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Determining Gestational Diabetes Mellitus Risk: Evaluation of the Role of Complete Blood Count Variables Measured in the First Two Trimesters

Gestasyonel Diabetes Mellitus Riskinin Belirlenmesi: İlk İki Trimesterde Ölçülen Tam Kan Sayımı Değişkenlerinin Rolünün Değerlendirilmesi

ABSTRACT

Objective:
To evaluate the value of first and second trimester complete blood count (CBC) parameters in predicting the risk of gestational diabetes mellitus (GDM).

Material and Methods:
This study was carried out from January 2017 to December 2018 at the Bağcılar Training and Research Hospital Gynecology and Obstetrics polyclinic. The CBC and biochemistry results, various indices calculated from CBC parameters, and other data of the study group consisting of pregnant women with and without GDM were obtained from medical records.

Results:
Age ($p<0.001$), fasting glucose ($p<0.001$), red blood cell count (RBC) ($p<0.001$), hemoglobin ($p=0.015$), hematocrit ($p<0.001$), red cell distribution width (RDW) ($p=0.001$), RDW-to-platelet ratio ($p<0.001$), and all glucose levels for 75 g OGTT tests ($p<0.001$ for all) were higher in women with GDM compared to controls. Platelet count ($p=0.002$), platelet-to-lymphocyte ratio ($p=0.006$) and platelet-to-MPV ratio ($p=0.021$) were lower in pregnant women with GDM compared to those without. We found advanced age ($p<0.001$), high RBC ($p=0.002$) and high RDW-to-platelet ratio ($p<0.001$) were independently associated with GDM. For the prediction of GDM, the area under curve (AUC) values were highest for RBC (AUC:0.619, 95%CI: 0.566-0.673; $p<0.001$) and RDW-to-platelet ratio (AUC:0.610, 95%CI: 0.556-0.663; $p<0.001$). RBC showed 57.0% sensitivity and 63.4% specificity, while RDW-to-platelet ratio demonstrated 31.7% sensitivity and 89.2% specificity.

Conclusion:
Increased RBC and increased RDW-to-platelet ratio measured in the early period of pregnancy are independent predictors of higher GDM risk. Comprehensive prospective studies assessing early determinants of GDM risk are needed.

Key Words:
Gestational diabetes, Risk, Complete blood count

ÖZ

Amaç:

Gestasyonel diyabetes mellitus (GDM) riskini öngörmede birinci ve ikinci trimester tam kan sayımı (CBC) parametrelerinin değerini değerlendirmek.

Gereç ve Yöntemler:

Bu retrospektif vaka kontrol çalışması, Ocak 2017 ile Aralık 2018 tarihleri arasında Bağcılar Eğitim ve Araştırma Hastanesi Kadın Hastalıkları ve Doğum Polikliniği'nde gerçekleştirildi. GDM'li gebeler ve sağlıklı gebelerden oluşan çalışma grubunun CBC ve biyokimya sonuçları, CBC parametrelerinden hesaplanan çeşitli indeksler ve diğer veriler tıbbi kayıtlardan elde edildi.

Bulgular:

Yaş (p<0,001), açlık kan glukozu (p<0,001), eritrosit sayısı (RBC) (p<0,001), hemoglobin (p=0,015), hematokrit (p<0,001), eritrosit dağılım genişliği (RDW) (p=0,001), RDW-trombosit oranı (p<0,001) ve 75 g OGTT testleri için tüm glukoz seviyeleri (tümü için p<0,001) GDM'li kadınlarda kontrollere kıyasla daha yüksekti. GDM'li gebelerde trombosit sayısı (p=0,002), trombosit/lenfosit oranı (p=0,006) ve trombosit/MPV oranı (p=0,021) sağlıklı gebelere göre daha düşüktü. Yüksek yaş (p<0,001), yüksek RBC (p=0,002) ve yüksek RDW-trombosit oranı (p<0,001) GDM için anlamlı bağımsız risk faktörleri olarak bulundu. GDM'nin öngörülmesinde, eğri altında kalan alan (AUC) değerleri en yüksek olan parametreler RBC (AUC:0,619, %95GA: 0,566-0,673; p<0,001) ve RDW-trombosit oranı (AUC:0,610, %95GA: 0,556-0,663; p<0,001) idi. RBC %57,0 duyarlılık ve %63,4 özgüllük gösterdi ve RDW-trombosit oranı %31,7 duyarlılık ve %89,2 özgüllük gösterdi.

