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The function of oral glucose tolerance test protocols in diagnosing and managing gestational diabetes: can insulin requirements be predicted?

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ABSTRACT

Aims: This study aims to evaluate the effectiveness of diagnostic tests, clinical, and laboratory markers in predicting insulin requirements in pregnant women diagnosed with gestational diabetes mellitus (GDM). Additionally, we assessed differences in maternal and neonatal outcomes between insulin-managed and diet-managed GDM patients.

Methods: A retrospective analysis was conducted on 406 pregnant women diagnosed with GDM at Ankara Etlik City Hospital between October 2022 and December 2024. Patients were categorized based on the diagnostic method used: the one-step 75 g oral glucose tolerance test (OGTT) or the two-step 100 g OGTT following a 50 g OGTT. Clinical, laboratory, and demographic data were compared between insulin-treated and diet-controlled groups. The predictive capacity of fasting plasma glucose (FPG), glucose levels at 1st, 2nd, and 3rd hours during OGTT, and HbA1c for insulin requirement were assessed using receiver operating characteristic (ROC) analysis.

Results: In the 75 g OGTT group, fasting, 1st-hour, and 2nd-hour glucose levels were significantly higher in the insulin-requiring group ($p<0.001$). ROC analysis indicated that fasting glucose >92 mg/dl and 2nd hour glucose >160 mg/dl were predictive of insulin requirement. HbA1c >5.25% was also a significant predictor ($p=0.009$). However, in the 100 g OGTT group, only the 2nd hour glucose level (>169 mg/dl, $p=0.032$) was predictive of insulin need, while HbA1c was not statistically significant. Birth outcomes showed that insulin-treated patients had an earlier gestational age at delivery ($p=0.001$), but neonatal outcomes were not significantly different between insulin-treated and diet-managed groups.

Conclusion: The findings suggest that glucose levels and HbA1c in the 75 g OGTT group are more effective in predicting insulin requirements in GDM patients than the 100 g OGTT. The study underscores the importance of identifying predictive markers for early intervention, potentially guiding clinicians in selecting optimal diagnostic methods and improving patient outcomes.

Keywords: Gestational diabetes mellitus, OGTT, insulin therapy, HbA1c, predictive markers, pregnancy outcomes

INTRODUCTION

Gestational diabetes mellitus (GDM) is a prevalent pregnancy condition identified during the second or third trimester [1]. The incidence of GDM ranges from 9.3% to 25.5%, influenced by ethnicity and the diagnostic methodology employed.[1-3] Besides the risk of acquiring type 2 diabetes mellitus, coronary artery disease, and hypertension later in life for women with GDM, exposure to hyperglycemia during pregnancy may result in long-term detrimental effects for both the mother and the infant.[4-7] GDM is concomitantly linked to numerous obstetric and neonatal complications, including polyhydramnios, macrosomia, preeclampsia, elevated cesarean section rates, preterm birth, birth traumas such as shoulder dystocia, neonatal hypoglycemia, hyperbilirubinemia, and a heightened incidence of neonatal intensive care unit (NICU) admissions.[8-10]

Approximately 15-30% of pregnant women diagnosed with GDM necessitate insulin therapy, which is recognized to reduce unfavorable pregnancy and neonatal outcomes associated with hyperglycemia.[11,12] Several studies have assessed the factors that predict insulin utilization in individuals diagnosed with GDM.[13,14] Given the significance of insulin therapy in regulating hyperglycemia in GDM, assessing prognostic markers may enhance patient management and facilitate timely referrals to appropriate facilities.

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Two approaches are employed for the diagnosis of GDM. The 75-g oral glucose tolerance test (OGTT), regarded as a single-step approach, and the 100-g OGTT conducted subsequent to the 50-g OGTT test, which constitutes a two-step method [Carpenter-Coustan (CC) criteria]. In 2010, the International Association of the Diabetes and Pregnancy Study Groups (IADPSG) endorsed the 75 g oral OGTT as a singular screening method for GDM.[15] Research indicates that the single-stage screening test, conducted in accordance with IADPSG guidelines, is more effective in diagnosing diabetes compared to the two-stage GDM screening test advocated by the American College of Obstetricians and Gynecologists (ACOG), which involves a 100-g OGTT following a 50-g OGTT result exceeding 130-140.[16-18] Moreover, research indicates that the single-step test endorsed by IADPSG decreases cesarean rates and composite neonatal outcomes while being cost-effective; yet, other studies assert that there is no distinction between the two methodologies.[17-19] A consensus on the appropriate test to utilize globally remains elusive. The American Diabetes Association (ADA) and ACOG advocate for a two-step diagnostic procedure, however the IADPSG endorses a single-step test.

