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Combined triple screening and BMI models for gestational diabetes prediction

Gebelik diyabetinin tahmininde üçlü tarama ve VKİ modellerinin birleştirilmesi

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Abstract

Objective: This study investigated whether routinely used second-trimester triple screening markers (alpha-fetoprotein, human chorionic gonadotropin, and unconjugated estriol) could help identify pregnancies at increased risk of gestational diabetes mellitus. In addition, several hematological inflammation indices were evaluated as potential adjunctive predictors.

Materials and Methods: Medical records of 405 singleton pregnancies were retrospectively reviewed. All participants underwent triple screening during gestational weeks 15-20 and subsequently underwent oral glucose tolerance testing during gestational weeks 24-28. Patients were categorized, according to oral glucose tolerance test findings, as either having gestational diabetes or as normoglycemic controls. Receiver operating characteristic analyses were performed to assess both the isolated and combined predictive capacities of measurements of alpha-fetoprotein, human chorionic gonadotropin, and unconjugated estriol. The impact of maternal body mass index on model performance was also analyzed.

Results: Alpha-fetoprotein, human chorionic gonadotropin, and unconjugated estriol levels showed poor discriminatory ability for identifying pregnancies complicated by gestational diabetes, both individually and in combined models. However, adding maternal body mass index to the combined biomarker model substantially improved predictive accuracy (area under the curve=0.809; p<0.001). None of the evaluated inflammatory indices demonstrated significant predictive performance for gestational diabetes mellitus.

Conclusion: Routine second-trimester triple screening markers appear to have limited standalone value for predicting gestational diabetes. Nevertheless, incorporating maternal body mass index considerably enhances model performance and may improve clinical risk stratification.

Keywords: Second trimester, gestational diabetes mellitus, AFP, hCG, estriol, inflammation markers

Öz

Amaç: Bu çalışmanın amacı, gebelik diyabetini öngörmede ikinci trimester üçlü tarama testi parametrelerinin (alfa-fetoprotein, insan koryonik gonadotropin ve konjuge olmayan estriol) performansını değerlendirmekti. Ayrıca, sistemik enflamasyon indeksleri ile gebelik diyabeti arasındaki ilişki de incelenmiştir.

Gereç ve Yöntemler: Bu retrospektif gözlemsel çalışmaya, gebeliğin 15. ve 20. haftaları arasında ikinci trimester üçlü tarama testi ve 24. ve 28. haftaları arasında oral glikoz tolerans testi yapılan 405 hamile kadın dahil edilmiştir. Oral glikoz tolerans testi sonuçlarına göre olgular, gebelik diyabeti ve kontrol gruplarına ayrılmıştır. Alfa-fetoprotein, insan koryonik gonadotropin ve konjuge olmayan estriol düzeylerinin bireysel ve kombine prediktif

PRECIS: Combining maternal body mass index with second-trimester triple screening markers significantly improves the prediction of gestational diabetes mellitus compared with biochemical markers alone.

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performansı alıcı işletim karakteristiği analizi kullanılarak değerlendirilmiştir. Ayrıca, vücut kitle indeksinin modele katkısı da incelenmiştir. Bunun yanı sıra obstetrik ve neonatal sonuç verileri hastane doğum kayıtları kullanılarak retrospektif olarak ayrıntılı ve istatistiksel açıdan karşılaştırmalı biçimde değerlendirilmiştir.

Bulgular: Alfa-fetoprotein, insan koryonik gonadotropin ve konjuge olmayan estriolün, tek başına veya kombinasyon halinde, gebelik diyabeti için anlamlı bir öngörü performansı sergilemediği saptanmıştır. Buna karşın, vücut kitle endeksinin üçlü belirteç modeline dahil edilmesi, ayırt edici performansı önemli ölçüde iyileştirmiştir (eğri altındaki alan=0,809; p<0,001). Enflamasyon indeksleri ile ilgili olarak anlamlı bir ilişki gözlemlenmemiştir.

