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Evaluation of Mean Platelet Volume and 25 Hydroxy Vitamin D Levels In Gestational Diabetic Women

Gestasyonel Diyabetli Kadınlarda Ortalama Platelet Hacmi ve 25 Hidroksi D Vitamini Düzeylerinin Değerlendirilmesi

Kadri Turan[1], Mine Adaş[2], Edip Erkus[3], Murat Kahramaner[1]

[1]Department of Internal Medicine, Cemil Tascioglu City Hospital, Istanbul, Turkey
[2]Department of Endocrinology, Cemil Tascioglu City Hospital, Istanbul, Turkey
[3]Department of Nephrology, Erzurum Regional Training and Research Hospital, Erzurum, Turkey

Abstract

Aim: According to few studies which tried to evaluate mean platelet volume (MPV) and 25 hydroxy vitamin D, have shown conflicting results in gestational diabetic patients. In this study we aimed to compare main platelet volume and 25 hydroxy vitamin D values between gestational diabetic patients and healty individual pregnant womens.

Material and Method: The patients were selected from 24-28 weeks pregnant people who made gestational diabetes screening and oral glucose tolerance test from obstetric-gynecology, diabetes and endocrinology polyclinics of Okmeydanı Training and Research Hospital. After the searching 52 gestational diabetic patients and 52 healty pregnant women included to the study. We estimated MPV and vitamin D level. In addition, demographic and clinical data of subjects were recorded.

Results: Mean platelet volume (MPV) value was found 8.5±1.0 fl and 8.3±1.1 fl. in gestational diabetic and control group respectively. There was no statistically significant differences in MPV value between case and the control group (p>0.05). Mean 25 hydroxy vitamin D value was found 20.5±11.0 ng/ml and 21.1±9.3 ng/ml. gestational diabetic and control group respectively. There was no statistically significant differences in 25 hydroxy (OH) vitamin D value between case and control group.

Conclusion: In our study we found no statistically significant differences in MPV and 25-OH vitamin D values between gastational diabetic pregnant group and healty pregnant group.

Keywords: Gestational diabetes, main platelet volume, vitamin D

Öz

Amaç: Gestasyonel diyabeti olan hastalarda ortalama trombosit hacmi (MPV) ve 25-OH hidroksi vitamin D düzeylerini değerlendirmeye çalışan az sayıdaki çalışmaya göre, çelişkili sonuçlar ortaya çıkmıştır. Bu çalışmada gestasyonel diyabetik ve sağlıklı gebelerde MPV ve serum 25-OH vitamin D düzeylerini değerlendirmeyi ve karşılaştırmayı amaçladık.

Gereç ve Yöntem: Hastalar Okmeydanı Eğitim ve Araştırma Hastanesi Kadın Hastalıkları ve Doğum, Diyabet ve Endokrinoloji polikliniklerinden gestasyonel diyabet taraması ve oral glukoz tolerans testi yapılmış 24-28 haftalık gebelerden seçildi. Araştırma sonucunda 52 gestasyonel diyabet hastası ve 52 sağlıklı gebe çalışmaya dahil edildi. MPV ve D vitamini seviyeleri tespit edildi. Ayrıca hastaların demografik ve klinik verileri kaydedildi.

Bulgular: Çalışmaya alınan gestasyonel diyabetik gebe grubunun ortalama MPV değeri 8,5±1,0 fl; kontrol grubunda ise ortalama MPV 8,3±1,1 fl saptandı. Çalışmaya alınan hasta grubu ile kontrol grubu arasında ortalama MPV değeri dağılımda istatistiksel olarak anlamlı bir farklılık görülmedi (p>0,05). Gestasyonel diyabetik gebe grubunun ortalama 25-OH vitamin D değeri 20,5±11,0 ng/ml; kontrol grubunda ise 21,1±9,3 ng/ml saptandı. Çalışmaya alınan hasta grubu ile kontrol grubu arasında ortalama 25-OH vitamin D değeri dağılımda istatiksel olarak anlamlı bir farklılık görülmedi (p>0,05)

Sonuç: Bizim çalışmamızda gestasyonel diyabetik gebe grubu ile sağlıklı gebe grubu arasında MPV ve 25-OH vitamin düzeyleri arasında istatistiksel olarak anlamlı bir fark saptanmadı.