Sonuç:

Gebeliğin erken döneminde saptanan artmış RBC ve artmış RDW-trombosit oranı, GDM riskinin artmasının bağımsız prediktörleridir. GDM riskinin erken belirleyicilerini değerlendiren kapsamlı prospektif çalışmalara ihtiyaç vardır.

Anahtar Kelimeler:

Gestasyonel diyabet, Risk, Tam kan sayımı

INTRODUCTION

Gestational diabetes mellitus (GDM) is diabetes diagnosed during pregnancy in women without diabetes before pregnancy (1). In the normal course of pregnancy, insulin resistance increases towards the end of the second trimester; however, individuals often remain normoglycemic owing to elevated insulin production. If this compensation is insufficient in responding to resistance, GDM may develop (2).

According to International Diabetes Federation data from 2017, more than 21 million births were affected by hyperglycemia during pregnancy and more than 18 million of these directly related with GDM (3). GDM is by far the most common disorder of the metabolism observed during pregnancy, with a reported prevalence of 17.8% (9.3-25.5%) (4, 5). GDM risk has been associated with various factors, including being overweight or obese, excessive gestational weight gain, unhealthy diet, genetic polymorphisms, polycystic ovary syndrome, micronutrient deficiencies, maternal age, and insulin resistance-related disease history in the family (6).

GDM poses a significant economic burden for health systems and it also has the potential to have serious adverse effects on the health of current and future generations through genetic and environmental mechanisms that are not yet fully understood (4). It has adverse effects including gestational hypertension and preeclampsia, and is associated with neonatal problems such as hyperinsulinemia, macrosomia, cesarean delivery, hypoglycemia, and obesity and Type 2 DM later in life (5). Improved health outcomes depend on early diagnosis and stringent glycemic control (7). Various diagnostic approaches have been used to identify mothers with GDM (8). The gold standard test is the oral glucose tolerance test (OGTT), administered between the 24th and 28th weeks of gestation. However, time and laboratory costs, the difficulty of drinking glucose solution, need for fasting before the test and low reproducibility are among the factors that cause difficulties in OGTT application. Additionally, OGTT is performed at a very late timepoint in the pregnancy and it cannot detect mild glucose intolerance (9). Therefore, being able to estimate GDM risk within the first two trimesters before OGTT can be performed, may be useful for early diagnosis and could prevent complications. Today, there is no accepted routine screening protocol for the diagnosis of GDM in the period before OGTT. In previous studies, some whole blood parameters, including platelet count, mean platelet volume (MPV) and neutrophil count, were reported to be useful in estimating GDM risk (10-13). We aimed to investigate complete blood count (CBC) parameters and indices measured during the first and second trimesters with respect to their value in predicting GDM risk.v This study has been prepared on the basis of the medical specialty thesis titled "Evaluation of the role of whole blood count variables in prediction of the risk of gestational diabetes mellitus", which we completed in 2019 under the supervision of specialist doctor M.A.

MATERIAL and METHODS

This retrospective study was conducted with 415 pregnant women between April January 2017 and December 2018 in Bağcılar Health Practice and Research Center, University of Health Sciences, Bağcılar, Turkey. Ethics committee approval for the study was obtained from Clinical Research Ethics Committee of Health Sciences University Istanbul Bağcılar Training and Research Hospital (decision no: 2019.03.1.03.022, date: 01/03/2019). All protocols were conducted in accordance with the principles of the Declaration of Helsinki.

Inclusion and exclusion criteria

Within the scope of the study, the health records of 221 pregnant women with GDM and 194 without GDM, who had applied to the Bağcılar Health Practive and Research Center, University of Health Sciences, between January 1, 2017 and December 31, 2018, were retrospectively analyzed. Pregnant women with diabetes diagnosis before pregnancy, those with eclampsia or preeclampsia, patients diagnosed with other chronic diseases, and subjects with infectious, rheumatological or connective tissue diseases were excluded.

For the diagnosis and follow-up of pregnancy in our clinic, a detailed obstetric history, personal and familial systemic disease history are questioned. Data on height, body weight, blood pressure and detailed physical/pelvic examinations are recorded and ultrasonography and various laboratory measurements are performed at the required gestational weeks. Obstetric USG of the pregnant women was performed with a 7.5 MHZ vaginal and abdominal probe on an Aloka prosound SSD 5500 ultrasound device.