Sonuç: İkinci trimester üçlü tarama parametrelerinin tek başına gebelik diyabetini öngörmede değeri sınırlıdır. Ancak, modele vücut kitle indeksinin eklenmesi, öngörü performansını önemli ölçüde iyileştirir.

Anahtar Kelimeler: İkinci trimester, gebelik diyabeti, AFP, hCG, estriol, enflamasyon belirteçleri

Introduction

Gestational diabetes mellitus (GDM) represents one of the most frequently encountered metabolic disorders during pregnancy and is associated with adverse maternal and neonatal outcomes[1]. Reported prevalence rates differ among populations; however, the global burden of GDM has increased steadily in parallel with rising obesity rates and delayed childbearing[2]. Beyond pregnancy-related complications, GDM has also been linked to long-term metabolic consequences affecting both mothers and their offspring[3].

Maternal complications such as hypertensive disorders, operative delivery, and obstetric trauma occur more frequently in pregnancies complicated by GDM, while neonatal risks include macrosomia, hypoglycemia, and future metabolic dysfunction[4]. Therefore, identifying women at increased risk before routine diagnostic testing remains an important clinical objective.

In current clinical practice, GDM is generally diagnosed using oral glucose tolerance testing performed during the late second trimester[5]. Because conventional screening occurs relatively late in gestation, considerable interest has focused on markers capable of identifying high-risk pregnancies earlier. Consequently, routine biochemical and clinical markers have been increasingly investigated for early GDM risk assessment.

Alpha-fetoprotein (AFP), human chorionic gonadotropin (hCG), and unconjugated estriol (uE3), which are routinely measured during second-trimester triple screening, primarily serve in fetal anomaly assessment but may also reflect placental and metabolic alterations occurring during pregnancy[6]. Accordingly, these biomarkers have attracted interest as possible indicators of metabolic complications including GDM. Previous studies evaluating their predictive utility have yielded inconsistent findings, and their clinical usefulness remains uncertain[7].

Increasing evidence suggests that low-grade chronic inflammation contributes to the pathophysiology of gestational diabetes[8]. Accordingly, systemic inflammation indices derived from complete blood counts—particularly the systemic immune-inflammation index (SII), the systemic inflammatory response index (SIRI), and the aggregate systemic inflammation index (AISI)—have been used in recent years to predict various metabolic and cardiovascular diseases[9]. However, available evidence regarding the predictive value of these indices during pregnancy remains limited and inconsistent, particularly for GDM[10].

The aim of this study was to evaluate the performance of second-trimester triple-screening parameters (AFP, hCG, and uE3), alone and in combination, in predicting GDM. Additionally, the potential contribution of the SII, SIRI, and AISI indices—which reflect inflammation and immune response—to the prediction of GDM was examined in an exploratory analysis. Additionally, we aimed to assess whether routinely available biochemical and hematological parameters could provide clinically useful information for early assessment of GDM risk.

Materials and Methods

A retrospective review was conducted in the Clinic of Obstetrics and Gynecology at Samsun Training and Research Hospital, based on records collected between July 2023 and January 2026. Pregnancies that were both followed and delivered at the same institution were identified through the institutional digital archive and reviewed. Approval for the study was obtained from the Samsun University Clinical Research Ethics Committee (approval number: 2023/15/8, date: 23.08.2023). Biochemical parameters of pregnant women who underwent the triple screening test during the second trimester were recorded; subsequently, the results of the oral glucose tolerance test (OGTT) administered to the same patients between the 24th and 28th weeks of gestation were evaluated. Participants were classified as either GDM cases or normoglycemic controls according to OGTT findings, and the predictive performance of second-trimester parameters was subsequently evaluated between groups. Delivery outcomes and neonatal characteristics were additionally assessed using archived obstetric records. Because the study was hospital-based and included only women with complete records for triple-screening, OGTT, delivery, and neonatal outcomes, the proportion of GDM cases observed in the study cohort should not be interpreted as reflecting the prevalence of GDM in the general obstetric population. The study was conducted in a tertiary referral

