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Correlation between diabetic kidney disease and platelet indices in type 2 diabetes mellitus

Mohamed Gaber Hamed, Ayman Fathy Arafa, Basma Ahmed Mohamed, Alaa Ezz Al-Arab Saad, Elsayed Anany Metwally

Internal Medicine Department, Faculty of Medicine, Zagazig University, Egypt

dralaaezz1993@gmail.com

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Abstract: the pathological alterations in diabetes that result in microvascular complications are mostly dependent on platelets. Given that platelet indices are measures of platelet activity, they might be helpful predictors of diabetes complications. This study set out to assess diabetes patients' platelet indices and establish a correlation between them and diabetic kidney damage. In this case-control study, we included 78 patients who were classified into 3 groups: 26 participants made up the first group, which was a control group; 26 participants made up the second group, which was T2DM without DKD; and 26 participants made up the third group, which was T2DM with DKD. All subjects were submitted to estimation of platelet indices (platelet count: PLT, mean platelet volume: MPV, platelet distribution width: PDW, and plateletcrit: PCT). The study found that compared to non-diabetic controls, MPV, PDW was considerably greater in diabetics. When comparing diabetics with DKD to those without DKD. A statistically significant difference was seen in MPV, PDW between non-diabetics and diabetics with and without DKD. These results prove that diabetic kidney disease can be predicted by MPV and PDW biomarkers.

Keywords: diabetic kidney disease, platelet indices, type 2 diabetes mellitus

Introduction: Diabetes mellitus is a chronic metabolic illness causing elevated blood glucose levels, dysregulation of lipid and protein metabolism, and insufficient insulin discharge. It can lead to severe damage to the heart, blood vessels, kidneys, nerves, and eyes as defined by WHO (World Health Organization, 2023). Diabetes prevalence has increased significantly, with 537 million adults worldwide estimated to have the condition in 2021, predicted to reach 783 million by 2045. It is also a growing public health concern in Egypt, with an estimated 9.8 million in 2019, expected to reach 16.9 million by 2045(Saeedi et al., 2019). Diabetic microvascular complications are linked to hyperglycemia severity and duration. (Holman et al., 2008).Diabetic kidney disease (DKD, previously termed diabetic nephropathy, DN) is a microvascular complication and progresses gradually over many

years in approximately 30–40% of individuals with T1D and T2D mellitus (Barrett et al., 2017).In addition to kidney failure, DKD is a strong independent risk factor for cardiovascular disease. The combination of diabetes and nephropathy increases cardiovascular disease risk by 20–40 fold, greatly increasing morbidity and mortality in patients with diabetes. Thus, the presence of microalbuminuria is an indication for surveillance and management of cardiovascular risk factors (Mattock et al., 1992).It has been established that diabetes mellitus (DM) is associated with an elevated platelet reactivity and a "prothrombotic tendency." There has been speculation that the microvascular complications associated with diabetes are related to this increased responsiveness. (Koltai et al., 2006).Platelets in diabetes mellitus (DM) are larger hyperactive, and release more granules as a result of metabolic abnormalities. They also have a higher propensity to thrombotic events, which can result in both macrovascular and microvascular complications, increasing morbidity and mortality. (Jindal et al., 2011; Kodiatte et al., 2012) Mean platelet volume (MPV), one of the platelet indices, shows variations in the rate of platelet synthesis or platelet stimulation. Platelet heterogeneity, which can be caused by either uneven demarcation of megakaryocytes or aging of the platelets, is measured by platelet distribution width (PDW). (Borkataky et al., 2009) .Increased MPV has been linked to diabetes, metabolic syndrome, and stroke. (Tavil et al., 2007) Recent research has demonstrated that patients with proliferative diabetic retinopathy had higher MPV levels. (Ates et al., 2009) Diabetes patients had considerably greater MPV, and it was theorized that platelets with changed morphology would be linked to a higher risk of vascular complications associated with the disease. (Papanas et al., 2004; Hekimsoy et al., 2004)
The aim of the present study is to explore the associations between platelet parameters and development of kidney dysfunction in patients with type 2 diabetes.