Anahtar Kelimeler: Gestasyonel diyabet, ortalama trombosit hacmi, D vitamini

Corresponding *(İletişim)*: Edip Erkuş, Department of Nephrology, Erzurum Regional Training and Research Hospital, Erzurum, Turkey
E-mail *(E-posta)*: dr.ediperkus@gmail.com
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INTRODUCTION

Gestational Diabetes Mellitus (GDM) is a glucose tolerance disorder that first appears during pregnancy or is diagnosed during pregnancy.[1] Its true incidence is not fully known; Data in the literature vary depending on the society in which the studies were conducted and the diagnostic criteria. According to IDF (International Diabetes Federation) 2013 data, the frequency of hyperglycemia in pregnant women between the ages of 20-49 is reported to be 16.9%. While the prevalence is 25% in Southeast Asia, it was found to be 10.4% in North America.[2] The frequency of GDM is increasing in studies conducted today. This may be due to the increased frequency of obesity or the decrease in threshold values in diagnosis and tests.[3]

It has been reported that there are changes in platelet function and morphology in diabetic patients.[4] These changes are associated with an increased risk of vascular disease and venous thromboembolism. Platelet volumes are an indicator of platelet synthesis. Platelet volume is one of the determinants of platelet functions because larger platelets are more metabolically active. Increased MPV indicates platelet functions and activation and is considered an indicator of increased cardiovascular disease risk. The slight increase in platelet aggregation that occurs during normal pregnancy causes an increase in platelet number and volume.[4,5] Increased MPV level may accompany acute myocardial infarction, acute ischemic stroke, preeclampsia and renal artery stenosis.[6] Conflicting results regarding MPV have been found in the few studies conducted in gestational diabetic patients.

Vitamin D level in pregnant women is also a subject that has attracted the attention of researchers. Some studies have shown that pregnant women are more prone to vitamin D deficiency[7] and that there is a relationship between vitamin D deficiency and insulin resistance.[8,9] In addition to studies showing the relationship between vitamin D deficiency and insulin resistance in pregnant women and that 25-OH vitamin D concentration is significantly lower in GDM patients than in the control group,[9] there are also studies showing that GDM rates are similar in those with and without vitamin D deficiency.[10]

Vitamin D receptors are expressed in tissues that play a role in the regulation of glucose metabolism, such as muscle and pancreas.[11] In our study, we wanted to study this issue, which has not been clarified in previous studies, in order to find answers to the questions of whether MPV levels can be a factor in the increase in thrombophilia in GDM and what is the relationship between vitamin D deficiency and GDM.

MATERIAL AND METHOD

The study was approved by the institutional ethics committee with 190 protocol no in 08.04.2014. Written informed consent was obtained from each subject following a detailed explanation of the protocol of the study. All study procedures were conducted in accordance with the ethical principles stated in the "Declaration of Helsinki".

Pregnant women aged 24-28 weeks who applied to Okmeydanı Training and Research Hospital Gynecology and Obstetrics, Diabetes and Endocrinology outpatient clinic for gestational diabetes screening between September 2013 and March 2014 were included in the study. These pregnant women underwent an oral glucose tolerance test (OGTT) with 50, 75g or 100g of glucose. Pregnant women whose glucose value was ≥140 mg/dl at the 2nd hour with 75 g glucose or at the 1st hour with 50 g glucose or who were diagnosed with gestational diabetes by a three-hour sugar loading test with 100 g glucose were included in the case group. Pregnant women who were not diagnosed with gestational diabetes by OGTT were included in the control group. Patients diagnosed with anemia, hemoglobinopathy, preeclampsia, pregestational diabetes, or a systemic disease were excluded from the study.

Of the 104 people included in the study, 52 were gestational diabetics and 52 were nondiabetic healthy pregnant women with similar ages and demographic characteristics. Demographic characteristics of both groups were recorded. Weight measurements were made with thin clothing and no shoes on the same scale (Arzum Peso Model AR535, China, 2008). Height measurements were made on bare foot. Body mass index (BMI) was calculated with the weight (kg)/height2 (m) formula. Waist circumference (WC) was measured with a measuring tape at the level of the umbilicus. Blood pressure of the patients was measured from both arms after a rest of at least 15 minutes using a sphygmomanometer (Erka, Germany).

