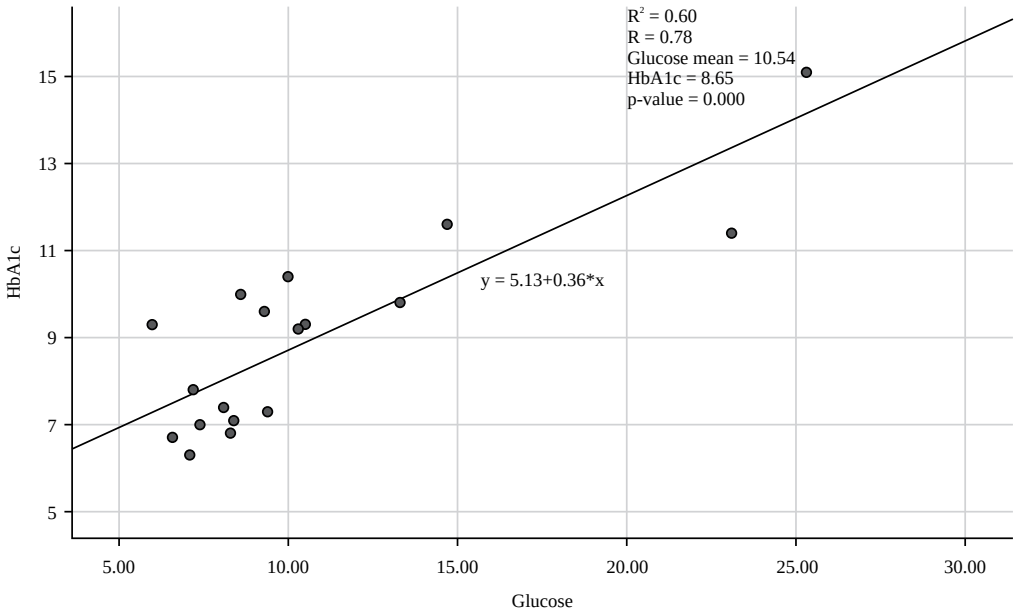

Fig. 3: Correlation between fasting blood glucose (mg dL^{-1}) with the percentage of HbA1c level

Table 3: Correlation between HbA1c level with blood chemistry (mg dL^{-1})

Markers	Mean±SD	r*	p-value
Sodium	140.5±2.4	0.175	0.825
Potassium	4.6±0.5	- 0.027	0.973
Chloride	105.5±3.3	0.196	0.804
Bi-carbonate	24.0±1.8	0.401	0.599
Anion	15.5±2.5	-0.430	0.570
Urea	7.7±2.8	-0.021	0.979
Creatinine	0.89±0.38	-0.146	0.590

*Pearson correlation

Table 4: Correlation between HbA1c levels with CBC parameters

Markers	Mean±SD	r*	p-value
WBCs (cell μL^{-1})	7.9±2.1	0.063	0.746
RBCs (cell μL^{-1})	5.1±0.5	0.399	0.029*
Hb (g dL^{-1})	13.3±1.8	-0.064	0.738
Hematocrit (%)	40.0±10	-0.022	0.908
MCV fl	81.1±8.6	-0.422	0.020*
MCH pg	26.2±3.4	-0.356	0.050*
MCHC (g dL^{-1})	311.5±54.2	0.036	0.851
RDW (%)	14.5±2.4	0.074	0.698
Platelets (cell μL^{-1})	303.0±83.8	0.152	0.423
MPV fl	10.4±2.2	-0.122	0.535
Neutrophils (%)	58.1±11.5	0.281	0.377
Lymphocytes (%)	29.4±8.8	-0.226	0.481
Monocytes (%)	8.8±2.5	-0.323	0.306
Eosinophils (%)	2.8±1.8	-0.140	0.665
Basophilic (%)	0.9±0.5	-0.339	0.281
NRBC count	0.0091±0.03	0.856	0.001*