This study aimed to assess the efficacy of diagnostic tests, clinical, and laboratory indicators in predicting the necessity of insulin treatment in pregnant women diagnosed with GDM. Our secondary objective was to assess the differences in pregnancy and newborn outcomes between pregnant women managing GDM with insulin and those controlling their blood sugar with dietary approaches. We assessed the predictive capacity of HbA1c, fasting blood glucose, and blood glucose levels at the 1st, 2nd, and 3rd hours during diagnostic tests for GDM.

METHODS

Ethics

This study covered patients diagnosed with GDM at Ankara Etlik City Hospital from October 2022 to December 2024. This study followed the Declaration of Helsinki on Research Involving Human Subjects and received approval from the Ankara Etlik City Hospital Scientific Researches Evaluation and Ethics Committee (Date: 25.12.2024, Decision No: AEŞH-BADEK–2024-1199).

Study Participants

A total of 406 individuals diagnosed with GDM using oral glucose tolerance testing at our hospital were included in the study. Patients diagnosed with GDM were divided into two groups: those diagnosed with a one-step method and those diagnosed with a two-step method. Of the 268 patients identified using the single-step approach following the 75 g OGTT test, 138 individuals were diagnosed using the two-step method. In the 75 g OGTT cohort, 49 patients (18.3%) were managed with insulin, whereas in the 100 g OGTT cohort, that number was 120 patients (87%). In our study, patient selection criteria were meticulously determined, and inclusion and exclusion criteria were determined as follows: 406 pregnant women who were diagnosed with GDM by OGTT at Ankara Etlik City Hospital during 24-28 weeks of pregnancy were included in the study. The patients included in the study were diagnosed with either single-stage 75 g OGTT or two-stage 100 g OGTT protocols. Inclusion criteria were gestational age of 18 years and above, being between 24-28 weeks of pregnancy, and GDM diagnosis was made according to the specified criteria. Exclusion criteria included type 1 or type 2 diabetes diagnosed before pregnancy, chronic metabolic diseases (e.g. polycystic ovary syndrome, Cushing syndrome), pregestational obesity (BMI>40 kg/m^2), thyroid diseases, chronic kidney or liver diseases, multiple pregnancies, and steroid use during pregnancy. In addition, patients with incomplete medical records or those for whom the necessary laboratory data could not be obtained were excluded from the study. Determining these criteria aims to conduct our study in a homogeneous patient group and to increase the reliability of the findings obtained. Demographic, clinical, laboratory, and ultrasonographic data of the cases were retrospectively acquired through the hospital data management system.

The sufficiency of the sample size acquired in our investigation was assessed by statistical power analysis. Power analysis is a technique for determining the likelihood of identifying a specific effect magnitude at a designated confidence level. In our investigation, the analyses conducted to assess the markers predicting insulin requirements in pregnant women with gestational GDM were based on an 80% power (1-β) and a 5% significance threshold (α=0.05) to identify significant differences. Based on calculations that accounted for effect sizes reported in analogous studies within the existing literature, it was concluded that the 406 patients included in our investigation constituted an adequate sample size to yield statistically significant results. The findings of our investigation are statistically valid and offer a solid foundation for the generalizability of the acquired data.

Methods for Diagnosing Gestational Diabetes

One step model: After measuring fasting plasma glucose (FPG) in women with 24-28 weeks of pregnancy, 75 g of glucose solution was loaded. Then, glucose levels were measured at 1st and 2nd hours. Patients with at least one positive value were diagnosed with GDM (FPG ≥92 mg/dl, 1st hour glucose ≥180 mg/dl and 2nd hour glucose ≥153 mg/dl).[20,21]

Two step model: Women at 24-28 weeks of gestation underwent a 50-g OGTT. Individuals with a glucose level of 140 mg/dl or higher were deemed positive and underwent a 100-g OGTT. FPG and glucose levels at the 1st, 2nd, and 3rd hours were assessed, and patients exhibiting two positive values were diagnosed as GDM (FPG >95 mg/dl, 1st hour glucose >180 mg/dl, 2nd hour glucose >155 mg/dl, and 3rd hour glucose >140 mg/dl).[20,21]