hospital serving a large regional population. Therefore, women with increased metabolic or obstetric risk may have been overrepresented in the study cohort compared with the general obstetric population. All procedures performed in this study were consistent with the ethical standards of the institutional research committee and with the principles of the Declaration of Helsinki. Written informed consent was obtained from all participants prior to inclusion in the study.
The study included women aged 18-45 with singleton pregnancies who underwent the necessary tests at the relevant gestational weeks; women with multiple pregnancies, diagnosed fetal structural or chromosomal anomalies, a pre-existing diagnosis of diabetes, chronic hypertension, renal failure, or other systemic diseases, and pregnant women under 18 or over 45 years of age were excluded. Additionally, patients with acute or chronic infections that could affect maternal inflammatory status, with hematological diseases, with immunological disorders, or with regular medication use (particularly steroid and immunosuppressive therapies), as well as those with incomplete laboratory or clinical data, were excluded from the analysis.
GDM screening was performed using a 75 g oral glucose tolerance test during gestational weeks 24-28. The fasting, 1 hour, and 2 hours plasma glucose levels measured during the test were evaluated using the following cutoff values: ≥92 mg/dL, ≥180 mg/dL, and ≥153 mg/dL, respectively. Patients exceeding at least one threshold value were classified as having GDM according to International Association of Diabetes and Pregnancy Study Groups recommendations[11].
As part of the study, demographic, clinical, biochemical, and hematological data for the cases were analyzed. Demographic and obstetric characteristics, including maternal age, body mass index (BMI), gravidity, parity, and parameters related to pregnancy outcomes (mode of delivery, birth weight, Apgar scores, presence of meconium, need for neonatal intensive care unit admission, and neonatal intubation status) were evaluated. Biochemical analyses included AFP, hCG, and uE3 levels obtained from second-trimester triple-screening tests; the predictive performance of these markers was evaluated both individually and in combination. As part of the hematological evaluation, composite indices reflecting systemic inflammation were calculated using white blood cell count, hemoglobin, hematocrit, platelet count, neutrophil count, lymphocyte count, and monocyte count obtained from a complete blood count. Systemic inflammatory indices, including SII, SIRI, and AISI, were derived from routinely collected complete blood count parameters. SII was calculated as platelet × neutrophil / lymphocyte, SIRI as neutrophil × monocyte / lymphocyte, and AISI as neutrophil × monocyte × platelet / lymphocyte. Hematological measurements were obtained using automated analyzers, and inflammatory indices were exploratorily assessed for their potential association with GDM.

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics for Windows, version 25.0 (IBM Corp., Armonk, NY, USA). Distribution characteristics of continuous variables were evaluated visually and statistically before analysis. Normality testing was performed using the Kolmogorov-Smirnov method. Because several variables exhibited non-normal distributions, nonparametric statistical methods were applied where appropriate. Continuous data were summarized using medians and ranges. For comparisons between two independent groups, the Mann-Whitney U test was used. A two-sided p-value below 0.05 was considered statistically significant. An receiver operating characteristic (ROC) analysis was performed to evaluate the predictive performance of second-trimester biochemical markers (AFP, hCG, and E3) for GDM. The area under the curve (AUC) was calculated for each parameter and model, along with the 95% confidence interval (CI). Optimal cutoff points were determined using the Youden index, and the corresponding sensitivity and specificity values were reported. Additionally, logistic regression models were constructed to evaluate the combined predictive effects of biochemical markers. In the first stage, a basic model was constructed that included the variables AFP, hCG, and E3; this model was then expanded by adding maternal BMI to obtain an extended model. The discriminative performance of the models was compared using ROC curves. Additionally, indices reflecting inflammation and immune response (SII, SIRI, and AISI) were evaluated using ROC analysis for exploratory purposes. Because significant right-skewness was observed in some variables, a logarithmic transformation was applied and sensitivity analyses were conducted. Similar findings obtained from transformation analyses supported the stability of the statistical results.