*Significant ($p<0.05$), r: Correlation coefficient, SD: Standard deviation, WBCs: White Blood Cells, RBCs: Red Blood Cells, MCV: Mean Cell Volume, MCH: Mean Cell Hemoglobin, MCHC: Mean Cell Hemoglobin Concentration, RDW: Red Blood Distribution Width, MPV: Mean Platelet volume and NRBC: Nucleated Red Blood Cell

DISCUSSION

In the current study, the proportion of men is 46.7% the proportion among females is 53.3%, the age group 16-28 is 23.3, the age group 42-54 is 26.7 and >55 is 50.0% HbA1c level plays a significant part in the diagnostic process type 2 diabetes and both of them are susceptible to anemia positive and negative strategies depending on the type of anemia, such as hemorrhage as well as hemolytic anemia, there are many treatment options can raise RBC revenue and lower HbA1c levels, but iron deficiency anemia and a drop in ferritin levels result in an increase in RBC lifetime, resultant in an elevation in HbA1c levels. According to current study findings, there is a substantial association between hemoglobin, MCV and the number of red blood cells in diabetics.

In comparison to earlier studies the results of this study revealed a link between MCV level and HBA1c. The adjustment is conceivable because increased MCV has been seen in T2DM patients with exceptionally elevated glucose levels. Pre-dilution of the blood in an isotonic medium, as well as the hyperosmolar state generated by increased glucose levels within the cell, may result in quick intracellular water diffusion in the counter. This process is dependent on temperature and has the potential to be reversible quickly[17]. The HbA1c levels were shown to be strong and were found to be significantly associated with MCV levels in 50 years old females[18]. Another study conducted by Rashed *et al.*[19] found a significant

negative correlation with the MCV level and the average MCV was significantly higher in non-diabetic patients than in pre-diabetic and diabetic patients. The lifetime span of red blood cells in hyperglycemia is smaller compared with normoglycemia[20]. The plasma glucose level determines the glycation process refers to the production of the terminal unit of the -chain in hemoglobin, which can be utilized to measure the level of metabolic control and the occurrence of problems in patients with T2DM and thus the standard of diabetes management[21].

Prior studies indicated that greater levels of C-reactive protein, fibrinogen and the number of leukocytes showed linked to a higher risk of cardiac events. Cells that are inflammatory were identified to have a significant impact on the progression of diabetes complications. Leukocytes might be triggered by glycation outcomes, oxidative stress and hyperglycemia-induced angiotensin II and can produce substances such as tumor necrosis factor and interleukin 1 that contribute to the development of diabetes complications[22].

On the other hand, current study data showed no link between WBC count and DM patients, which contradicts prior studies carried out in Libya[23], Ethiopia[24], India[25], Nigeria[26], Ghana[27] and Turkey[28]. The WBC indices have also been reported to be altered in diabetic patients. An elevated WBC count has been described as a sign of chronic inflammation, which has been linked to microvascular problems in type 2 diabetes. Furthermore, elevated WBC counts, even within the normal range, have been linked to micro and macrovascular problems[29]. The epidemiological literature supports a correlation between the WBC count, nonspecific inflammatory indices and diabetes risk[30].

Current study findings revealed no causal relationship between platelets, lipids and electrolytes in diabetic patients. Research, on the other hand, found that BMI is substantially and independently related to the incidence of T2DM[31]. Obesity is significantly connected to high blood pressure, hypertriglyceridemia and elevated cholesterol levels, with fat distribution being an essential factor. Index of inflammation, with changes in cytokine concentrations and platelet count being directly linked[32].

Diabetes mellitus (DM) was recently identified as a 'prothrombotic state' with increased platelet reactivity[33], with studies discovering morphological abnormalities in platelets as well as increased platelet activity in diabetic individuals[34].