Statistical Analysis

The data analysis was performed using IBM Corporation SPSS version 22.0 (IBM Corporation, Armonk, NY, USA). The figures were created using Office 2021 (Microsoft, Albuquerque, New Mexico, USA). The Kolmogorov-Smirnov test was used to analyze conformity to normal distribution. Descriptive statistics of continuous variables are shown as "mean±standard deviation" for those with normal

distribution. and as "median (interquartile range)" for those that do not. Categorical variables were compared using the chi-squared test or Fisher's exact test. Continuous variables that were and were not normally distributed were compared using the independent sample T test and the Mann-Whitney U test. respectively. Receiver operating characteristic (ROC) curve was applied to calculate and compare the areas under the curve (AUC) and determine the best cutoff values according to Youden Index. Statistical significance for all tests was defined as p-value of less than 0.05.

RESULTS

Among the patients evaluated using the 75 g OGTT, when comparing the insulin-treatment group with the diet-only group, the mean age of those requiring insulin was significantly lower (31.9±5.9 years) with statistical significance of p=0.016. The frequency of insulin use was significantly lower in the nulliparous cohort (p=0.031). Higher HgbA1c levels were noted in the insulin group (p=0.009), and white blood cell and lymphocyte counts showed statistically significant variations (p=0.014 and p=0.031, respectively). However, serum albumin levels were significantly lower in the insulin group (p<0.001) (Table 1).

Table 1. Characteristics and laboratory results of patients diagnosed with GDM with 75 g OGTT according to need for insulin treatment

	GDM-regulated with insulin n: 49 (18.3%)	GDM-regulated with diet n: 219 (81.7%)	p-value
Maternal age (year)	31.9±5.9	34.2±5.6	0.016[a]
Gravida	2 (3)	3 (1)	0.169[b]
Parity	1 (2)	1 (1)	0.154[b]
Nulliparous	139 (63.5%)	39 (79.6%)	0.031[c]
In vitro fertilization	1 (6.4%)	2 (4.1%)	0.744[d]
Height (cm)	161±6	162±5.4	0.081[a]
Weight (kg)	81.9±14.7	84.6±12.7	0.254[a]
BMI (kg/m$^{2)}$	31.7±5.6	32±4.3	0.735[a]
Family history of diabetes mellitus	4 (1.8%)	5 (10.2%)	0.012[d]
Hemoglobin (g/dl)	11.80 (1.5)	12 (1.6)	0.130[b]
White blood cell count (10^9/L)	9.81 (3.05)	10.17 (3.16)	0.014[b]
Lymphocyte count (10^9/L)	1.86 (0.72)	2.02 (0.79)	0.031[b]
Neutrophil count (10^9/L)	7.24 (2.54)	7.23 (2.72)	0.077[b]
Monocyte count (10^9/L)	0.59 (0.25)	0.62 (0.27)	0.112[b]
Platelet count (10^9/L)	234.5 (78)	252.00 (83)	0.013[b]
TSH (mU/ml)	1.79 (1.67)	1.71 (1.15)	0.792[b]
AST (IU/L)	15 (6)	15 (5)	0.376[b]
ALT (IU/L)	11 (5.5)	11 (8)	0.132[b]
Albumin (g/dl)	35.65 (4.15)	37.75 (2.7)	<0.001[b]
Fibrinogen (mg/dl)	465 (116)	485 (141)	0.730[b]
HgbA1c (%)	5.3 (0.8)	5 (0.6)	0.009[b]

Data are expressed as n (%), mean±standard deviation or median (interquartile range) where appropriate. A p-value of <0.05 indicates a significant difference and statistically significant p-values are in bold. GDM: Gestational diabetes mellitus, OGTT: Oral glucose tolerance test, BMI: Body-mass index, TSH: Thyroid stimulating hormone, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, HgbA1c: Hemoglobin A1c, [a]: Student T test, [b]: Mann-Whitney U test, [c]: Pearson chi-square, [d]: Fisher's exact test

Analysis of birth outcomes revealed that the delivery week occurred sooner in the insulin therapy cohort (p=0.001). A notable disparity was seen between the groups regarding infant gender; it was established that the offspring of patients undergoing insulin therapy were predominantly male (p=0.011). In addition, no statistical significance was observed between the rates of NICU admission and other neonatal complication rates in this group (Table 2).