Results

Among the 405 pregnancies evaluated, 272 women (67.2%) were diagnosed with GDM, whereas 133 women (32.8%) had normal glucose tolerance. A comparison of maternal and neonatal characteristics revealed no statistically significant difference in maternal age between the groups (p=0.928). Gestational age, gravidity, and parity were likewise comparable between GDM and control patients (p=0.958, p=0.895, and p=0.312, respectively). Women who developed GDM had significantly higher maternal BMI values than normoglycemic controls (p<0.001). Neonatal birth weight was significantly increased in pregnancies complicated by GDM (p<0.001). Fasting glucose levels were significantly higher in the GDM group (p<0.001). Similarly, both first- and second-hour OGTT glucose measurements were significantly higher in women with GDM than in controls (p<0.001 for each comparison). No meaningful between-group differences were identified for second-trimester triple screening markers, including hCG, AFP, and E3 levels (p=0.717, p=0.500, and

Table 1. Comparison of maternal and neonatal characteristics according to the presence of gestational diabetes

	Presence of gestational diabetes				p-value
	GDM (n=272)		Control (n=133)		
	Mean ± SD	Median (min-max)	Mean ± SD	Median (min-max)	
Maternal age (years)	31.15±5.15	31.00 (20.00-44.00)	31.05±5.59	31.00 (20.00-43.00)	0.928
Neonatal birth weight (g)	3,814.00±464.52	3,800.00 (2570-5200)	3,474.14±411.664	3,450.00 (2670-4500)	<0.001
Maternal BMI	31.43±5.36	30.00 (21.00-44.00)	25.72±5.56	24.00 (19.00-42.00)	<0.001
Gestational age (weeks)	38.11±1.37	38.00 (35.00-40.00)	38.11±1.36	38.00 (35.00-40.00)	0.958
Gravida	2.34±1.31	2.00 (1.00-7.00)	2.38±1.44	2.00 (1.00-7.00)	0.895
Parity	1.08±0.98	1.00 (0.00-4.00)	1.00±1.03	1.00 (0.00-4.00)	0.312
Fasting blood glucose (mg/dL)	105.45±19.72	100.90 (74.30-181.00)	86.40±5.15	89.90 (70.30-91.00)	<0.001
Hcg	44,045.56±33,629.73	36,297.32 (7,831-264,400)	43,005.84±26,981.58	33,574.00 (2,789-171,555)	0.717
AFP	41.52±17.96	38.20 (0.99-125.10)	41.00±19.38	37.05 (2.00-124.30)	0.500
Estriol	1.49±1.02	1.36 (0.01-14.20)	1.46±0.57	1.35 (0.50-4.00)	0.565
OGTT 1 (1 hour glucose tolerance test) (mg/dL)	194.51±39.54	194.90 (75.10-339.40)	156.62±24.82	164.80 (82.30-189.30)	<0.001
OGTT 2 (2 hours glucose tolerance test) (mg/dL)	157.93±56.41	153.75 (57.70-764.70)	125.85±29.17	122.00 (56.90-188.70)	<0.001
Apgar Score (1st minute)	8.40±1.31	9.00 (4.00-9.00)	8.89±0.59	9.00 (5.00-9.00)	<0.001
Apgar Score (5th minute)	8.70±1.44	9.00 (0.00-10.00)	9.71±0.88	10.00 (5.00-10.00)	<0.001

Mann-Whitney U test
BMI: Body mass index, OGTT: Oral glucose tolerance test, SD: Standard deviation, GDM: Gestational diabetes mellitus

p=0.565, respectively). With respect to neonatal outcomes, both 1 minute and 5 minutes Apgar scores were significantly lower in the GDM cohort (p<0.001 for both) (Table 1).

