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The Neutrophil/Lymphocyte and Platelet/Lymphocyte Ratios of Pregnant Women Who Underwent the 75-g Oral Glucose Tolerance Test to Predict Gestational Diabetes

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Abstract: Gestational diabetes mellitus (GDM) is one of the most common medical complications of pregnancy. Early diagnosis and treatment are important; the condition can cause both maternal and foetal complications. Today, single-/double-bolus oral 50-100-g glucose tolerance tests (OGTTs) are preferred. We explored whether the peripheral blood platelet/lymphocyte ratio (PLR) and/or neutrophil/lymphocyte ratio (NLR) could guide diabetes screening of a target group (rather than all pregnant women). This retrospective study was conducted at the Obstetrics and Gynecology Clinic of Sanko University Hospital from January 2010 to January 2020. Pregnant women in gestational weeks 24 to 28 who underwent 75-g OGTTs were included. Patients were evaluated by dividing them into two groups. Group 1 included 300 women with GDM. Group 2 included 300 healthy pregnant women who were negative on the OGTT test. We retrieved patient ages, gestational weeks, all blood count data derived during pregnancy, fasting blood glucose levels, heights and weights, and body mass indices. Leukocyte and neutrophil counts were significantly higher in the diabetic patient group than in the control group (both $p<0.01$). The NLR and PLR differed significantly between the two groups (both $p<0.01$), but the demographic data did not. Increase in white blood cell count, and elevations in the PLR and NLR, independently predicted GDM. Blood NLR and PLR can also be used as a GDM screening test. The NLR and PLR (markers of inflammation) were significantly increased in pre-diabetic and diabetic patients. The NLR and PLR may usefully predict pre-diabetes and GDM. ©2023 NTMS.

Keywords: Gestational diabetes; Platelet-to-lymphocyte ratio; Pregnancy; Neutrophil-to-lymphocyte ratio.

1. Introduction

Gestational diabetes mellitus (GDM), a common medical complication in pregnancy is a glucose metabolization disorder that develops in the second trimester and disappears after pregnancy [1].

GDM affects 10–15% of all pregnant women; there is some regional/country variability [2]. The cases are divided into those who were diabetic before pregnancy but were first diagnosed with diabetes only during

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pregnancy, and cases who develop diabetes during pregnancy (pregestational and gestational diabetes, respectively) [3]. To ensure that the foetus receives the glucose it requires, placental secretion of cortisol, growth hormone, oestrogen, progesterone, prolactin, and (especially) human placental lactogen all increase; triggering hyperinsulinemia, insulin resistance, fasting hypoglycemia, and postprandial hyperglycemia. This enhances the need for insulin; pancreatic hypertrophy and hyperplasia develop when the need is met [4, 5]. Foetal macrosomy, neonatal hypoglycemia, hyperbilirubinemia, and shoulder dystocia increase the frequencies of operative birth and birth trauma. Gestational hypertension, pre-eclampsia, a need for caesarean delivery, related complications, and type 2 diabetes are common. Early diagnosis and the treatment of gestational diabetes is vital; the condition can trigger maternal and foetal complications [6, 7].

Screening programmes for gestational diabetes are in place in many countries worldwide. Screening tests are performed in the second trimester (at gestational weeks 24-28) after the ingestion of 75 g (one bolus) or 50-100 g (two boluses) of glucose; venous plasma glucose levels are calculated [8, 9]. It is appropriate to use the tolerance test using 75-g oral glucose (OGTT) to evaluate all pregnant women in Turkey (the type 2 diabetes prevalence is high in our country). The test is well-tolerated, performed only once, and yields a single value [10]. We thus applied this test.

The platelet/lymphocyte ratio (PLR) and neutrophil/lymphocyte ratio (NLR) are simple markers of systemic inflammatory response (SIR) obtained from full blood count examined from peripheral blood [11]. Recent studies have shown that these markers are of prognostic utility in cancer patients; those with bowel and ischemic heart diseases; and patients with endometriosis, pre-eclampsia, and hyperemesis gravidarum [12-17]. Today, screening for diabetes is routine for all pregnant women. NLR and PLR have been studied in many diseases such as inflammatory bowel diseases, ischemic heart diseases, endometriosis, many malignancies, endometriosis. Based on past knowledge, inflammation in the etiology of GDM has always been investigated. In many studies, SIR markers such as NLR and PLR have been studied in GDM or DM patient groups. In some studies, significant statistics were obtained, while in others no significant statistics were found. The main purpose of our study is to conduct a study for the particularly prone group among all pregnancies screened for GDM, so that there will be no need to perform glucose loading tests on all pregnants [13-18]. Here, we explored whether the NLR and PLR could be used to screen a target group (thus not all pregnant women) in terms of gestational diabetes.