I. Subjects and methods

A. Subjects

This study was a case and control study conducted at Internal medicine department and Medical Biochemistry& Molecular Biology Departments, Faculty of Medicine, Zagazig University, Egypt and ethically approved by the institutional bioethical committee. The study was carried out on 78 subjects: They were divided into three groups; healthy, type 2 diabetic patients without DKD, and type 2 diabetic patients with DKD having 26 subjects each. Informed consent was obtained from all subjects. They were 32 males and 46 females, age (25-75 years). Type 2 diabetic patients with or without DKD were selected as per the criteria established by American Diabetes Association [ADA, 2023]: Fasting blood glucose ≥ 126 mg/Dl, 2-h post prandial bl. glucose levels >200 mg/dL, HbA1c > 6.5 % in patients with classic symptoms of hyperglycemia or hyperglycemic crisis, Patients with abnormal oral glucose tolerance test. DKD patients was defined in accordance with the consensus reached by American Diabetes Association [ADA, 2023]: GFR <60
mL/min, OR albumin creatinine ratio> 30 mg/g lasting for more than 3 months.All subjects were submitted to full history taking, clinical examination, and laboratory investigations

includ- ing measurement of serum total cholesterol, triglyceride, LDL-c, HDL-c, serum urea, creatinine, fasting, postprandial blood glucose, glycated hemoglobin (HbA1c), Urine analysis (micro albumin and creatinine) and Albumin creatinine ratio.

B. Methods

After 6-8 hours after the last meal, 6 ml of venous blood were withdrawn by sterile vein-puncture and divided as follow.

–1 ml of blood was transferred into EDTA tube for quantitative colorimetric determination of glycated hemoglobin.

–1 ml of blood was transferred into sodium fluoride tube for enzymatic colorimetric determination of blood glucose.

–2 ml was transferred into a plain tube and allowed to clot at 37 °C, centrifuged for 10 min at 4000 round per minute. The clear supernatant serum was separated from the clot and kept frozen at − 80 °C for colorimet- ric determination of serum urea , creatinine , total cholesterol ,triglyceride , HDL-c , while LDL-c was calculated from TC, HDL-c, and TG according to Friedewald formula.

First morning urine samples were collected under complete sterile condition. NaOH/HCL 1 mol/L was added to adjust the pH at 7.0.

Results

Regarding the demographic data in our study, we included three groups: 1st group was a control group and consisted of 26 participants, the 2nd group was T2DM without kidney disease, and the 3rd group was T2DM with kidney disease, each of them had the same number of patients (26). The three groups were age and gender -matched with no statistically significant difference. (Table 1) But as regards BMI, the mean BMI was highest in diabetics with DKD followed by diabetics without DKD. The controls have significantly lower BMI compared to both diabetic groups. However, there was no significant difference in BMI between the two diabetic groups. (Table 1)

Comparison between Type 2 diabetic patients with DKD, Type 2 diabetic patients without DKD and Controls regarding demographic data.

			Type 2 diabetic patients with DKD	Type 2 diabetic patients without DKD	Controls	t. test	P. value	LSD
Age (years)	Mean ± SD		55.58± 7.81	51.92± 10.82	51.62± 8.69	1.492	.231	
Gender	Female	No	16	14	16	X2	.809	
		%	61.5%	53.8%	61.5%	.424		
	Male	No	10	12	10			
		%	38.5%	46.2%	38.5%			
BMI	Mean ± SD		32.60± 4.67	31.30± 5.09	26.95± 1.90	13.276	.000	P1=.262 P2=.000 P3=.000

The mean duration of diabetes was longest in diabetics with DKD versus diabetics without DKD. However, this difference was not statistically significant. There were significant differences in diabetes duration when comparing both diabetic groups to the control group. In terms of SBP and DBP, there is significant in diabetics with DKD compared to both diabetics without DKD and controls. (table2)

COMPARISON BETWEEN TYPE 2 DIABETIC PATIENTS WITH DKD, TYPE 2 DIABETIC PATIENTS WITHOUT DKD AND CONTROLS REGARDING Duration of DM, blood pressure.