Table 2. Characteristics and laboratory results of patients diagnosed with GDM with 100 g OGTT according to need for insulin treatment

	GDM-regulated with insulin n: 120 (87%)	GDM-regulated with diet n: 18 (13%)	p-value
Maternal age (year)	32.3±5.6	32.1±6.8	0.925[a]
Gravida	2 (2)	3 (2)	0.894[b]
Parity	1 (2)	1 (2)	0.513[b]
Nulliparous	87 (72.5%)	10 (55.6%)	0.142[c]
In vitro fertilization	6 (5%)	1 (5.6%)	1[d]
Height (cm)	161±6.1	161.1±5.6	0.914[a]
Weight (kg)	83.3±13.9	87.7±11.9	0.209[a]
BMI (kg/m^2)	32.1±4.9	33.7±4.3	0.188[a]
Family history of diabetes mellitus	2 (1.7%)	3 (16.7%)	0.016[d]
Hemoglobin (g/dl)	12 (0.8)	11.85 (1.5)	0.495[b]
White blood cell count (10^9/L)	9.73 (2.01)	10.19 (3.11)	0.951[b]
Lymphocyte count (10^9/L)	1.91 (0.52)	1.77 (0.52)	0.466[b]
Neutrophil count (10^9/L)	7.27 (1.44)	7.50 (2.7)	0.792[b]
Monocyte count (10^9/L)	0.61 (0.18)	0.59 (0.28)	0.371[b]
Platelet count (10^9/L)	241 (63)	239 (75)	0.493[b]
TSH (mU/ml)	1.34 (0.88)	1.63 (1.07)	0.441[b]
AST (IU/L)	16 (5)	16 (7)	0.544[b]
ALT (IU/L)	10 (4)	11 (8)	0.631[b]
Albumin (g/dl)	36.30 (2.6)	36.80 (4.5)	0.680[b]
Fibrinogen (mg/dl)	458.5 (123)	470 (145.5)	0.919[b]
HgbA1c (%)	5.10 (0.7)	5.05 (0.8)	0.572[b]

Data are expressed as n (%), mean±standard deviation or median (interquartile range) where appropriate. A p-value of <0.05 indicates a significant difference and statistically significant p-values are in bold. GDM: Gestational diabetes mellitus, OGTT: Oral glucose tolerance test, BMI: Body-mass index, TSH: Thyroid stimulating hormone, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, HgbA1c: Hemoglobin A1c, [a]: Student T test, [b]: Mann-Whitney U test, [c]: Pearson chi-square, [d]: Fisher's exact test

No significant differences were seen between the insulin-regulated group and the diet-regulated group regarding maternal age, gravida, parity, BMI, and other laboratory parameters in patients assessed with a 100 g OGTT. Nonetheless, family history of diabetes was found to be higher in the insulin-treated group (p=0.016). No significant difference was seen between the groups regarding serum HgbA1c levels and glucose measurements (Table 3). Birth outcomes indicated that birth week and birth weights were comparable in both groups, with no statistical significance observed in neonatal results (Table 4).

In the comparison of serum glucose levels between insulin-regulated and diet-regulated GDM patients diagnosed via the 75 g OGTT (Table 5), fasting, 1st-hour, and 2nd hour glucose levels were significantly higher in the insulin-requiring group

Table 3. Birth characteristics and neonatal outcomes of newborns of patients diagnosed with GDM by 75 g OGTT

	GDM-regulated with insulin n: 49 (18.3%)	GDM-regulated with diet n: 219 (81.7%)	p-value
Gestational age at delivery (week)	38 (1)	38 (2)	0.001[a]
Cesarean section	34 (69.4%)	134 (61.2%)	0.283[b]
Birth weight (gram)	3239±609	3238±407	0.989[c]
Gender			0.011[b]
Female	20 (40.8%)	133 (60.7%)	
Male	29 (59.2%)	86 (39.3%)	
Apgar score at 1st minute	9 (0)	9 (0)	0.270[a]
Apgar score at 5th minute	10 (0)	10 (0)	0.752[a]
CAPO	12 (24.5%)	36 (16.4%)	0.184[b]
NICU admission	4 (8.2%)	5 (2.3%)	0.061[d]
Umbilical cord pH	7.38 (0.06)	7.36 (0.08)	0.180[a]
Preterm birth	7 (14.3%)	20 (9.1%)	0.279[d]
Transient tachypnea of the newborn	5 (10.2%)	12 (5.5%)	0.220[d]
Neonatal sepsis	0 (0%)	0 (0%)	NA
Fetal distress	2 (4.1%)	19 (8.7%)	0.385[d]
Respiratory distress syndrome	2 (4.1%)	4 (1.8%)	0.302[d]
Continues positive airway pressure	4 (8.2%)	14 (6.4%)	0.751[d]
Mechanical ventilation	3 (6.1%)	14 (6.4%)	1[d]
Phototherapy for neonates	2 (4.1%)	11 (5%)	1[d]
Neonatal hypoglycemia	9 (18.4%)	22 (10%)	0.135[b]
Interventricular hemorrhage	0 (0%)	0 (0%)	NA
Necrotizing enterocolitis	0 (0%)	0 (0%)	NA