ROC curve analysis demonstrated that second-trimester triple-screening markers (AFP, hCG, and uE3) had limited independent predictive ability for GDM. The calculated AUC values were 0.521 for AFP (95% CI: 0.460-0.582; p=0.500), 0.489 for hCG (95% CI: 0.430-0.548; p=0.717), and 0.482 for uE3 (95% CI: 0.421-0.543; p=0.565), indicating weak discriminatory performance for all three markers. Combining these biochemical parameters into a single model did not improve predictive accuracy, with the combined model yielding an AUC of 0.507 (95% CI: 0.446-0.568; p=0.830). However, the incorporation of maternal BMI into the model resulted in a substantial increase in discriminatory capacity. The BMI-adjusted model achieved an AUC of 0.809 (95% CI: 0.757-0.860; p<0.001), reflecting significantly improved predictive performance. Using an optimal cutoff value of 0.55, the model demonstrated 88% sensitivity and 68% specificity (Table 2).

Figure 1 shows the ROC curves for the model based on the three screening parameters and for the model to which BMI was added. The curve for the triple-marker model lies closer to the diagonal, while the curve for the model incorporating BMI lies closer to the upper-left corner. Correspondingly, discriminatory performance improves with the inclusion of BMI (Figure 1).

To further clarify the independent contribution of maternal BMI to the combined model's predictive performance, an additional ROC analysis was performed using maternal BMI alone. Maternal BMI demonstrated good discriminatory performance in predicting GDM, with an AUC of 0.806 (95% CI: 0.755-60.858; p<0.001). The combined model, including AFP, hCG, E3, and BMI, showed a slightly higher AUC of 0.809 (Figure 2).

When the role of inflammation and immune response indices in predicting GDM was evaluated in an exploratory analysis, no significant discriminatory performance was observed for SII, SIRI and AISI. The AUC value for SII was 0.516 (95% CI: 0.453-0.578; p=0.609), 0.546 for SIRI (95% CI: 0.488-0.605; p=0.129), and 0.540 for AISI (95% CI: 0.481-0.599; p=0.189) (Table 3).

Logistic regression analysis identified maternal BMI as an independent predictor of GDM development. Multivariate analysis demonstrated that increasing BMI was significantly associated with a higher likelihood of GDM (odds ratio: 1.17; 95% CI: 1.100-1.257; p<0.001). No significant relationship was detected between GDM and AFP, hCG, uE3, or the evaluated hematological variables in regression analyses (p>0.05) (Table 4).

Discussion

The present study evaluated whether second-trimester triple-screening markers could predict GDM and found that AFP, hCG, and uE3 had limited ability to distinguish pregnancies complicated by GDM. Predictive performance improved substantially after maternal BMI was incorporated into the model.

Table 2. Second-trimester biochemical parameters and the predictive performance of combined models for gestational diabetes (ROC analysis)

	AUC (95% CI)	p-value	Cut-off (Youden)	Sensitivity	Specificity
AFP	0.521 (0.460-0.582)	0.500	30.75	0.73	0.32
hCG	0.489 (0.430-0.548)	0.717	7503	1.00	0.02
Estriol	0.482 (0.421-0.543)	0.565	0.70	0.94	0.08
AFP + hCG + estriol	0.507 (0.446-0.568)	0.830	0.66	0.72	0.32
BMI	0.806 (0.755-0.858)	<0.001	22.5	0.91	0.68
AFP + hCG + estriol + BMI	0.809 (0.757-0.860)	<0.001	0.55	0.88	0.68

BMI: Body mass index, AUC: Area under the curve, ROC: Receiver operating characteristic, hCG: Human chorionic gonadotropin, AFP: Alpha-fetoprotein, CI: Confidence interval