		Type 2 diabetic patients with DKD	Type 2 diabetic patients without DKD	Controls	t. test	P. value	LSD
Duration of DM (yrs)	Mean ± SD	10.44± 3.56	9.88± 4.52	-	10.44± 3.56	P1=.262 P2=.000 P3=.000	P1=.548 P2=.000 P3=.000
SBP (mmHg)	Mean ± SD	124.27± 4.33	120.69± 3.70	119.88± 3.39	9.642	.000	P1=.001 P2=.000 P3=.450
DBP (mmHg)	Mean ± SD	82.73± 2.14	77.62± 4.72	74.19± 3.69	35.464	.000	P1=.000 P2=.000 P3=.001

In our research, mean values for FBS, PPBG and HbA1c were highest in diabetics without DKD followed closely by those with DKD, with both being significantly higher than controls. However, the differences in FBS and PPBG between the two diabetic groups were not significant with high p values. HbA1c showed a small but significant difference, being lower in diabetics with DKD (7.90%) versus without DKD (8.41%). (Table 3)

COMPARISON BETWEEN TYPE 2 DIABETIC PATIENTS WITH DKD, TYPE 2 DIABETIC PATIENTS WITHOUT DKD AND CONTROLS REGARDING FBS, 2 HR PPBG and HbA1c(%).

		Type 2 diabetic patients with DKD	Type 2 diabetic patients without DKD	Controls	t. test	P. value	LSD
FBS(mg/dl)	Mean ± SD	187.88± 45.48	175.42± 38.22	102.08± 5.38	47.117	.000	P1=.196 P2=.000 P3=.000
2 HR PPBG(mg/dl)	Mean ± SD	285.00± 37.11	284.46± 46.25	122.96± 7.36	190.502	.000	P1=.955 P2=.000 P3=.000
HbA1c (%)	Mean ± SD	7.90± .875	8.41± 1.22	4.91± .319	117.745	.000	P1=.045 P2=.000 P3=.000

Our Data showed that there was a statistically significant increase in Albumin/creatinine ratio in the diabetics with DKD compared to diabetics without DKD and controls, the difference in ACR between diabetics without DKD and controls was statistically insignificant (p=0.957). Serum albumin was significantly lower in DKD group compared to diabetic group which was significantly lower compared to controls. There was a statistically significant

elevation in Serum urea and creatinine levels in T2DM with DKD compared to other groups. However, the difference between diabetics without DKD and controls was statistically not significant. Regarding eGFR, it was significantly lower in
T2DM with DKD group compared to other groups. The eGFR is lower in non- DKD diabetics versus controls, this difference was statistically significant. (Table 4)

COMPARISON BETWEEN TYPE 2 DIABETIC PATIENTS WITH DKD, TYPE 2 DIABETIC PATIENTS WITHOUT DKD AND CONTROLS REGARDING alb/ creat ratio, s. albumin, kidney functions, Estimated GFR.

		Type 2 diabetic patients with DKD	Type 2 diabetic patients without DKD	Controls	t. test	P. value	LSD
alb/ creat ratio.	Mean ± SD	501.92± 272.74	10.18± 3.92	7.82± 4.37	84.8 82	.000	P1=.000 P2=.000 P3=.957
s. albumin(g/dl)	Mean ± SD	3.07± .3 04	3.90± .3 69	4.13± .3 09	74.1 85	.000	P1=.000 P2=.000 P3=.015
S. creat(mg/dl)	Mean ± SD	4.01± .6 11	.827± .1 20	.777± .1 47	650. 794	.000	P1=.000 P2=.000 P3=.628
bl urea(mg/dl)	Mean ± SD	104.55± 14.99	28.73± 8.36	26.75± 5.46	472. 533	.000	P1=.000 P2=.000 P3=.495
Estimated GFR(ml/mnt/ 1.73m^2)	Mean ± SD	14.54± 2.84	92.65± 9.76	103.15± 6.72	1229 .543	.000	P1=.000 P2=.000 P3=.000