Glucose, total, very-low-density lipoprotein (VLDL) and high-density lipoprotein (HDL)-cholesterol, triglyceride and insulin levels of the patients were measured in the venous blood sample drawn after 12-hour fasting by a clinical biochemistry otoanalyzer (Olympus AU2700). LDL-cholesterol value was calculated using the Fridewalt formula.

Hemogram, MPV and 25-OH vitamin D levels were checked. For complete blood count, blood is taken into 2 cc EDTA tubes; The study was carried out with the LH 789 device from Beckman Coulter. 25-OH vitamin D level in serum was analyzed by the HLPC method with commercial kits (Immuchrom GmbH, Happenheim, Germany) on an HLPC device (Agilent 1100, Minneapolis, USA). A 25-OH vitamin D level <30 ng/ml was considered vitamin D deficiency.

Pregnant women who were diagnosed with gestational diabetes with a 75 g OGTT two-hour or 50-g OGTT 1st-hour glucose value ≥140 mg/dl and a 100-g OGTT three-hour glucose loading test performed on patients who applied for gestational diabetes screening at 24-28 weeks of gestation were included in the case group was included. The control group included healthy pregnant women who applied for routine gestational diabetes screening at 24-28 weeks of gestation and who were not diagnosed with gestational diabetes by OGTT. Patients diagnosed with anemia, hemoglobinopathy, preeclampsia, pre-gestational diabetes, or a systemic disease were excluded from the study.

Statistical analyses were conducted using the SPPSS 22.0 program. Descriptive statistics of the data were used mean, standard deviation, median, minimum-maximum, rate and frequency values. The distribution of variables were checked with the Kolmogorov Smirnov test. Unpaired t test and Mann Whitney U test was used for comparisons based on the distribution pattern of the numerical data. Chi-square test was used to compare categorical data. Associations between the parameters were evaluated with the Pearson and Spearman's correlation. Analyses where apporpriate. Results were evaluated as significant when $p<0.05$ with in a 95% confidence interval.

RESULTS

The average age of the GDM group was found to be 31.2±3.4 years. The average age of the control group was 31.0±4.7 years. There was no statistically significant difference between the ages, heights, body weights, BMI, number of pregnancies, and number of weeks of gestation of the GDM group included in the study and the control group. ($p>0.05$) (**Table 1**). The rate of DM history in first-degree relatives of the GDM group was significantly higher than the control group ($p<0.05$) (**Table 1**). While the presence of DM in first-degree relatives was seen in 38.5% of the GDM group; It was seen in 13.5% in the control group.

The average MPV value of the GDM group was 8.5±1.0 fl; In the control group, it was found to be 8.3±1.1 fl. MPV was found to be higher in the patient group included in the study, but the difference with the control group was not significant ($p>0.05$) (**Table 2**).

The average 25-OH vitamin D value of the GDM group was 20.5±11.0 ng/ml; In the control group, it was found to be 21.1±9.3 ng/ml. There was no statistically significant difference between the average 25-OH vitamin D value between the patient group included in the study and the control group ($p>0.05$) (**Table 2**)

There was no statistically significant difference between the patient and control groups in terms of the prevalence of 25-OH vitamin D deficiency ($p>0.05$) (**Table 2**).

There was no statistically significant difference between mean haemoglobin (Hb), platelet (PLT), platelet distribution width (PDW), parathormone (PTH), calcium, phosphorus, alkaline phosphatase (ALP), albumin values between the patient group included in the study and the control group. ($p>0.05$).

The average HbA1C value was 5.3±0.5 (%) in the GDM group and 4.6±0.3 (%) in the control group. A statistically significant difference was detected between the mean HbA1C values of the patient and control groups included in the study ($p<0.05$).

The correlation analysis of the patients' MPV and serum 25-OH vitamin D levels with other clinical and laboratory data is shown in **Table 4**.