Diabetic individuals had increased platelet hyperreactivity and baseline platelet activation. This is produced by a combination of factors such as insulin effects, hyperglycemia, excessive cholesterol levels, endothelial cell dysfunction, oxidative damage and an inflammatory state. As shown by the detection of immature, reticulated circulating platelets, both inflammation and oxidative stress are associated with quicker platelet renewal in DM patients in comparison to healthy people[35].

This study revealed no link between platelets and diabetes, which is consistent with another study that reported no significant differences in platelets between patients with and without diabetes[36].

Despite the fact that diabetes that is uncontrolled causes challenges with the functioning of the kidneys, the study findings reveal no causal relationship between diabetes and renal function. Include undertaking an additional study to determine the actual mechanism of diabetes' influence on red blood cell mean cell volume and whether this is related to the degree of oxidative stress.

CONCLUSION

It can be concluded that HbA1c which major measurement criterion of diabetes mellitus has a significant impact on RBC count as well as the same effect on the MCV of the erythrocyte. Diabetes' effect on hemoglobin inevitably leads to a drop in red blood cell efficiency and a decrease in average cell size, resulting in the elimination of red blood cells from the blood before prematurely.

SIGNIFICANCE STATEMENT

This study discovered that HbA1c, a primary diabetes mellitus measuring criterion, has a considerable impact on RBC count as well as MCV of the erythrocyte. The effect of diabetes on hemoglobin necessarily leads to a decrease in the efficiency of the red blood cell and a decrease in the average cell size, which leads to the removal of red blood cells from the blood before completing their life span. This study will assist the researcher in determining hyperglycemia consequences, which could be a useful and critical tool for optimizing treatment approaches and reducing therapeutic delays.

ACKNOWLEDGMENT

This publication was supported by the Deanship of Scientific Research at Prince Sattam Bin Abdulaziz University.

REFERENCES

1. Pretorius, E., J.N. du Plooy, P. Soma, I. Keyser and A.V. Buys, 2013. Smoking and fluidity of erythrocyte membranes: A high resolution scanning electron and atomic force microscopy investigation. Nitric Oxide, 35: 42-46.