Laboratory analysis

Laboratory test results for the period before OGTT (before the 24th gestational week) were recorded from medical records. Blood glucose tests were performed on the Beckman-Coulter AU-5800 model device. HbA1c testing was done with the Arkray-Adams A1cHA-8180, while CBC evaluations were done with Sysmex XN-9000 device. Various indices were calculated from CBC results, including neutrophil-to-lymphocyte ratio, platelet-to-neutrophil ratio, platelet-to-lymphocyte ratio, platelet-to-MPV ratio, and red blood distribution width (RDW)-to-platelet ratio.

Oral glucose tolerance test

All pregnant women screened for GDM were between 24-28 weeks gestational age. Some of the pregnant women underwent 50 g OGTT and some underwent 75 g OGTT. Pregnant women with positive test results in the first group underwent a 100 g oral glucose loading test (OGTT) for diagnosis. The 75 g glucose loading test was performed for both screening and diagnostic purposes. Since there is no clear consensus in the world on which test should be used to diagnose GDM, both tests are used. The methods and limits recommended by the ADA were used for both screening tests.

Before the 50 g glucose loading test, pregnant women were not required to be hungry. However, at least 8 hours of fasting was required before the 75 g and 100 g tests. Before the OGTT, pregnant women were asked to take uninterrupted diet for at least three days. Pregnant women were restricted in terms of physical activity during the test period.

For the 50 g loading test, the threshold value for the first hour blood glucose ≥ 140 mg/dl was accepted. Impaired glucose tolerance was considered in patients with first hour blood glucose levels between 140 and 180 mg/dl and a 100 g OGTT test was performed. For the 75 g loading test, venous plasma threshold values were accepted as fasting ≥ 92 mg/dl, 1st hour ≥ 180 mg/dl, 2nd hour ≥ 153 mg/dl. Patients with a high value of 75 g OGTT were diagnosed with GDM. For 100 g OGTT, the cut-off values in venous plasma were accepted as fasting ≥ 95 mg/dl; 1st hour ≥ 180 mg/dl; 2nd hour ≥ 155 mg/dl; 3rd hour ≥ 140 mg/dl according to Carpenter and Coustan (C&C) criteria. GDM was diagnosed if there were two or more threshold elevations in 100 g OGTT.

Statistical analysis

The IBM SPSS software for Windows, Version 25.0 (IBM, Armonk, NY, USA) was used for analyses and significance threshold was set at $p < 0.05$. Normality of distribution was tested with histogram and Q-Q plots. Continuous data are summarized with mean ± standard deviation or median (1st quartile - 3rd quartile) in the presence of normal or non-normal distribution, respectively. Number and percentage were used to summarize categorical data. Normally distributed variables were analyzed with the independent samples t-test, while the Mann-Whitney U test was used for those without normal distribution. Categorical variables were compared with chi-square tests (continuity correction, Pearson, Fisher Exact). Prediction performances were evaluated by using Receiver Operating Characteristic (ROC) curve analysis, and cut-off values were determined by using the Youden index. Multiple logistic regression analysis (forward conditional method) was performed to determine the best predictive factors associated with GDM.

RESULTS

Mean age was 30.27 ± 5.87 years and 221 of patients were diagnosed with GDM. Age ($p<0.001$), fasting glucose ($p<0.001$), red blood cell (RBC) ($p<0.001$), hemoglobin ($p=0.015$), hematocrit ($p<0.001$), red cell distribution width (RDW) ($p=0.001$) and RDW-to-platelet ratio ($p<0.001$) of pregnant women with GDM diagnosis values were significantly higher than healthy pregnant women. Fasting glucose value ($p<0.001$), 1st hour glucose value ($p<0.001$) and 2nd hour glucose value ($p<0.001$) of 75 g OGTT test of pregnant women with GDM were significantly higher than healthy pregnant women. Platelet count ($p=0.002$), platelet-to-lymphocyte ratio ($p=0.006$) and platelet-to-MPV ratio ($p=0.021$) values were higher in pregnant women with GDM compared to those without (Table I).