Composite adverse perinatal outcomes include the presence of at least one of the following adverse outcomes: 5th-minute APGAR score <7, transient tachypnea of the newborn, respiratory distress syndrome, need for continuous positive airway pressure, need for mechanical ventilation, neonatal intensive care unit admission, preterm birth, neonatal hypoglycemia, need for phototherapy, intraventricular hemorrhage and neonatal sepsis. Data are expressed as n (%), mean±standard deviation or median (interquartile range) where appropriate. A p-value of <0.05 indicates a significant difference and statistically significant p-values are in bold. GDM: Gestational diabetes mellitus, OGTT: Oral glucose tolerance test, CAPO: Composite adverse perinatal outcome, NICU: Neonatal intensive care unit, NA: Not applicable, [a]: Mann-Whitney U test, [b]: Pearson chi-square, [c]: Student T test, [d]: Fisher's exact test

Table 4. Birth characteristics and neonatal outcomes of newborns of patients diagnosed with GDM by 100 g OGTT

	GDM-regulated with insulin n: 18 (13%)	GDM-regulated with diet n: 120 (87%)	p-value
Gestational age at delivery (week)	38 (2)	38 (2)	0.869[a]
Cesarean section	13 (72.2%)	77 (64.2%)	0.503[b]
Birth weight (gram)	3186±514	3232±587	0.752[c]
Gender			0.125[d]
Female	14 (77.8%)	69 (57.5%)	
Male	4 (22.2%)	51 (42.5%)	
Apgar score at 1st minute	9 (1)	9 (1)	0.243[a]
Apgar score at 5th minute	10 (1)	10 (1)	0.752[a]
CAPO	3 (16.7%)	36 (30%)	0.241[b]
NICU admission	0 (0%)	6 (5%)	1[d]
Umbilical cord pH	7.39 (0.1)	7.36 (0.09)	0.450[a]
Preterm birth	2 (11.1%)	26 (21.6%)	0.529[d]
Transient tachypnea of the newborn	1 (5.6%)	12 (10%)	1[d]
Neonatal sepsis	0 (0%)	0 (0%)	NA
Fetal distress	1 (5.6%)	9 (7.5%)	1[d]
Respiratory distress syndrome	0 (0%)	3 (2.5%)	1[d]
Continues positive airway pressure	1 (5.6%)	10 (8.3%)	1[d]
Mechanical ventilation	0 (0%)	7 (5.8%)	0.594[d]
Phototherapy for neonates	1 (5.6%)	5 (4.2%)	0.575[d]
Neonatal hypoglycemia	1 (5.6%)	15 (12.5%)	0.694[d]
Interventricular hemorrhage	0 (0%)	0 (0%)	NA
Necrotizing enterocolitis	0 (0%)	0 (0%)	NA

Data are expressed as n (%), mean±standard deviation or median (interquartile range) where appropriate. A p-value of <0.05 indicates a significant difference and statistically significant p-values are in bold. GDM: Gestational diabetes mellitus, OGTT: Oral glucose tolerance test, CAPO: Composite adverse perinatal outcome, NICU: Neonatal intensive care unit, NA: Not applicable, [a]: Mann-Whitney U test, [b]: Pearson chi-square test, [c]: Student T test, [d]: Fisher's exact test

Table 5. Comparison of serum glucose levels in patients diagnosed with GDM by 75 g OGTT

	GDM-regulated with insulin n: 49 (18.3%)	GDM-regulated with diet n: 219 (81.7%)	p-value
Fasting	97 (25)	89 (19)	<0.001[a]
1st hour	203 (37)	187 (35)	<0.001[a]
2nd hour	163 (58)	139 (48)	0.001[a]