2. Material and Methods

This retrospective study was conducted in the 10-year period covering the dates of January 2010 and January 2020 at Sanko University Hospital Obstetrics and Gynecology Clinic between 24 weeks and 28 weeks. Pregnant women who apply between 24 and 28 weeks gestational weeks and have undergone a 75g oral glucose tolerance test included. In our study, 300 pregnant women diagnosed with gestational diabetes and 300 healthy pregnants with negative OGTT test were included as a control group. Patients' ages, gestational weeks, complete blood count parameters during pregnancy, fasting blood glucose, height and weight, BMI (body mass index) was scanned in patient files. The patient and control group included patients who applied to the obstetrics and general internal medicine clinic for routine control. Patients and control groups with a diagnosis of malignancy, patients with any infection, patients receiving steroid or immunosuppressive therapy, patients receiving chemotherapy or radiotherapy, patients with hematological diseases, patients with type 1 or type 2 diabetes mellitus were excluded from the study. The protocol of the study was approved by Sanko University Non-Interventional Clinical Research Ethics Committee (File no:07/07/2020, 2020/09) and written informed consent was obtained from all participants.

Patients were classified into two groups. Group 1 included 300 pregnant women diagnosed with gestational diabetes. Group 2 included 300 healthy pregnant women with negative OGTT test. The blood tests examined in all pregnant groups were taken in the outpatient clinic.

2.1. Statistical Analysis

Demographic distribution and statistical comparison of the data made in our study by SPSS (23. Version) program. Data are presented as mean, standard deviation, median, minimum, maximum, percentage and number. The normal distribution of continuous variables was analyzed using the Shapiro Wilk test. In the comparisons betten two groups with numerical variables, the Independent Samples T test was used when the normal distribution condition was met, and the Mann Whitney U test was used if it was not. In the comparison of continuous variables with more than two groups, the ANOVA test was used when the normal distribution condition was met, and the Kruskal Wallis test was used when it was not. The comparison between categorical variables was made with Chi-square test and Fisher's Exact test. In the comparison of two continuous variables, Pearson correlation test was used if the normal distribution condition is met, and the Spearman correlation test was used if it was not, and the statistical significance level was accepted as $p<0.05$.

3. Results

A total of 600 pregnant women with 300 pregnant OGTT tests positive and 300 pregnant OGTT tests negative were included in the study. The sociodemographic charecterictics of the patients and controls according to the diagnosis is shown in table 1. There were no significant differences between the

groups in terms of age, gravida, parite and body mass index (BMI). There was a significant difference between group 1 and the group 2 in terms of neutrophil and platelet counts.

In terms of lymphocyte count, group 1 were found to be higher when compared with the control group. There was no significant difference in lymphocyte count between group 1 and group 2 (Table 2).

Table 1: The sociodemographic charecterictics of the patients and controls according to the diagnosis.

	GDM group n=300	Control group n=300	p
Age	35.58±1.56	34.41±1.90	0.152
Gravida	3.14±0.21	2.98±0.52	0.321
Parity	3.02±0.18	2.78±0.39	0.187
Live Birth	2.98±0.16	2.64±0.28	0.110
BMI	27.5±1.21	26.9±1.14	0.210

Table 2: Comparison of groups according to neutrophil, lymphocyte and platelet levels.

	GDM group n=300	Control group n=300	p
Neutrophil	5750.26±312.7	2870.46±265.5	<0.001
Lymphocyte	2215.72±90.1	2045.51±65.2	0.121
Platelets	321458.21±7451.2	254129±9564.7	<0.001

There was a significant difference between patients and control group in terms of NLR and PLR, ($p<0.001$ for both). The NLR and PLR value were significantly higher in patients than control group (Table 3)

A significantly positive correlation was found between neutrophil count and patients ($p=0.242$), platelet count and patients ($p=0.313$) and a significantly negative correlation was found between lymphocyte count and patients ($p=-0.201$).

Table 3: Comparison of groups according to NLR and PLR.