Table I. Summary of variables with regard to gestational diabetes mellitus

		Gestational DM		
	Total (n=415)	Absent (n=194)	Present (n=221)	p
Age (years)	30.27 ± 5.87	28.75 ± 5.80	31.60 ± 5.60	**<0.001**
OGTT				
75-g	304 (73.3%)	194 (100.0%)	110 (49.8%)	**<0.001**
100-g	111 (26.7%)	0 (0.0%)	111 (50.2%)	
Fasting glucose (mg/dL)	89 (82 - 96)	83 (80 - 87)	95 (90 - 101)	**<0.001**
75-g OGTT (mg/dL), n=304				
Fasting glucose	87 (82 - 95)	83 (80 - 87)	98.5 (94 - 105)	**<0.001**
1-hour glucose	136 (116.5 - 161)	128 (109 - 148)	163 (130 - 191)	**<0.001**
2-hour glucose	107 (91 - 128)	99 (86 - 113)	127 (107 - 149)	**<0.001**
100-g OGTT (mg/dL), n=111				
Fasting glucose	92 (86 - 97)	-	92 (86 - 97)	N/A
1-hour glucose	203 (190 - 218)	-	203 (190 - 218)	N/A
2-hour glucose	174 (163 - 186)	-	174 (163 - 186)	N/A
3-hour glucose	125 (107 - 143)	-	125 (107 - 143)	N/A
RBC (10^6/mcL)	3.98 ± 0.42	3.89 ± 0.40	4.07 ± 0.42	**<0.001**
Hemoglobin (g/dL)	11.40 ± 1.15	11.25 ± 1.11	11.52 ± 1.16	**0.015**
Hematocrit (%)	34.57 ± 3.18	33.95 ± 2.89	35.12 ± 3.33	**<0.001**
Leukocyte (x10^3/mcL)	10.34 ± 2.24	10.42 ± 2.12	10.27 ± 2.35	0.499
Neutrophil (%)	71.08 ± 5.94	71.38 ± 5.35	70.82 ± 6.42	0.340
Neutrophil (x10^3/mcL)	7.38 ± 1.90	7.47 ± 1.75	7.30 ± 2.03	0.369
Lymphocyte (%)	19.9 (17.1 - 23.2)	19.6 (17.1 - 22.9)	20.1 (17.2 - 23.8)	0.353
Lymphocyte (x10^3/mcL)	2.03 (1.66 - 2.41)	2.05 (1.68 - 2.38)	2.02 (1.66 - 2.46)	0.839
Platelet (x10^3/mcL)	248.83 ± 64.68	259.05 ± 63.52	239.86 ± 64.50	**0.002**
MPV (fL)	10.0 (8.9 - 10.9)	10.1 (9.2 - 10.8)	10.0 (8.7 - 11.0)	0.948
RDW (%)	13.5 (12.8 - 14.6)	13.2 (12.5 - 14.3)	13.7 (13.0 - 14.7)	**0.001**
Platelet to neutrophil ratio	33.73 (26.00 - 41.67)	34.43 (26.85 - 42.55)	32.71 (25.57 - 40.52)	0.078
Platelet to lymphocyte ratio	120.51 (97.78 - 150.00)	124.25 (100.40 - 156.28)	113.53 (93.60 - 140.40)	**0.006**
Platelet to MPV ratio	24.71 (20.33 - 30.61)	26.15 (21.01 - 31.36)	23.72 (19.47 - 30.43)	**0.021**
RDW to platelet ratio	5.70 (4.71 - 6.92)	5.35 (4.60 - 6.52)	6.09 (4.85 - 7.34)	**<0.001**

Data are given as mean ± standard deviation or median (1st quartile - 3rd quartile) for continuous variables according to normality of distribution and as frequency (percentage) for categorical variables

Multiple logistic regression was used to determine factors independently associated with GDM. We found that higher age significantly increased the likelihood of GDM development (p<0.001). Individuals with high RBC (>4.0) had a 1.968-fold greater risk for GDM than those with lower values (OR: 1.968, 95% CI: 1.295 - 2.989, p=0.002). Individuals with high RDW-to-platelet ratio (>7.15) had a 3.706-fold greater risk for GDM than those with lower values (OR: 3.706, 95% CI: 2.129 - 6.449, p<0.001). Other variables included in the model, hemoglobin (p=0.293), hematocrit (p=0.596), platelet (p=0.297), RDW (p=0.087), platelet-to-lymphocyte ratio (p=0.065) and platelet-to-MPV ratio (p=0.106) were found to be non-significant (Table II).