As regard to platelet indices, our study shows that mean platelet count is significantly lower in diabetics with DKD versus those without DKD with a p value of 0.001. The mean platelet count is similar between controls and diabetics with DKD, and between controls and those without DKD. However, higher MPV in diabetics with DKD compared to non- DKD diabetics and controls. MPV was also elevated in non- DKD diabetics versus controls. Also, PDW levels were highest in the diabetic patients with DKD. (Table 5)

COMPARISON BETWEEN TYPE 2 DIABETIC PATIENTS WITH DKD, TYPE 2 DIABETIC PATIENTS WITHOUT DKD AND CONTROLS REGARDING platelet indices.

		Type 2 diabetic patients with DKD	Type 2 diabetic patients without DKD	Controls	t. test	P. value	LSD
PLT (x103/uL)	Mean ± SD	221.19± 83.79	296.92± 86.67	218.58± 69.34	7.985	.001	P1=.001 P2=.907 P3=.001
MPV (fL)	Mean ± SD	11.43± .852	9.23± 1.12	8.43± .882	67.644	.000	P1=.000 P2=.000 P3=.004
PDW (fL)	Mean ± SD	16.23± 3.12	12.50± 1.73	11.61 ± 1.15	33.239	.000	P1=.000 P2=.000 P3=.144
PCT(%)	Mean ± SD	.242± .090	.270± 085	.180± .070	8.161	.001	P1=.224 P2=.008 P3=.000

Discussion

Diabetes mellitus, a metabolic disease causing hyperglycemia due to insulin defects, is predicted to affect 366 million people globally by 2030, affecting nearly 5% of the global population. (Ahmed et al., 2013).Diabetic kidney disease is a common microvascular complication of diabetes that may eventually require dialysis. Not all diabetic patients develop kidney disease, but about one-third of patients with diabetes eventually develop this complication. (Conway et al., 2022). Microvascular problems arise from the elevated prothrombotic and atherosclerotic potential associated with diabetes, particularly when the condition is poorly managed or extended. (Avogaro et al., 2007) The higher morbidity and death rates associated with diabetes are caused by these complications, which are predictive indicators of cardiovascular disease. (Rosenson et al., 2011) According to earlier research, platelet indices might help predict the microvascular complications associated with diabetes. (Demirtas et al., 2015) It is claimed that there is a relationship between platelet function and size. A higher propensity for thrombotic events is associated with larger platelets. Since it is hypothesized that persistently high and uncontrolled blood sugar levels may lead to the formation of large-sized platelets, platelet hyperactivity in diabetes mellitus is also linked to hyperglycemia. (Kakouros et al., 2011). Platelet indices that we studied included – Platelet count, MPV, PDW, and PCT. In our study we found that higher MPV in diabetics with DKD compared to non-DKD diabetics and controls. MPV was also elevated in non-DKD diabetics versus controls. Also, PDW levels were highest in the diabetic patients with DKD compared to both diabetic patients without DKD and controls while there was no significant difference between diabetic patients without DKD and controls. PCT levels were highest in diabetic patients without DKD versus diabetic patients with DKD and controls. The only significant differences were between diabetic patients without DKD versus controls (p=.008) and diabetic patients with DKD versus controls (p=.000). No significant difference existed between the two diabetic groups with and without DKD (p=.224). The mean platelet