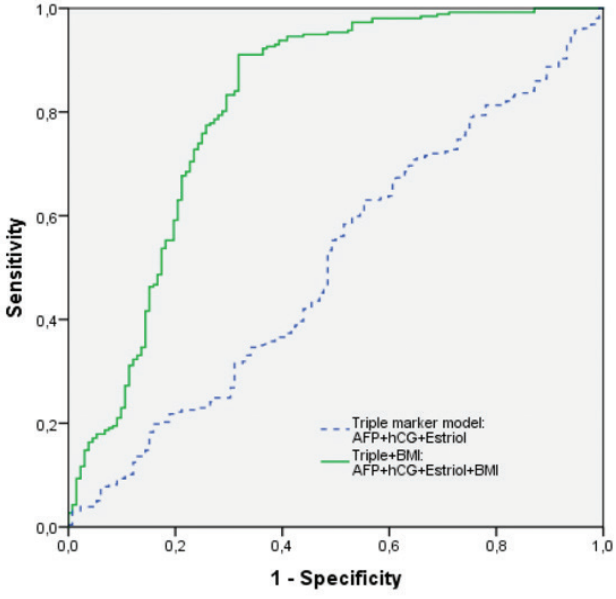

Figure 1. Receiver operating characteristic curves for the triple marker model and the model including BMI

BMI: Body mass index, AFP: Alpha-fetoprotein, hCG: Human chorionic gonadotropin

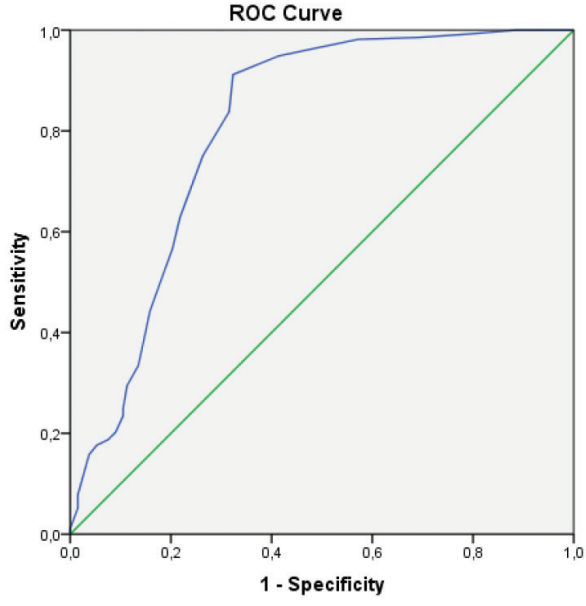

Figure 2. ROC curve of maternal BMI for predicting gestational diabetes mellitus

BMI: Body mass index, ROC: Receiver operating characteristic

Table 3. Results of an exploratory ROC analysis of inflammation and immune combination indices for gestational diabetes

	AUC (95% CI)	p-value	Cut-off (Youden)	Sensitivity	Specificity
SII	0.516 (0.453-0.578)	0.609	545	0.88	0.68
SIRI	0.546 (0.488-0.605)	0.129	1.26	0.88	0.12
AISI	0.540 (0.481-0.599)	0.189	330	0.85	0.19

SII: Systemic immune-inflammation index, SIRI: Systemic inflammatory response index, AISI: Aggregate systemic inflammation index, AUC: Area under the curve, CI: Confidence interval, ROC: Receiver operating characteristic

Table 4. An analysis of the effects of ındependent variables on the probability of gestational diabetes using binary logistic regression

	GDM		Univariate		Multiple	
	No	Yes	OR (95% CI)	p-value	OR (95% CI)	p-value
Age	31.05±5.59	31.15±5.15	1.00 (0.965-1.044)	0.855	0.98 (0.918-1.065)	0.765
BMI	25.72±5.56	31.43±5.36	1.24 (1.181-1.319)	<0.000	1.17 (1.100-12.57)	<0.000
White blood cells	9.85±2.35	10.08±2.27	1.04 (0.955-1.147)	0.333	1.04 (0.819-1.329)	0.729
Hemoglobin	11.54±1.32	11.43±1.31	0.93 (0.797-1.096)	0.405	1.18 (0.530-2.634)	0.683
Hematocrit	35.43±3.40	34.86±3.46	0.95 (0.896-1.012)	0.116	0.88 (0.642-1.206)	0.427
Platelets	246.82±68.34	247.17±64.65	1.00 (0.997-1.003)	0.960	1.00 (0.993-1.006)	0.902
Lymphocytes	1.98±0.71	2.65±12.14	1.01 (0.958-1.074)	0.633	1.15 (0.568-2.350)	0.691
Monocytes	0.63±0.19	0.69±0.53	2.21 (0.828-5.930)	0.113	1.79 (0.177-18.094)	0.622
Neutrophils	8.08±3.17	8.05±2.81	0.99 (0.929-1.070)	0.928	0.96 (0.848-1.104)	0.621
hCG	43,574.20±27,666.82	47,414.25±55,720.46	1.00 (1.00-1.056)	0.462	1.00 (1.00-1.00)	0.118
AFP	41.00±19.38	41.52±17.96	1.00 (0.990-1.013)	0.793	1.00 (0.983-1.021)	0.864
Estriol	1.46±0.57	1.49±1.020	1.04 (0.811-1.333)	0.757	0.72 (0.492-1.071)	0.106