Table II. The best predictive factors for gestational diabetes mellitus, multiple logistic regression analysis

	β coefficient	Standard Error	p	Exp(β)	95.0% CI for Exp(β)	
Age	0.086	0.019	**<0.001**	1.090	1.050	1.131
RBC (>4.0)	0.677	0.213	**0.002**	1.968	1.295	2.989
RDW to platelet ratio (>7.15)	1.310	0.283	**<0.001**	3.706	2.129	6.449
Constant	-3.037	0.591	<0.001	0.048		

Exp: exponential value CI: confidence interval; Dependent variable: Gestational diabetes mellitus; Nagelkerke R^2=0.188

The greatest area under curve (AUC) values for the detection of GDM were found to be for RBC (AUC: 0.619, 95% CI: 0.566 - 0.673; p<0.001) and for RDW-to-platelet ratio (AUC: 0.610 95% CI: 0.556 - 0.663; p<0.001). The sensitivity and specificity values of RDW-to-platelet ratio to detect GDM were found to be 31.7% and 89.2%, respectively. The diagnostic capabilities of parameters demonstrating notable significance for GDM detection are summarized in Table III.

Table III. Performance of various parameters to predict gestational diabetes mellitus

	Cut-off	Sensitivity	Specificity	Accuracy	PPV	NPV	AUC (95.0% CI)	p
RBC (10^6/mcL)	>4.0	57.0%	63.4%	60.0%	64.0%	56.4%	0.619 (0.566 - 0.673)	<0.001
Hemoglobin (g/dL)	>11.49	56.1%	59.8%	57.8%	61.4%	54.5%	0.566 (0.511 - 0.621)	0.020
Hematocrit (%)	>35.3	48.9%	67.5%	57.6%	63.2%	53.7%	0.599 (0.545 - 0.654)	<0.001
Platelet (x10^3/mcL)	≤200	33.0%	83.5%	56.6%	69.5%	52.3%	0.584 (0.529 - 0.639)	0.003
RDW (%)	>13.2	65.6%	51.0%	58.8%	60.4%	56.6%	0.598 (0.543 - 0.653)	0.001
Platelet-to-lymphocyte ratio	≤135.99	72.9%	40.2%	57.6%	58.1%	56.5%	0.578 (0.523 - 0.633)	0.006
Platelet-to-MPV ratio	≤18.1	22.6%	90.7%	54.5%	73.5%	50.7%	0.566 (0.511 - 0.621)	0.021
RDW-to-platelet ratio	>7.15	31.7%	89.2%	58.6%	76.9%	53.4%	0.610 (0.556 - 0.663)	<0.001

PPV: Positive predictive value, NPV: Negative predictive value, AUC: Area under ROC curve, CI: Confidence intervals

DISCUSSION

Maintaining blood sugar levels in GDM reduces maternal and neonatal morbidity and therefore, earlier detection can yield better outcomes. CBC is inexpensive and may provide diagnostic data (14, 15). This study showed that, despite having very poor sensitivity, RDW-to-platelet ratio had very good specificity for GDM diagnosis, which suggests that GDM risk is exceedingly low in patients with values below the cut-off (7, 15). However, since advanced ageage and RBC were also found to be independently associated with GDM risk, it appears that assessing patients with a single indice would be insufficient.

Hyperglycemia prevalence in pregnancy increases with age (3, 6). Savvidou et al., and Mertoğlu et al., reported that the age of women diagnosed with GDM was higher than healthy controls (16, 17). In the study of Çolak et al., increasing age was reported as an independent risk factor for GDM (18). Similarly, in the current study, the median age of the GDM group was found to be higher compared to controls and age increase was one of the independent predictors of GDM development. It is therefore evident that closer follow may be beneficial in older pregnant women.