There was no significant ($p>0.05$) correlation between MPV level and 25-OH vitamin D value, Hb, PDW, HbA1C, PTH, phosphorus, ALP, albumin, and number of pregnancies. There was a significant ($p<0.05$) negative correlation between MPV value, PLT value and gestational week. There was a significant ($p<0.05$) positive correlation between the MPV value and the calcium value (**Table 4**).

There was no significant ($p>0.05$) correlation between 25-OH vitamin D level and Hb, PLT, PDW, HbA1C, PLT, calcium, phosphorus, ALP, albumin, pregnancy number, and gestational week. There was a significant ($p<0.05$) negative correlation between 25-OH vitamin D level and PTH level (**Table 4**)

Table 1. Averages of demographic and anthropometric characteristics of the patient and control groups

		Patient GroupGDM)			Control Group			p-value
		Mean + s.d./n-%	Median	min-max	Mean + s.d./n-%	Median	min-max	
Ageyears)		31.2±3.4	32	24.0 - 37.0	31.0±4.7	30	24 - 40	0.462
Heightcm)		160.5±5.1	160	150.0 - 172.0	160.1±5.3	160	150 - 170	0.674
Body weightkg)		74.8±7.7	75	60.0 - 92.0	74.1±13.0	72	55 - 120	0.233
BMIkg/m2)		29.1±3.2	29	23.1 - 37.8	28.9±4.6	29	22 - 44	0.393
First degree relatives of patients with DM	Yes No	20 38.5% 32 61.5%			7 13.5% 45 86.5%			**0.004**
Number of pregnancy		2.2±0.9	2	1.0 - 4.0	2.2±1.0	2	1 - 5	0.522
Gestational Week		26.2±1.6	26	24.0 - 28.0	26.0±1.4	26	24 - 28	0.493

Mann-whitney u test / Chi-squared test

Table 2. Average MPV, 25-OH vitamin D and 25-OH vitamin D deficiency averages of the patient and control groups.

		Patient Group(GDM)		Control Group		
		Mean±s.d./n-%	Median (min-max)	Mean + s.d./n-%	Median (min-max)	p-value
MPV(fl)		8.5±1.0	8 (6.5 - 10.7)	8.3±1.1	8 (7 - 12)	0.303
25 OH Vit D (ng/ml)		20.5±11.0	21 (4.2 - 62.0)	21.1±9.3	22 (4 - 50)	0.477
Vitamin D deficiency <30	No Yes	8 15.4% 44 84.6%		6 11.5% 46 88.5%		0/566

Independent!Samples t test / Mann-whitney u test / Chi-squared test

Table 3. Mean laboratory parameter of case and control groups

	Patient Group (GDM)			Control Group			p-value
	Mean±s.d.	Median	min-max	Mean±s.d.	Median	min-max	
Hb (g/dl)	11.5±0.9	12	9.5 - 13.3	11.4±0.7	11	10 - 13	0.563
PLT (x10^3)	206.3±41.0	202	122.0 - 336.0	211.3±40.7	212	133 - 282	0.411
PDW	17.1±0.7	17	16.1 - 19.0	17.0±0.6	17	1·6 - 19	0.225
H bAIC (%)	5.3±0.5	5	4.5 - 7.1	4.6±0.3	5	4 - 6	**0.000**
PTH (pg/ml)	33.3±13.4	32	12.0 - 67.5	32.8±16.3	33	11 - 104	0.587
Calcium (mg/dl)	9.1±0.4	9	8.0 - 10.0	9.2±0.4	9	8 - 11	0.136
Phosphorus(mg/dl)	3.4±0.4	3	2.7 - 5.0	3.3±0.4	4	2 - 4	0.995
ALP (U/L)	78.3±19.1	78	43.0 - 123.0	87.2±23.0	87	49 - 153	0.067
Albumin(g/dl)	3.4±0.3	3	2.9 - 3.9	3.4±0.3	3	3 - 4	0.536

Independent Samples t test I Mann-whitney test

Table 4. Correlation between MPV, serum 25-0H vitamin D level of patients and other clinical with laboratory datas.