2. Zhou, Z., A. Mahdi, Y. Tratsiakovich, S. Zahorán and O. Kövamees *et al*., 2018. Erythrocytes from patients with type 2 diabetes induce endothelial dysfunction via arginase I. J. Am. Coll. Cardiol., 72: 769-780.
3. Blaslov, K., I. Kruljac, G. Mirošević, P. Gaćina, S.O. Kolonić and M. Vrkljan, 2019. The prognostic value of red blood cell characteristics on diabetic retinopathy development and progression in type 2 diabetes mellitus. Clin. Hemorheol. Microcirc., 71: 475-481.
4. Kor, C.T., Y.P. Hsieh, C.C. Chang and P.F. Chiu, 2018. The prognostic value of interaction between mean corpuscular volume and red cell distribution width in mortality in chronic kidney disease. Sci. Rep., Vol. 8. 10.1038/s41598-018-19881-2.
5. Ang, L., V. Palakodeti, A. Khalid, S. Tsimikas and Z. Idrees *et al*., 2008. Elevated plasma fibrinogen and diabetes mellitus are associated with lower inhibition of platelet reactivity with clopidogrel. J. Am. Coll. Cardiol., 52: 1052-1059.
6. Tominaga, M., H. Eguchi, H. Manaka, K. Igarashi, T. Kato and A. Sekikawa, 1999. Impaired glucose tolerance is a risk factor for cardiovascular disease, but not impaired fasting glucose. The funagata diabetes study. Diabetes Care, 22: 920-924.
7. Tong, P.C., K.F. Lee, W.Y. So, M.H. Ng and W.B. Chan *et al*., 2004. White blood cell count is associated with macro- and microvascular complications in Chinese patients with type 2 diabetes. Diabetes Care, 27: 216-222.
8. Weyer, C., P.A. Tataranni and R.E. Pratley, 2000. Insulin action and insulinemia are closely related to the fasting complement C3, but not acylation stimulating protein concentration. Diabetes Care, 23: 779-785.
9. Angiolillo, D.J., A. Fernandez-Ortiz, E. Bernardo, C. Ramírez and M. Sabaté *et al*., 2005. Platelet function profiles in patients with type 2 diabetes and coronary artery disease on combined aspirin and clopidogrel treatment. Diabetes, 54: 2430-2435.
10. Winocour, P.D., C. Watala and R.L. Kinglough-Rathbone, 1992. Membrane fluidity is related to the extent of glycation of proteins, but not to alterations in the cholesterol to phospholipid molar ratio in isolated platelet membranes from diabetic and control subjects. Thromb. Haemostasis, 67: 567-571.
11. Keating, F.K., B.E. Sobel and D.J. Schneider, 2003. Effects of increased concentrations of glucose on platelet reactivity in healthy subjects and in patients with and without diabetes mellitus. Am. J. Cardiol., 92: 1362-1365.
12. Assert, R., G. Scherk, A. Bumbure, V. Pirags, H. Schatz and A.F.H. Pfeiffer, 2001. Regulation of protein kinase C by short term hyperglycaemia in human platelets *in vivo* and *in vitro*. Diabetologia, 44: 188-195.
13. Narjis, M., M. Noreen, S.Z. Safi, N.E. Ilahi, S.Y. Alomar and A.F. Alkhuriji, 2021. Cross talk between complete blood count and progression of type II diabetes mellitus. J. King Saud Univ. Sci., Vol. 33. 10.1016/j.jksus.2021.101492.
14. Bianconi, E., A. Piovesan, F. Facchin, A. Beraudi and R. Casadei *et al*., 2013. An estimation of the number of cells in the human body. Ann. Hum. Biol., 40: 463-471.
15. Gilstrap, L.G., M.E. Chernew, C.A. Nguyen, S. Alam and B. Bai *et al*., 2019. Association between clinical practice group adherence to quality measures and adverse outcomes among adult patients with diabetes. JAMA Netw. Open, Vol. 2. 10.1001/jamanetworkopen.2019.9139.
16. Mora, S., N. Rifai, J.E. Buring and P.M. Ridker, 2009. Comparison of LDL cholesterol concentrations by friedewald calculation and direct measurement in relation to cardiovascular events in 27 331 women. Clin. Chem., 55: 888-894.
17. Alamri, B.N., A. Bahabri, A.A. Aldereihim, M. Alabduljabbar and M.M. Alsubaie *et al*., 2019. Hyperglycemia effect on red blood cells indices. Eur. Rev. Med. Pharmacol. Sci., 23: 2139-2150.
18. Simmons, D. and T. Hlaing, 2014. Interpretation of HbA_{1c}: Association with mean cell volume and haemoglobin concentration. Diabetic Med., 31: 1387-1392.
19. Rashed, E.R., Y. Abhishek, A. Abhishek, C.R. Shyam and S. Aradhana, 2020. The effects of red blood cells parameters on HbA1c and random blood sugar levels in diabetics diagnosis. Int. J. Diabetes Clin. Res., Vol. 7. 10.23937/2377-3634/1410128.
20. Rio, M.B., M. Tiwari, L.I. Amodu and J. Cagliani and R.H.L. Rilo, 2016. Glycated hemoglobin, plasma glucose, and erythrocyte aging. J. Diabetes Sci. Technol., 10: 1303-1307.
21. Leow, M.K.S., 2016. Glycated hemoglobin (HbA1c): Clinical applications of a mathematical concept. Acta Inf. Med., 24: 233-238.
22. Boussageon, R., F. Gueyffier and C. Cornu, 2016. Metformin as firstline treatment for type 2 diabetes: Are we sure? BMJ, Vol. 352. 10.1136/bmj.h6748.
23. Arkew, M., T. Yemane, Y. Mengistu, K. Gemechu and G. Tesfaye, 2021. Hematological parameters of type 2 diabetic adult patients at Debre Berhan Referral Hospital, Northeast Ethiopia: A comparative cross-sectional study. PLoS ONE, Vol. 16. 10.1371/journal.pone.0253286.
24. Biadgo, B., M. Melku, S.M. Abebe and M. Abebe, 2016. Hematological indices and their correlation with fasting blood glucose level and anthropometric measurements in type 2 diabetes mellitus patients in Gondar, Northwest Ethiopia. Diabetes Metab. Syndr. Obesity: Targets Ther., 9: 91-99.
25. Harish, K.S., S.V. Srinivasa and K. Prabhakar, 2017. Haematological profile of diabetes and non-diabetes patients in rural tertiary centre. Int. J. Adv. Med., 4: 1271-1275.
26. Umeji, L.C., A.O. Paul, S.O. Felix, C.N. Umeji and A.A. Folake *et al*., 2019. Haematological profile of diabetes and non-diabetes patients in Abuja, Nigeria. Int. J. Res. Sci. Innovation, 6: 274-277.