Erythrocytes are highly unique cells that, when mature, lose all membrane-bound organelles to accommodate for their essential functions and are more susceptible to any metabolic disturbances. Glucose metabolism disorders alter the morphology and disrupt the functions of erythrocytes, causing insufficient microcirculation perfusion and hypoxia, particularly in patients with DM. Indices associated with the erythrocyte (RBC, hemoglobin, RDW), a cell that is closely affected by blood sugar changes, may provide some actionable information regarding diabetes likelihood (19). Some researchers revealed that GDM causes higher hemoglobin concentrations compared to women without GDM and other studies have also shown that early-pregnancy levels of hemoglobin can predict GDM risk (8, 20, 21). However, it must be noted that conflicting results exist, some researchers have shown lower hemoglobin levels in women with GDM while others have found similar levels in women with and without GDM (17, 22, 23). The natural physiological changes during pregnancy cause a decreasing trend of RBC until the 28th week of pregnancy, while this is followed by an increase after the 28th week. Additionally, RBC may be higher in the presence of GDM (24). It is reported that data obtained by repeated measurements of RBC (during the first trimester and early second trimester) can be utilized for the early prediction of GDM (8). In the study of Yang et al., it was reported that RBC was significantly higher in women with GDM, but an independent relationship between these parameters could not be found (25). There are also studies reporting no difference in terms of RBC between pregnant women with and without GDM (8). In addition to RBC and hemoglobin values, RDW can be directly measured through CBC (26). RDW, an inflammatory marker, is significantly elevated in diabetic patients (27). In previous studies, authors reported that RDW was higher in pregnant women with GDM compared to controls and RDW was found to be an independent predictor of GDM (28, 29). In the present study, it was found that the hemoglobin, RBC, RDW and RDW-to-platelet ratio values of pregnant women with GDM were higher than that of healthy controls, and furthermore, higher RBC and RDW-to-platelet ratio values were revealed as independent risk factors for GDM. In addition, for the diagnosis of GDM, it was observed that RBC had a sensitivity of 57.0% and a specificity of 63.4%, while RDW-to-platelet ratio had a sensitivity of 31.7% and a specificity of 89.2%. It was concluded that determining pregnant women with GDM risk before OGTT can be performed by use of RBC and RDW-to-platelet ratio, and that this approach may be useful for assessing GDM risk in the early period.

Platelets critically contribute to atherothrombosis which represents one of the main underlying causes of morbidity / mortality in diabetes (27). Platelet-related indices can be useful in GDM screening as they are inexpensive and routinely evaluated markers whose importance are often overlooked (30). In the study of Erikçi et al., it was reported that the platelet count was lower in the presence of GDM (10). In the study by Fashami et al., platelet count was similarly found to be lower in subjects with GDM compared to controls, and furthermore, platelet count was identified to be independently associated with GDM risk (31). In the current study, platelet count was significantly lower and RDW-to-platelet ratio was higher in pregnant women with GDM. Despite these results, it should be noted that various previous studies reported no difference in platelet counts between pregnant women with and without GDM (11, 17, 18, 22, 23, 32). Furthermore, some rare studies described higher platelet count in subjects with GDM (25, 29). These considerable differences in the literature are likely to be explained by a number of factors; however, the most prominent of these factors can be listed as follows: differences in gestational age at time of measurements, the age groups of pregnant women, possible comorbidities and confounding factors within and between studies, and methodological variations in CBC measurement. On the other hand, based on the results we found in the study, it was concluded that the platelet count (particularly because it affects the RDW-to-platelet ratio) may be a useful parameter that could contribute to the estimation of the risk of GDM during early pregnancy.

This study was planned retrospectively and it was not community-based, which establish its primary limitations. These limitation may question the generalizability of the results to the population. Secondly, the results of some highly-conclusive parameters (like HbA1C) were not included in the analysis due to lack of measurements in the majority of patients (especially subjects without GDM). Also, CBC results included in the study were measured at different timepoints in each subject; thus, this wide time interval covering the first two trimesters could have intro-

duced bias with respect to the changes in respective reference intervals throughout the pregnancy. Another limitation may be noted as the significantly higher mean age of the GDM group compared to controls; however, since age is a risk factor for GDM, this difference was largely unavoidable. Lastly, hemoglobin electrophoresis was not performed and the diagnosis of thalassemia was not questioned. In our clinic, oral iron prophylaxis is started at the 12th gestational week; however, vitamin B12 use was not questioned. Nonetheless, our study is important as it shows relationships between GDM risk and many easily-accessible CBC parameters measured in the early period of pregnancy.

CONCLUSION

In the light of the analyses, it was determined that increases in age, RBC and RDW-to-platelet ratio could be valuable to distinguish pregnant women with GDM risk. Evaluating early-pregnancy levels of RBC and RDW-to-platelet ratio in pregnant women (with respect to age) may have value in identifying patients with high or low risk for GDM before OGTT can be performed. Further studies on this topic must be conducted to assess whether these findings can be replicated in different populations. Given that such relationships (or others) can be shown, it may be possible to devise new strategies for the identification and timely management of pregnancies at high risk for GDM.