OR: Odds ratio, CI: Confidence interval, BMI: Body mass index, hCG: Human chorionic gonadotropin, GDM: Gestational diabetes mellitus

Furthermore, inflammatory indices derived from complete blood count parameters did not meaningfully contribute to GDM prediction.

Maternal obesity has consistently been identified as one of the strongest clinical risk factors associated with GDM development because of its close relationship with insulin resistance and altered metabolic regulation[12]. Similarly, BMI remained independently associated with GDM in both univariate and multivariate analyses in our cohort. The marked improvement in AUC observed after adding BMI indicates that clinical variables may provide stronger predictive information than isolated biochemical markers during the second trimester. These findings suggest that combined risk assessment models may offer greater clinical utility than single-marker approaches[13].

The association between maternal age and the development of gestational diabetes has been extensively studied in the literature; it has been reported that advanced maternal age is a significant risk factor for GDM, as it is associated with increased insulin resistance and a decrease in pancreatic β-cell reserve[14]. Numerous epidemiological studies have shown that the incidence of GDM increases significantly, particularly among pregnant women aged 30-35[15]. However, it is also emphasized that this association is not consistent across all populations and that the effect of age may vary depending on factors such as obesity, lifestyle, and genetic predisposition[16]. In the present study, however, no statistically significant association was found between maternal age and the development of GDM. This may be due to the relatively homogeneous age distribution in the study group, the predominant influence of stronger metabolic markers such as BMI, or the effect of potential confounding factors. Indeed, the fact that BMI emerged as an independent risk factor in the multivariate analysis suggests that age alone may not be a decisive parameter. This finding appears consistent with the literature indicating that maternal age is a risk marker that contributes to the development of GDM but is not sufficient on its own[17].

Previous investigations examining the relationship between triple screening markers and GDM have produced inconsistent findings. AFP has been proposed as a potential marker because of its relationship with placental physiology; however, reported associations with GDM remain controversial[18]. In this study, the low AUC value for AFP and the statistically non-significant results indicate that AFP plays a limited role in predicting GDM. Similarly, although hCG is a placental hormone and might be expected to be associated with metabolic processes, the current study found that hCG levels did not significantly contribute to the prediction of GDM. The presence of studies in the literature supporting an association between hCG and GDM, as well as studies that failed to find a significant association, highlights the uncertainty surrounding this issue[19,20]. Although the association between uE3 levels and GDM has been less extensively studied, some studies have suggested that high uE3 levels may be associated with GDM[21]. However, the results obtained for uE3 in the current study indicate that this parameter is not a significant biomarker for predicting GDM. This suggests that these biochemical parameters measured in the second trimester may not adequately reflect maternal metabolic changes.

The failure to achieve significant predictive performance, despite combining triple-screening test parameters, suggests that these biomarkers may not be directly pathophysiologically

linked to GDM or that this association is weak. However, the significant increase observed with the addition of BMI underscores the importance of evaluating clinical parameters in conjunction with these biochemical markers. This finding suggests that approaches relying solely on laboratory data may be insufficient for predicting GDM, highlighting the need to develop multidisciplinary and multiparameter models[22].

