



# Predicting Gestational Diabetes Mellitus Using The Systemic Immune-Inflammation Index in The First Trimester

## İlk Trimesterde Sistemik İmmün-İnflamasyon İndeksini Kullanarak Gestasyonel Diabetes Mellitus'u Tahmin Etme

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### Abstract

**Aims:** Gestational diabetes mellitus (GDM) is an inflammatory disorder. GDM raises the risk of pregnancy complications. Early recognition of GDM is critical to prevent complications. Systemic Immune-Inflammation Index (SII) is an index that shows the inflammatory response, we hypothesized that it might be associated to GDM. The purpose of this study was to determine the relationship between GDM and SII, as well as whether SII in the first trimester can predict GDM.

**Material and Method:** This retrospective cohort study was conducted between January 2021 and January 2022. 100 pregnant women were included in the study. The study group included 50 pregnant women who had been diagnosed with GDM. The control group consisted of the remaining 50 pregnant women who had not been diagnosed with GDM. SII values were calculated from the hemogram values of the patients at the first visit in the first trimester.

**Results:** There was a statistically significant difference between GDM and control groups in terms of SII, platelet, neutrophil, FT3, apgar 1 min and apgar 5 min measurements ( $p<0.05$ ). The SII level cut-off value for predicting GDM was determined to be 607.32.

**Conclusion:** SII was found to be significantly higher in people with GDM in the study. It can be used to predict GDM in the first trimester of pregnancy by calculating SII with a simple hemogram. By regulating their diet, patients in the first trimester can reduce the complications of diabetes that can occur during pregnancy.

**Keywords:** Systemic Immune-Inflammation Index, GDM, pregnancy

### Öz

**Amaç:** Gestasyonel diyabetes mellitus (GDM) inflamatuvar bir hastalıktır ve gebelik komplikasyonlarını artırır. GDM'nin erken tanınması, komplikasyonları önlemek için kritik öneme sahiptir. Sistemik İmmün-İnflamasyon İndeksi (SII), inflamatuvar yanıtı gösteren bir indeks olup, GDM ile ilişkili olabilir. Bu çalışmanın amacı, GDM ve SII arasındaki ilişkiyi özellikle ilk trimesterdeki SII'nin GDM'yi tahmin edip edemeyeceğini belirlemektir.

**Gereç ve Yöntem:** Çalışma, Ocak 2021 ile Ocak 2022 tarihleri arasında retrospektif kohort çalışması olarak dizayn edildi. Çalışmaya 100 gebe dahil edildi. Çalışma grubu GDM tanısı almış 50 gebeyi içermektedir. Kontrol grubu ise GDM tanısı almamış kalan 50 gebeden oluşturuldu. Hastaların ilk trimesterde ilk ziyaretlerindeki hemogram değerlerinden SII değerleri hesaplandı.

**Bulgular:** SII, trombosit sayısı, nötrofil sayısı, FT3, apgar 1. dk ve apgar 5. dk ölçümleri açısından GDM ve kontrol grupları arasında istatistiksel olarak anlamlı fark vardı ( $p<0,05$ ). GDM'yi öngörmek için SII düzeyi cut-off değeri 607,32 olarak belirlendi.

**Sonuç:** Çalışmada GDM'li kişilerde SII anlamlı olarak daha yüksek bulundu. Basit bir hemogram tetkiki ile SII hesaplanarak gebeliğin ilk trimesterinde GDM'yi predikte etmek için kullanılabilir. İlk trimesterdeki riskli hastalar diyetlerini düzenleyerek, hamilelik sırasında oluşabilecek diyabet komplikasyonlarını azaltabilirler.

**Anahtar kelimeler:** Sistemik İmmün-İnflamasyon İndeksi, GDM, gebelik



## INTRODUCTION

Glucose intolerance that does not occur before pregnancy and occurs during pregnancy is defined as gestational diabetes mellitus (GDM). The projected 7% prevalence of GDM is expected to increase in the coming years, primarily as a result of the impact of the rising trends in maternal age, obesity, sedentary behavior, and poor diet.<sup>[1,2]</sup> It has the potential to cause a wide range of fetal problems. GDM raises the risk of miscarriage, macrosomia, shoulder dystocia, infant hypoglycemia, hyperbilirubinemia, and stillbirth, and is thus linked to greater incidence of cesarean birth and surgical vaginal delivery.<sup>[3,4]</sup> GDM has been associated to long-term maternal consequences in addition to unfavorable fetal outcomes. These include a higher likelihood of recurrence in subsequent pregnancies and a higher rate of progression to cardiometabolic illnesses such as type 2 diabetes mellitus, atherosclerotic disease, and metabolic syndrome.<sup>[5-7]</sup> Early detection of GDM should be critical for physicians to ensure timely diagnosis and treatment.