Ethics Committee Approval:
Ethics committee approval for the study was obtained from Clinical Research Ethics Committee of Health Sciences University Istanbul Bağcılar Training and Research Hospital (decision no: 2019.03.1.03.022, date: 01/03/2019). All protocols were conducted in accordance with the principles of the Declaration of Helsinki.

Author Contributions:
Concept – E.Y., M.A.; Design - E.Y., M.A.; Supervision - E.Y., M.A.; Resources - E.Y.; Materials - E.Y., M.A.; Data Collection and/or Processing - M.A.; Analysis and/ or Interpretation - E.Y., M.A.; Literature Search - E.Y., M.A.; Writing Manuscript - E.Y., M.A.; Critical Review - E.Y., M.A.

Conflicts of Interest:
The authors declare that they have no conflicts of interest concerning this article.

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REFERENCES

1. Association AD. 2. Classification and diagnosis of diabetes: standards of medical care in diabetes-2018. Diabetes Care 2018; 41(Supplement 1):S13-S27.

2. Abell SK, De Courten B, Boyle JA, Teede HJ. Inflammatory and other biomarkers: role in pathophysiology and prediction of gestational diabetes mellitus. Int J Mol Sci 2015; 16(6):13442-73.

3. Cho N, Shaw J, Karuranga S, Huang Y, Da Rocha Fernandes J, Ohlrogge A, Malanda B. IDF Diabetes Atlas: Global estimates of diabetes prevalence for 2017 and projections for 2045. Diabetes Res Clin Pract 2018; 138:271-81.

4. Johns EC, Denison FC, Norman JE, Reynolds RM. Gestational diabetes mellitus: mechanisms, treatment, and complications. Trends Endocrinol Metab 2018; 29(11):743-54.

5. Sacks DA, Hadden DR, Maresh M, Deerochanawong C, Dyer AR, Metzger BE, Lowe LP, Coustan DR, Hod M, Oats JJ. Frequency of gestational diabetes mellitus at collaborating centers based on IADPSG consensus panel–recommended criteria: the Hyperglycemia and Adverse Pregnancy Outcome (HAPO) Study. Diabetes Care 2012; 35(3):526-8.

6. Plows JF, Stanley JL, Baker PN, Reynolds CM, Vickers MH. The pathophysiology of gestational diabetes mellitus. Int J Mol Sci 2018; 19(11):3342.

7. Mpondo BCT, Ernest A, Dee HE. Gestational diabetes mellitus: challenges in diagnosis and management. J Diabetes Metab Disord 2015; 14(1):42.

8. Shaarbaf Eidgahi E, Nasiri M, Kariman N, Safavi Ardebili N, Salehi M, Kazemi M, Zayeri F. Diagnostic accuracy of first and early second trimester multiple biomarkers for prediction of gestational diabetes mellitus: a multivariate longitudinal approach. BMC Pregnancy Childbirth 2022; 22(1):13.

9. Amini M, Kazemnejad A, Zayeri F, Montazeri A, Rasekhi A, Amirian A, Kariman N. Diagnostic accuracy of maternal serum multiple marker screening for early detection of gestational diabetes mellitus in the absence of a gold standard test. BMC Pregnancy Childbirth 2020; 20(1):375.

10. Erikçi AA, Muhçu M, Dündar Ö, Öztürk A. Could mean platelet volume be a predictive marker for gestational diabetes mellitus? Hematology 2008; 13(1):46-8.

11. Bozkurt N, Yılmaz E, Biri A, Taner Z, Himmetoğlu Ö. The mean platelet volume in gestational diabetes. J Thromb Thrombolysis 2006; 22(1):51-4.

12. Kong M, Zhang H, Liu X, Ge Y, Zhang Z, Zhao R, Li Y, Huang S, Xiong G, Yang X. Association of maternal neutrophil count in early pregnancy with the development of gestational diabetes mellitus: a prospective cohort study in China. Gynecol Endocrinol 2022; 38(3):258-62.

13. Huang Y, Chen X, You ZS, Gu F, Li L, Wang D, Liu J, Li Y, He S. The value of first-trimester platelet parameters in predicting gestational diabetes mellitus. J Matern Fetal Neonatal Med 2022; 35(11):2031-5.