27. Antwi-Baffour, S., R. Kyeremeh, S.O. Boateng, L. Annison and M.A. Seidu, 2018. Haematological parameters and lipid profile abnormalities among patients with type-2 diabetes mellitus in Ghana. Lipids Health Dis., Vol. 17. 10.1186/s12944-018-0926-y.
28. Duman, T.T., G. Aktas, B.M. Atak, M.Z. Kocak, E. Erkus and H. Savli, 2019. Neutrophil to lymphocyte ratio as an indicative of diabetic control level in type 2 diabetes mellitus. Afr. Health Sci., 19: 1602-1606.
29. Pan, L., Y. Ye, M. Wo, D. Bao and F. Zhu *et al*., 2018. Clinical significance of hemostatic parameters in the prediction for type 2 diabetes mellitus and diabetic nephropathy. Dis. Markers, Vol. 2018. 10.1155/2018/5214376.
30. Jiang, H., W.H. Yan, C.J. Li, A.P. Wang, J.T. Dou and Y.M. Mu, 2014. Elevated white blood cell count is associated with higher risk of glucose metabolism disorders in middle-aged and elderly Chinese people. Int. J. Environ. Res. Public Health, 11: 5497-5509.
31. Ganz, M.L., N. Wintfeld, Q. Li, V. Alas, J. Langer and M. Hammer, 2014. The association of body mass index with the risk of type 2 diabetes: A case-control study nested in an electronic health records system in the United States. Diabetol. Metabol. Syndrome, Vol. 6. 10.1186/1758-5996-6-50.
32. do Nascimento Ferreira, L.C.C., H.J.G. da Silva, T.A. Lins and W.L. do Prado, 2013. Relationship between lipid and hematological profiles with adiposity in obese adolescents. Rev. Bras. Hematol. Hemote, 35: 163-166.
33. Jindal, S., S. Gupta, R. Gupta, A. Kakkar, H.V. Singh, K. Gupta and S. Singh, 2011. Platelet indices in diabetes mellitus: Indicators of diabetic microvascular complications. Hematology, 16: 86-89.
34. Malladi, N., E. Johny, S.K. Uppulapu, V. Tiwari, M.J. Alam, R. Adela and S.K. Banerjee, 2021. Understanding the activation of platelets in diabetes and its modulation by allyl methyl sulfide, an active metabolite of garlic. J. Diabetes Res., Vol. 2021. 10.1155/2021/6404438.
35. Kim, J.H., H.Y. Bae and S.Y. Kim, 2014. Response: Clinical marker of platelet hyperreactivity in diabetes mellitus (*Diabetes Metab J* 2013;37:423-8). Diabetes Metab. J., 38: 160-161.
36. Chen, X., L. Fang, H. Lin, P. Shen and T. Zhang *et al*., 2017. The relationship between type 2 diabetes and platelet indicators. Iran. J. Public Health, 46: 1211-1216.