Interleukins and leukocytes interact to cause the inflammatory condition known as GDM, and low-grade chronic inflammation is thought to be a critical factor in the pathogenesis of the condition.<sup>[8,9]</sup> The complete blood cell count test is useful in determining the severity of systemic inflammation. The previous studies have been conducted to evaluate the neutrophil-to-lymphocyte ratio (NLR) and platelet to lymphocyte ratio (PLR) value in pregnancies complicated by GDM.<sup>[10-12]</sup> Recently, it was discovered that the "Systemic Immune-Inflammation Index" (SII), which is derived from peripheral blood neutrophil, platelet, and lymphocyte counts, is a boosting index. SII has been linked to negative neonatal outcomes such as abortion and preterm premature rupture of membranes (PPROM), according to researchs.<sup>[13,14]</sup>

The purpose of this study was to determine the relationship between GDM and SII, as well as whether SII in the first trimester can predict GDM.

## MATERIAL AND METHOD

This retrospective cohort study was conducted between January 2021 and January 2022. The study was carried out with the permission of Gazi University Ethics Committee (Date: 10.02.2022, Decision No: 2022-183). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

One hundred pregnant women were screened retrospectively. Patients with abnormal thyroid function test results and patients with additional maternal disease were excluded from the study (n=20). 100 pregnant women were included in the study. The study group included 50 pregnant women who had been diagnosed with GDM. The control group consisted of the remaining 50 pregnant women who had not been diagnosed with GDM.

Age, gravida, parity, complete blood count, and thyroid function test values were recorded in the patients' first visit file records. Hemoglobin, platelet, white blood cell, lymphocyte, and neutrophil counts were examined as complete blood count values. Thyroid stimulating hormone (TSH), fT3, and fT4 levels were measured during thyroid function tests. All patients' 75 g oral glucose tolerance test results at 24-28 weeks of gestation were considered in the follow-up. The time of birth, mode of delivery, birth weight and baby apgar score were obtained from the file records of the patients.

Diagnostic criteria for GDM include fasting blood glucose levels of 5.1 mmol/l [92 mg/dl], one-hour plasma glucose levels of 10 mmol/l [180 mg/dl], and two-hour plasma levels of 8.5 mmol/l [153 mg/dl]. The (neutrophil  $\times$  platelet / lymphocyte) formula was used to produce the SII. SII values were calculated from the hemogram values of the patients at the first visit in the first trimester.

Using IBM SPSS Statistics 23, data were analyzed. Frequency distributions (number, percentage) for categorical variables and descriptive statistics (mean, standard deviation) for numerical variables are provided when analyzing the study's data. The difference between the two groups was checked with the independent sample t-test and the chi-square test. Pearson correlation analysis was used to examine the relationship between numerical variables. In addition, an SII cut off value that could predict GDM was looked at.  $P < 0.05$  was accepted for significance.

## RESULTS

In terms of age, gravida, parity, delivery week, mode of delivery, and birth weight, there was no statistically significant difference between GDM conditions ( $p > 0.05$ ) (**Table 1**).

There was no statistically significant difference between GDM and control groups in terms of hemoglobin, lymphocyte, TSH and fT4 levels ( $p > 0.05$ ). There was a statistically significant difference between GDM and control groups in terms of SII, platelet, neutrophil, fT3, apgar 1 min and apgar 5 min measurements ( $p < 0.05$ ) (**Table 2**). As a result, while SII, platelet, and neutrophil levels were higher in the GDM group than in the control group, the control group had higher fT3, apgar 1 min, and apgar 5 min values than the GDM group.

**Table 2. The SII level cut-off value for predicting GDM (n=100)**

SII value	Sensitivity	Specificity	p	AUC (95 CI)
607.32	0.800	0.520	0.004*	0.665 (0.557-0.773)
682.80	0.720	0.560		
721.87	0.660	0.600		
765.16	0.640	0.680		

\*:  $p < 0,05$  SII: Systemic Immune-Inflammation Index, AUC: Area Under Curve, CI: Confidence Interval