count is significantly lower in diabetics with DKD versus those without DKD with a p value of 0.001. On the other hand it is similar between controls and diabetics with DKD, and between controls and those without DKD. Our study agrees in some findings and disagrees in others with the research of Chu et al. (2010), who declared that regarding MPV was significantly higher in diabetic patients compared to controls. In addition, PDW was also higher in diabetic subjects as compared to controls and also diabetic patients with kidney disease as compared to controls. However, the platelet count was similar in the three groups **.** The findings of Besada et al. (2021), Showed that MPV was not significantly different between diabetic patients and diabetic patients with kidney disease. However, there was highly significant difference in MPV in the diabetic group than the controls. On the other hand, PDW was significantly higher in diabetic patients with kidney disease compared to control group. An earlier study by Demirtas et al showed lower MPV in diabetic cases compared to the controls with no statistical significant difference. On the other hand, PDW was also significantly higher in diabetic subjects compared to controls. (Demirtas et al., 2004) **.**In agreement with a study done by Jindal et al, our study shows significantly higher MPV in diabetics with complications than without complications. Also, observed a statistically significant higher PDW in diabetics with complications than without complications. (Jindal et al., 2011). In comparison to diabetic and control groups, Kshirsagar et al. 2019 found lower PLT in DKD. They also found higher MPV in diabetic patients with complications compared to diabetic patients without complications, though the difference was not statistically significant. Finally, they found no significant difference in PDW between diabetic patients with complications, diabetic patients without complications, and nondiabetic groups. Few research are available concerning PCT. There was no discernible difference in PCT levels between the diabetics and the controls in the Kshirsagar et al. 2019 research, nor was there a meaningful relationship between PCT and microvascular problems. Alhadas et al. (2016), however, found that both diabetics and diabetics with chronic problems had higher PCT.

References:

1. World Health Organization. (2023). Diabetes . World Health Organization. https://www.who.int/westernpacific/health-topics/diabetes
2. Saeedi P, Petersohn I, Salpea P, Malanda B, Karuranga S, Unwin N, Colagiuri S, Guariguata L, Motala AA, Ogurtsova K, Shaw JE, Bright D, Williams R, and IDF Diabetes Atlas Committee (2019). Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: Results from the International Diabetes Federation Diabetes Atlas, 9th edition. Diabetes Res Clin Pract, 157:107843. doi:10.1016/j.diabres.2019.107843.
3. Barrett E J, Liu Z, Khamaisi M, King G L, Klein R, Klein B E and Bowden D W (2017). Diabetic microvascular disease: an endocrine society scientific statement. The Journal of Clinical Endocrinology & Metabolism, 102(12):4343-4410.
4. Mattock M B, Morrish N J, Viberti G, Keen H, Fitzgerald A P and Jackson G (1992). Prospective study of microalbuminuria as predictor of mortality in NIDDM. Diabetes, 41(6):736-741.