		25 OH Vit D	Hb	PLT	PDW	HbAIC	PTH
MPV (fl)	r	0.002	0.126	-0.396	0.152	0.141	-0.106
	P	0.983	0.204	**0.000**	0.124	0.153	0.285
25OH vit D (ng/ml)	r		0.088	0.017	-0.117	-0.028	-0.356
	P		0.377	0.866	0.235	0.776	**0.000**
		Calcium	**Phosphorus**	**ALP**	**Albumin**	**Number of pregnancy**	**Gestational Week**
MPV (fl)	r	0.205	0.030	-0.168	0.144	-0.077	-0.208
	P	**0.036**	0.763	0.088	0.144	0.438	**0.034**
25OH vit D (ng/ml)	r	0.134	0.046	-0.101	-0.043	-0.128	0.064
	P	0.174	0.643	0.310	0.663	0.197	0.519

Spearman Correlation

DISCUSSION

Studies have shown that larger platelets are more active and clot better. Large platelets collapse more easily with platelet aggregation agonists such as ADP, collagen, and adrenaline. These larger platelets produce more prothrombotic and vasoactive factors such as arachidonic acid metabolites, serotonin and ATP, and have denser granules.[12,13]

Changes in platelet morphology have been reported in diabetic patients.[14] Increased platelet aggregation is seen in diabetic patients and this correlates with increased cardiovascular events. Platelet activation is increased in diabetic patients compared to nondiabetic patients.[15]

Increased platelet and leukocyte activity increases adhesion to endothelial cells, leading to inflammation and thrombosis. During normal pregnancy, MPV is constant.[12,16-18] There is no difference between MPV values in Type 1 and Type 2 diabetes mellitus.[12,17] In diabetes mellitus, hemostasis shifts towards a prethrombotic state, leading to microangiopathic late complications. It has been found that MPV in diabetic patients is higher than in the normal population. It is known that this height is one of the factors causing impaired hemostasis and prethrombotic state in diabetes. It is a matter of debate whether tight metabolic control can normalize this hyperactivity in diabetes. There are also studies linking this volume increase in platelets to stem cell dysfunction in the megakaryocyte series.[16,19] Although some studies found that MPV levels of macroangiopathic diabetic patients were higher than normal controls, no statistical relationship was found between vascular complications and MPV in many other studies.[19,20] Studies have reported that changes in MPV, rather than qualitative changes in platelet functions, are responsible for hypercoagulable platelets, as in diabetes mellitus.[21]

MPV was found to be high in diabetics with or without complications, but no correlation could be shown between high glucose levels and glycated hemoglobin (HbA1c) and MPV. In type 1 diabetes patients, platelet activation may be associated with poor metabolic control.[21] When blood sugar drops effectively, MPV decreases significantly.[6] MPV levels are higher in diabetic patients than in the control group.[22] High MPV levels have also been reported in prediabetic patients.[23]

Different results have been reported in the few studies conducted on MPV in GDM patients. While several of these studies reported that MPV levels were significantly higher in gestational diabetic pregnant women than in healthy pregnant women, no significant difference was found in other studies. In our study, no statistically significant difference was shown between pregnant women with gestational diabetes and healthy pregnant women in terms of both MPV and platelet count.

Bozkurt et al.[24] showed that gestational diabetic patients had higher MPV levels and lower platelet counts than the control group, and explained the low platelet count with the shorter platelet lifespan in diabetic patients.

In a similar study conducted by Balkan et al.[25] on a total of 89 pregnant women, 38 with gestational diabetes and 51 healthy pregnant women; MPV and HbA1C values of the gestational diabetic group were found to be significantly higher than those of healthy pregnant women.

Having a history of diabetes in first-degree relatives is considered a risk factor in the development of gestational diabetes.[26] In our study, presence of a history of diabetes in first-degree relatives; It was found to be 38.5% in the gestational diabetes patient group and 13.5% in the healthy pregnant group, and was found to be statistically significantly higher (**Table 1**).

In our study, in the correlation analysis of the MPV level of the patients with other clinical and laboratory data; There was a significant negative correlation between MPV value, platelet count and gestational week. There was a significant positive correlation between MPV value and calcium value. However, this was not statistically significant (**Table 4**).