	GDM group n=300	Control group n=300	p
NLR	2.78±1.4	1.59±1.2	<0.001
PLR	149.65±70.2	89.10±31.3	<0.001

4. Discussion

Subclinical inflammation and insulin resistance are the principal pathophysiological features of diabetes [18]. Several previous studies have reported correlations between subclinical inflammation and insulin resistance [19, 20]. Current studies have shown that inflammation, endothelial dysfunction and procoagulation disorder play a role in the occurrence of diabetes, insulin resistance and diabetes-related complications [21]. NLR, PLR and platelet index are low-cost, practical laboratory tests that are calculated from full blood counts examined during routine controls and are studied in most centers. Since there is no easy way to predict maternal GDM in pregnancy, inflammatory and platelet count detection by studying complete blood count in pregnant women in the first half of pregnancy contributes to maternal health in early detection of GDM. Pattanathaiyanon et al. showed that higher leukocyte numbers at early in the gestation process belonged with a greater risk of developing GDM [23]. However, Gorar et al. [23] reported that white blood cell, neutrophil, or lymphocyte parameters did not correlate significantly with GDM.

We found that the NLR and PLR indicated whether the OGTT test for gestational diabetes was required by all pregnant women or only a high-risk subgroup thereof. The NLR and PLR are simple, rapid, and convenient biological indicators of systemic inflammation. A study of 2753 pregnant women showed that women with gdm had a significant increase in the number of leukocytes in the first trimester.(compared to normoglycemic women) [24]. In another study, there was no significant difference between the GDM group and the normal healthy pregnant group in terms of NLR and PLR [25]. In the study conducted by Sahbaz et al., PLR and NLR increases were found to be significant between pregnants with gdm and healthy groups [26]. Friis et al. [27] study that inflammation markers (CRP, IL1-Rα, IL-6, TNF receptor II, monocyte-chemoattractant protein-1 and IL-10) increased from early- to mid-pregnancy, but not toward the end of pregnancy. Liu et al. [28] reported similar results.

NLR has been observed as an example of increased complications such as hearing loss in diabetic patients [29]. Indices of the systemic inflammatory response (the NLR and PLR) were associated with the the

development of diabetic retinopathy in patients lacking relevant family histories [30]. We showed earlier that, in T2DM patients, the serum CRP level/blood NLR combination served as a biomarker of Escherichia coli of β-lactamase-producing in urinary tract infections [31]. The PLR reflects the chronic inflammatory response; many studies have shown that the PLR usefully estimates the status of patients with tumors, diabetes, and neurological diseases [32, 33].

Fashami et al. [34] found that increases in the platelet and inflammatory indices of the complete blood count during the second trimester reflected the risk of GDM. Our results support this proposition. Onalan et al. [35] suggested that haematological parameters (the haematocrit and mean platelet volume), the PLR, and the NLR (they can be easily calculated from the exact count taken from the patients.) might seve as its cost-effective is appropriate in predicting microvascular complications of diabetes.

Today, gestational diabetes screening is performed on all pregnant women. However, many pregnant women oppose this screening test by drinking glucose. The aim of our study is to develop a method for glucose loading test by determining the risk group instead of all pregnants. The NLR and PLR values in our study were significantly higher in the gestational diabetic group. We recommend that glucose loading test should definitely be performed for patients in this group. We think that pregnant women who do not want to have the glucose loading test should insist on having a glucose loading test if at least the NLR and PLR values are high. The limitations of our study include the retrospective nature there of and there are no records of insulin levels and insulin resistance. The sample size was relatively small. Additional prospective studies are required to evaluate changes in the levels of inflammatory markers and platelet counts from the first trimester of the pregnancy to the end of pregnancy.

5. Conclusions

We found that an increased white blood cell count and a higher PLR and NLR independently predicted GDM. We recommend that PLR and NLR can be used as screening tests to distinguish pregnant women who may have GDM. An increased leukocyte count is very important marker for GDM; an elevation reflects subclinical inflammation. It is important to diagnose GDM early. Future studies focusing on the first trimester may improve patient outcomes by facilitating early interventions. Additional randomised controlled studies evaluating the relationships among the PLR and NLR, and GDM status, are required

Limitations of the Study

The limitations of the study is small sample size

Acknowledgement

None.

Conflict of Interests

We declare that we have no confict of interest.

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Author Contributions

Constructing the idea or hypothesis for research – Topdagi YE, Sahin AZ; Planning the design of the work- Topdagi YE, Demiroglu C; Execution of the experiments, patient follow-up - Topdagi YE, Sahin AZ; Analysis and interpretation of data - Topdagi YE, Demiroglu C; Providing financial support, tools and instruments – none; Biological materials, reagents and referred patients - Topdagi YE; Literature Review - Topdagi YE; Critical Review - Demiroglu C, Sahin AZ; Final approval of hthe cersion to be published - Topdagi YE, Demiroglu C, Sahin AZ.

Ethical Approval

Ethics committee approval was received for this study from the ethics committee of SANKO University.

Data sharing statement

All data relevant to the study are included in the article.

Consent to participate

All participants read the consent form and understand the study being described.

Informed Statement

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

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