5. Koltai, K., Feher, G., Kesmarky, G., Keszthelyi, Z., Czopf, L., & Toth, K. (2006). The effect of blood glucose levels on hemorheological parameters, platelet activation and aggregation in oral glucose tolerance tests. Clinical hemorheology and microcirculation, 35(4), 517–525.
6. Jindal S, Gupta S, Gupta R, Kakkar A, Singh H. V, Gupta Ketal., (2011). Platelet indices in diabetes mellitus: indicators of diabetic microvascular complication Hematology16:86-90
7. Kodiatte, T. A., Manikyam, U. K., Rao, S. B., Jagadish, T. M., Reddy, M., Lingaiah, H. K., & Lakshmaiah, V. (2012). Mean platelet volume in Type 2 diabetes mellitus. Journal of laboratory physicians, 4(1), 5–9. https://doi.org/10.4103/0974-2727.98662
8. Borkataky, S., Jain, R., Gupta, R., Singh, S., Krishan, G., Gupta, K., & Kudesia, M. (2009). Role of platelet volume indices in the differential diagnosis of thrombocytopenia: a simple and inexpensive method. Hematology (Amsterdam, Netherlands), 14(3), 182–186. https://doi.org/10.1179/102453309X426182
9. Tavil, Y., Sen, N., Yazici, H. U., Hizal, F., Abaci, A., & Cengel, A. (2007). Mean platelet volume in patients with metabolic syndrome and its relationship with coronary artery disease. Thrombosis research, 120(2), 245–250. https://doi.org/10.1016/j.thromres.2006.10.005
10. Ateş, O., Kiki, I., Bilen, H., Keleş, M., Koçer, I., Kulaçoğlu, D. N., & Baykal, O. (2009). Association of mean platelet volume with the degree of retinopathy in patients with diabetes mellitus. Eur J Gen Med, 6(2), 99-102.
11. Papanas, N., Symeonidis, G., Maltezos, E., Mavridis, G., Karavageli, E., Vosnakidis, T. H., & Lakasas, G. (2004). Mean platelet volume in patients with type 2 diabetes mellitus. Platelets, 15(8), 475-478.
12. Hekimsoy, Z., Payzin, B., Örnek, T., & Kandoğan, G. (2004). Mean platelet volume in Type 2 diabetic patients. Journal of Diabetes and its Complications, 18(3), 173-176.
13. Conway B, Goddard J, Jaap A and Patrick A (2022). Management of Diabetic Nephropathy. In Primer on Nephrology .Springer, Cham, 671-690.
14. Avogaro, A., Giorda, C., Maggini, M., Mannucci, E., Raschetti, R., Lombardo, F., Spila-Alegiani, S., Turco, S., Velussi, M., Ferrannini, E., & Diabetes and Informatics Study Group, Association of Clinical Diabetologists, Istituto Superiore di Sanità (2007). Incidence of coronary heart disease in type 2 diabetic men and women: impact of microvascular complications, treatment, and geographic location. Diabetes care, 30(5), 1241–1247. https://doi.org/10.2337/dc06-2558
15. Rosenson, R. S., Fioretto, P., & Dodson, P. M. (2011). Does microvascular disease predict macrovascular events in type 2 diabetes?. Atherosclerosis, 218(1), 13–18. https://doi.org/10.1016/j.atherosclerosis.2011.06.029
16. Demirtas, L., Degirmenci, H., Akbas, E. M., Ozcicek, A., Timuroglu, A., Gurel, A., & Ozcicek, F. (2015). Association of hematological indicies with diabetes, impaired glucose regulation and microvascular complications of diabetes. International journal of clinical and experimental medicine, 8(7), 11420–11427.
17. Kakouros, N., Rade, J. J., Kourliouros, A., & Resar, J. R. (2011). Platelet function in patients with diabetes mellitus: from a theoretical to a practical perspective. International journal of endocrinology, 2011, 742719. https://doi.org/10.1155/2011/742719
18. ChuS.G, Becker R.C, Berger P.B, Bhatt D.L, Eikelboom J. W, Konkle B etal.,(2010). Mean platelet volume as apredicator of cardiovascular risk: asystematic review of platelet dysfunction and meta-analysis.JThromb.Haemost.8;148-156 10.1111/j.1538-7836.2009.03584.
19. Besada, M. S. D., Elsayed, A. A., Ali, A. E., & Hashem, A. A. (2021). Platelet indicies as an indicators of diabetic nephropathy. SVU-International Journal of Medical Sciences, 4(1), 41-48. doi: 10.21608/svuijm.2021.112026
20. Demirtas L, Degirmenci H, Akbas E, Ozcicek A, Timuroglu A,Gure etal., (2004). World Health Organization Guideline.Type I diabetes: recentdevelopments. BMJ; 328:750-754.

21. Kshirsagar, Ravindra & Deoke, Shilpa & Akhtar, Shamim. (2019). Platelet indices in type 2 diabetes mellitus and their association with microvascular complications. Panacea Journal of Medical Sciences. 9. 23-28. 10.18231/j.pjms.2019.007.

22. Alhadas, K. R., Santos, S. N., Freitas, M. M. S., Viana, S. M. S., Ribeiro, L. C., & Costa, M. B. (2016). Are platelet indices useful in the evaluation of type 2 diabetic patients?. Jornal Brasileiro de Patologia e Medicina Laboratorial, 52, 96-102.

23. ElSayed, N. A., Aleppo, G., Aroda, V. R., Bannuru, R. R., Brown, F. M., Bruemmer, D., Collins, B. S., Hilliard, M. E., Isaacs, D., Johnson, E. L., Kahan, S., Khunti, K., Leon, J., Lyons, S. K., Perry, M. L., Prahalad, P., Pratley, R. E., Seley, J. J., Stanton, R. C., Gabbay, R. A., … on behalf of the American Diabetes Association (2023). 16. Diabetes Care in the Hospital: Standards of Care in Diabetes-2023. Diabetes care, 46(Suppl 1), S267–S278.