14. Alfadhli EM. Gestational diabetes mellitus. Saudi Med J 2015; 36(4):399-406.

15. Mcpherson RA, Pincus MR. Henry's clinical diagnosis and management by laboratory methods E-book, Elsevier Health Sciences 2021.

16. Savvidou M, Nelson SM, Makgoba M, Messow C-M, Sattar N, Nicolaides K. First-trimester prediction of gestational diabetes mellitus: examining the potential of combining maternal characteristics and laboratory measures. Diabetes 2010; 59(12):3017-22.

17. Mertoglu C, Gunay M, Gungor M, Kulhan M, Kulhan NG. A study of inflammatory markers in gestational diabetes mellitus. Gynecol Obstet Reprod Med 2019; 25(1):7-11.

18. Colak E, Ozcimen EE, Ceran MU, Tohma YA, Kulaksızoglu S. Role of mean platelet volume in pregnancy to predict gestational diabetes mellitus in the first trimester. J Matern Fetal Neonatal Med 2020; 33(21):3689-94.

19. Wang Y, Yang P, Yan Z, Liu Z, Ma Q, Zhang Z, Wang Y, Su Y. The relationship between erythrocytes and diabetes mellitus. J Diabetes Res 2021; 2021:6656062.

20. Yong HY, Shariff ZM, Yusof BNM, Rejali Z, Tee YYS, Bindels J, Van Der Beek EM. Early pregnancy hemoglobin is associated with the risk of gestational diabetes mellitus: a retrospective cohort study. Br J Nutr 2022:1-8.

21. Wang C, Lin L, Su R, Zhu W, Wei Y, Yan J, Feng H, Li B, Li S, Yang H. Hemoglobin levels during the first trimester of pregnancy are associated with the risk of gestational diabetes mellitus, pre-eclampsia and preterm birth in Chinese women: a retrospective study. BMC Pregnancy Childbirth 2018; 18(1):263.

22. Güdücü N, Görmüş U, Herman İ, Yİğİter AB, Dünder İ. Mean platelet volume in gestational diabetes mellitus. İstanbul Bilim Üniversitesi Florence Nightingale Tıp Dergisi 2015; 1(1):7-10.

23. Şentürk HSA, Şentürk M, Kara OF. The role of the platelet profile in the prediction of gestational diabetes. Kastamonu Med J 2021; 1(2):50-4.

24. Zhang Y, Zhang Y, Zhao L, Shang Y, He D, Chen J. Distribution of complete blood count constituents in gestational diabetes mellitus. Medicine 2021; 100(23):e26301.

25. Yang H, Zhu C, Ma Q, Long Y, Cheng Z. Variations of blood cells in prediction of gestational diabetes mellitus. J Perinat Med 2015; 43(1):89-93.

26. Montagnana M, Cervellin G, Meschi T, Lippi G. The role of red blood cell distribution width in cardiovascular and thrombotic disorders. Clin Chem Lab Med 2012; 50(4):635-41.

27. Nada AM. Red cell distribution width in type 2 diabetic patients. Diabetes Metab Syndr Obes 2015; 8:525-33.

28. Eren P, Beyazit F. Gestasyonel Diabetes Mellituslu Hastalarda Basit Hematolojik Belirteçlerin Değerlendirilmesi: Vaka-Kontrol Çalışması. Bozok Tıp Dergisi 2021; 11(3):19-24.

29. Yılmaz ZV, Yılmaz E, İçer B, Küçüközkan T. Association of complete blood count parameters with gestational diabetes mellitus. Gynecol Obstet Reprod Med 2017; 23(2):65-9.

30. Sahbaz A, Cicekler H, Aynioglu O, Isik H, Ozmen U. Comparison of the predictive value of plateletcrit with various other blood parameters in gestational diabetes development. J Obstet Gynaecol 2016; 36(5):589-93.

31. Fashami MA, Hajian S, Afrakhteh M, Khoob MK. Is there an association between platelet and blood inflammatory indices and the risk of gestational diabetes mellitus? Obstet Gynecol Sci 2020; 63(2):133-40.

32. Baldane S, Ipekci SH, Kebapcilar A. Relationship between insulin resistance and mean platelet volume in gestational diabetes mellitus. J Lab Physicians 2015; 7(02):112-5.