Although the role of inflammation in the pathogenesis of GDM is increasingly recognized, it is noteworthy that the inflammatory indices evaluated in this study (SII, SIRI, AISI) did not demonstrate significant predictive performance for GDM. Some studies in the literature have reported that these indices are associated with insulin resistance and metabolic syndrome[23]. However, physiological changes during pregnancy may affect hematological parameters and, as a result, reduce the specificity of inflammatory markers. The findings of this study suggest that these markers may not be sufficiently sensitive or specific for predicting GDM in the second trimester.

A review of studies investigating various biomarkers in GDM suggests that, in recent years, GAS6, periostin, and various adipokines have been evaluated as potential biomarkers[24,25]. Although some studies have reported that these biomarkers show promising results, there is not yet sufficient evidence to support their use in clinical practice. This situation highlights that, due to the multifactorial nature of GDM, predicting the condition with a single biomarker is difficult and more comprehensive biomarker panels are needed.

Among the strengths of our study are that the data were collected at a single center using standardized protocols and that the study included a large patient cohort. Furthermore, the evaluation of biochemical parameters obtained during routine clinical practice in the second trimester enhances the study's clinical applicability. Furthermore, combined analysis of biochemical markers, clinical (BMI), and hematological parameters has enabled a multidimensional perspective and strengthened the interpretability of the findings.

Study Limitations

Several limitations should be acknowledged when interpreting the findings of this study. Because the data were obtained from a single institution, the applicability of the results to broader populations may be restricted. In addition, the relatively high proportion of women with GDM in the study cohort likely reflects several methodological and population-related factors. First, the retrospective hospital-based design and the inclusion of only women with complete triple-screening, OGTT, delivery, and neonatal outcome records may have introduced selection bias. Second, our institution serves as a tertiary referral center, resulting in a higher proportion of pregnancies at increased metabolic and obstetric risk. Finally, the relatively high maternal BMI may also have contributed to the increased frequency of GDM observed in this cohort. Therefore, the GDM rate reported in the present study should not be interpreted as representative of the prevalence in the general obstetric population. The analysis of inflammatory indices was exploratory; further multicenter studies involving larger patient populations are required to clarify the clinical relevance of these markers for predicting GDM. Biomarkers were measured at a single time point, which limits the assessment of dynamic changes and time-dependent variations during pregnancy. In addition, the failure to account for potential confounding factors (such as nutritional status, physical activity, and genetic predisposition) may limit the interpretation of the results. Future studies should focus on predictive models that incorporate repeated measurements at different gestational stages and integrate biochemical and clinical parameters, and these studies should be conducted in multicenter settings with larger populations. This approach will contribute to the development of more reliable and clinically applicable methods for the early prediction of GDM.

Conclusion

This study demonstrates that second-trimester triple screening test parameters have limited value in predicting GDM. However, adding BMI to these models significantly improved predictive performance. These findings highlight the value of incorporating simple and readily available clinical variables into GDM risk assessment models. Inflammatory indices, however, were found to make no significant contribution to the prediction of GDM. Future studies focusing on multivariate models that evaluate different biomarkers and clinical parameters together may contribute to the development of more effective strategies for the early prediction of GDM.

Ethics

Ethics Committee Approval: Approval for the study was obtained from the Samsun University Clinical Research Ethics Committee (approval number: 2023/15/8, date: 23.08.2023).

Informed Consent: Written informed consent was obtained from all participants prior to inclusion in the study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: N.G., S.M.A., Concept: N.G., K.G.Ş., Ne.G., Design: N.G., M.A., Ne.G., Data Collection or Processing: S.M.A., M.A., K.G.Ş., Analysis or Interpretation: S.M.A., M.A., K.G.Ş., Ne.G, Literature Search: Ne.G., Writing: Ne.G.

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manuscript, ChatGPT (OpenAI) was used to assist with English-language editing and improving scientific wording. All generated content was critically reviewed, revised, and approved by the authors, who accept full responsibility for the final version of the manuscript.

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