In studies where the MPV value is found to be significantly higher, the gestational week is generally 32-36 weeks. In our study, MPV values at 24-28 weeks of gestation were evaluated. The fact that the MPV value did not show a statistically significant difference between the two groups in our study suggested that this might be due to the fact that the study was conducted at an earlier gestational week.

Vitamin D deficiency is quite common in the general population, and its prevalence in the pregnant population has been known for a long time.[27] Vitamin D has been associated with many negative health outcomes, starting from the preconception period, pregnancy, perinatal period, childhood and adulthood.[27,28] There is also increasing evidence regarding the role of adequate vitamin D levels in maintaining normal glucose homeostasis. It has been observed in the literature that studies evaluating the effect of vitamin D deficiency in patients with gestational diabetes have contradictory results.

There is no international consensus on the reference range of serum 25-OH vitamin D level that best reflects vitamin D status in the normal population and pregnant women. The standard definition of normal values of vitamin D levels in the normal population is the 25-OH vitamin D level that will not cause an increase in PTH level.[32] In our study, when vitamin D deficiency was categorized according to the cut-off value of <30 ng/ml, the deficiency rates were found to be 84.6% in the gestational diabetes group and 88.5% in the healthy pregnant group. The average 25-OH vitamin D level of the gestational pregnant group was found to be lower than that of healthy pregnant women, but no statistically significant difference was shown between them in terms of both rate and level.

When the literature was reviewed in terms of data showing the relationship between vitamin D deficiency and gestational diabetes in pregnant women, in a cross-sectional study conducted by Maghbooli et al.[9] at 24-28 weeks of gestation, the rate of severe vitamin D deficiency was found to be statistically significantly higher in the GDM group than in the control group. Additionally, it was shown that the average 25-OH vitamin D levels were statistically significantly lower in the GDM group than in the control group.

Similarly, in the case-control study conducted by Zhang et al.[11] it was shown that vitamin D deficiency was higher in the GDM group than in the control group, and the average maternal plasma 25-OH vitamin D concentration was statistically significantly lower in the GDM group than in the control group. There are also studies in the literature that do not associate vitamin D deficiency with the risk of GDM. In the case-control study conducted by Baker et al.[29] the relationship between vitamin D deficiency and GDM in the first trimester was evaluated. In this study, first trimester maternal 25-OH vitamin D deficiency rates were found to be similarly low in the GDM group and healthy controls.

In another case-control study by Makgoba et al.[30] in which the relationship between the development of GDM and the first trimester 25-OH vitamin D level was evaluated, no statistically significant difference was detected in the GDM group and the normoglycemic control group in terms of vitamin D deficiency. In a cross-sectional study conducted by Farrant et al.[10] 25-OH vitamin D levels were found to be similar in the GDM group and the healthy pregnant group, and the prevalence of vitamin D deficiency was shown to be 66%.

Studies have reported vitamin D deficiency in pregnant women at rates ranging from 7.2% (2-53) to 78.4%.[31] The prevalence of vitamin D deficiency in our study is higher than other studies. These differences are thought to be caused by many factors that can affect serum 25-OH vitamin D levels, such as the ethnic group in which the study was conducted, clothing style, physical activity status, BMI, and socioeconomic status. There is also not enough data to measure vitamin D levels during pregnancy and evaluate the effectiveness of vitamin D replacement if deficiency is detected. In cases where women during pregnancy and lactation require at least 600 IU vitamin D per day and 25-OH vitamin D levels are <20 ng/ml, 1000-2000 IU/day vitamin D replacement is recommended by The American Congress of Obstetricians and Gynecolgists (ACOG).[33,34]

CONCLUSION

As a result, in our study, consistent with the literature, the presence of a history of diabetes in first-degree relatives was found to be higher in the GDM group than in the control group. For this reason, we believe that pregnant women with a history of diabetes in their first-degree relatives should be closely monitored for gestational diabetes.

However, vitamin D deficiency was found to be quite common in all pregnant women. Therefore, we believe that measuring vitamin D in all pregnant women is useful.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of İstanbul Okmeydan Training and Research Hospital Clinical Researches Ethics Committee (Date: 08.04.2014, Decision No: 190).

Informed Consent: All patients signed the free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

Financial Disclosure: The Work was developed at Van Training and Research Hospital, Van, Turkey.

Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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