**Table 1: Relationship between variables and GDM status (n=100)**

	Control Group Mean±SD	GDM Mean±SD	Total Mean±SD	Test	p
Age	32.12±4.53	33.46±6.09	32.79±5.38	-1.249	0.215
Gravida	2.04±1.14	2.26±1.48	2.15±1.32	-0.831	0.408
Parity	0.70±0.76	0.66±0.80	0.68±0.78	0.256	0.798
Delivery week	37.84±1.97	37.05±2.37	37.44±2.21	1.827	0.071
Mode of delivery				3.405	0.065
Caesarean section	26 (52%)	35 (70%)	61 (61%)		
Vaginal	24 (48%)	15 (30%)	39 (39%)		
Birth weight	3201.86±530.96	3140.72±566.18	3171.29±546.94	0.557	0.579
Apgar score 1 minute	8.98±0.14	8.42±1.60	8.70±1.17	2.478	0.017*
Apgar score 5 minute	9.92±0.27	9.62±0.83	9.77±0.63	2.426	0.018*
SII	711.04±400.80	916.42±363.02	813.73±394.19	-2.686	0.009*
Hb	11.89±1.38	12.08±1.20	11.98±1.29	-0.760	0.449
Platelet	228.46±67.25	258.92±67.40	243.69±68.71	-2.262	0.026*
Lymphocyte	2216.80±1131.32	2117.40±541.15	2167.10±883.70	0.560	0.577
Neutrophil	6125.40±2923.91	10294.8±2433.00	8210.10±3398.70	-7.751	0.000*
TSH	2.07±1.19	2.02±1.33	2.05±1.25	0.177	0.860
Free T3	3.20±0.33	1.26±1.58	1.84±1.60	8.151	0.000*
Free T4	0.77±0.13	0.78±0.59	0.78±0.45	-0.148	0.883

1: Independent sample t test, 2:chi-square test\*;p<0,05. GDM: Gestational diabetes mellitus, SII: Systemic Immune-Inflammation Index, Hb: Hemoglobine TSH: Thyroid stimulating hormone

The SII level cut-off value for predicting GDM was determined to be 607.32. This value's area was found to be 0.665. (0.557-0.773). Furthermore, the selectivity is 0.520 and the sensitivity is 0.800 for these values.

## DISCUSSION

SII was found to be significantly higher in people with GDM in the study. We showed that the SII value measured in the first trimester can be used to predict GDM. To the best of our knowledge, this is the first study in the literature to use SII to predict adverse neonatal outcomes in GDM-complicated pregnancies. The platelet and neutrophil ratios were also significantly different between the groups.

SII is a good marker in demonstrating local immune response and systemic inflammation, according to another study by Huang et al.<sup>[15]</sup> SII was assessed in cervical cancer patients in this study, and it was noticed to be linked to a poor prognosis. In a different study, Orgul et al. looked into how maternal NLR, PLR, and SII levels were affected by the administration of neuroprotective magnesium sulfate. Magnesium sulfate has been shown to increase systemic inflammation via cytokines in previous studies.<sup>[16,17]</sup> In this study, it was discovered that magnesium sulfate administration led to a significant increase in SII.

In another study by Turgut et al, looked into whether SII could be used to predict miscarriages. High SII values in early pregnancy have been highlighted as being important in predicting miscarriages. Abortions occur for a variety of reasons. There is clearly an inflammatory process in the uterus during this process. SII is also important in demonstrating the inflammatory response, according to this study.<sup>[14]</sup> Tanacan et al. studied the link between PPRM

and SII in another study. Inflammatory response occurs in pregnant women complicated with PPRM. SII was found to be significantly higher in the PPRM group, and it was found to be more effective than NLR in detecting negative pregnancy outcomes.<sup>[13]</sup>

Only one study in the literature has investigated the correlation between SII and diabetes. The link between diabetic depression and SII was demonstrated in that study. Patients with DM who were depressed had significantly higher SII levels than those who were not depressed, according to Wang et al.<sup>[18]</sup>

Although there has yet to be a study showing GDM to SII, there have been studies comparing NLR and PLR to GDM, which are two other inflammatory markers in the blood count. Because it is an index that shows the SII inflammatory response, we hypothesized that it might be associated to GDM, which induces the inflammatory process. Increased platelet number and volume have been linked to diabetes, impaired fasting glucose, and insulin resistance in previous studies.<sup>[19]</sup>

The study's limitation is that it is retrospective design. Randomized controlled studies on this subject will shed more light on the role of this index in screening.

## CONCLUSION

We found a relation between GDM and SII in this study. It can be used to predict GDM in the first trimester of pregnancy by calculating SII with a simple hemogram. By regulating their diet, patients in the first trimester can reduce the complications of diabetes that can occur during pregnancy.

## ETHICAL DECLARATIONS

**Ethics Committee Approval:** The study was carried out with the permission of Gazi University Ethics Committee (Date: 10.02.2022, Decision No: 2022-183)

**Informed Consent:** Because the study was designed retrospectively, no written informed consent form was obtained from patients.

**Referee Evaluation Process:** Externally peer-reviewed.

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

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**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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