Data are expressed as n (%) or median (interquartile range) where appropriate. A p-value of <0.05 indicates a significant difference and statistically significant p-values are in bold. GDM: Gestational diabetes mellitus, OGTT: Oral glucose tolerance test, [a]: Mann-Whitney U test

Table 6. Comparison of serum glucose levels in patients diagnosed with GDM by 100 g OGTT

	GDM-regulated with insulin n: 18 (13%)	GDM-regulated with diet n: 120 (87%)	p-value
Fasting	90 (23)	83 (17.5)	0.090[a]
1st hour	200 (39)	193 (27)	0.164[a]
2nd hour	189 (39)	162 (36)	0.032[a]
3rd hour	140 (25)	125 (41)	0.141[a]

Data are expressed as n (%) or median (interquartile range) where appropriate. A p-value of <0.05 indicates a significant difference and statistically significant p-values are in bold. GDM: Gestational diabetes mellitus, OGTT: Oral glucose tolerance test, [a]: Mann-Whitney U test

(p<0.001, p<0.001, and p=0.001, respectively). Similarly, in patients diagnosed with GDM using the 100 g OGTT (Table 6), the 2nd hour glucose level was significantly higher in the insulin-requiring group (p=0.032), while fasting, 1st hour, and 3rd hour glucose levels did not show statistically significant differences.

ROC analysis evaluating the ability of serum glucose levels to predict insulin requirements (Table 7) demonstrated that fasting glucose >92 mg/dl in all patients (AUC=0.657, p<0.001), >94 mg/dl in 75 g OGTT patients (AUC=0.669, p<0.001), 1st-hour glucose >196 mg/dl (AUC=0.667, p<0.001), and 2nd hour glucose >160 mg/dl (AUC=0.656, p=0.001) were predictive of insulin requirement. Among 100 g OGTT patients, a 2nd hour glucose level >169 mg/dl was associated with insulin use (AUC=0.661, p=0.032).

Table 7. Evaluation of serum glucose levels to predict insulin requirements in patients diagnosed with GDM by using ROC analysis

	LR+	LR-	Cut-off*	Sensitivity	Specificity	AUC	95% CI	p-value
Fasting (with all patients)	1.52	0.68	>92	58.2%	61.7%	0.657	0.58-0.73	<0.001
Fasting (for 75 g OGTT)	1.58	0.67	>94	57.1%	63.8%	0.669	0.58-0.76	<0.001
1st hour (for 75 g OGTT)	2.09	0.50	>196	65.3%	68.8%	0.667	0.58-0.76	<0.001
2nd hour (for 75 g OGTT)	2.27	0.59	>160	55.1%	75.7%	0.656	0.57-0.75	0.001
2nd hour (for 100 g OGTT)	1.72	0.57	>169	64.7%	62.4%	0.661	0.51-0.81	0.032

*Cut-off values were found according to Youden Index, GDM: Gestational diabetes mellitus, ROC: Receiver operating characteristic, LR+: Positive likelihood ratio, LR-: Negative likelihood ratio, AUC: Area under the curve, CI: Confidence interval, OGTT: Oral glucose tolerance test

Evaluation of HbA1c for predicting insulin requirement in 75 g OGTT-diagnosed GDM patients (Table 8) revealed that an HbA1c cutoff of >5.25% had an AUC of 0.633 (p=0.009), with a sensitivity of 53.5% and specificity of 71.4%. However, in patients diagnosed with the 100 g OGTT, HbA1c was not predictive of insulin need (AUC=0.544, p=0.573).

Finally, the ability of HbA1c to predict composite adverse perinatal outcomes (Table 9) was significant in 75 g OGTT patients, with an AUC of 0.662 (p=0.003) at a cutoff of >5.25%. However, in patients diagnosed with the 100 g OGTT, HbA1c did not significantly predict adverse outcomes (AUC=0.475, p=0.704). Serum glucose levels and insulin requirements; ROC analysis indicated that fasting blood glucose levels obtained during the 75 g OGTT, namely at the 1st and 2nd hour, were significant predictors of insulin requirements (p<0.001). The threshold value established for the 2nd hour glucose level (>160 mg/dl) exhibited 55.1% sensitivity and 75.7% specificity in forecasting insulin necessity (Figure 1). The study of HgbA1c revealed that a threshold value over 5.25 significantly predicted insulin demand (p=0.009), however statistical significance was not attained for the 100 g OGTT group (Figure 2).

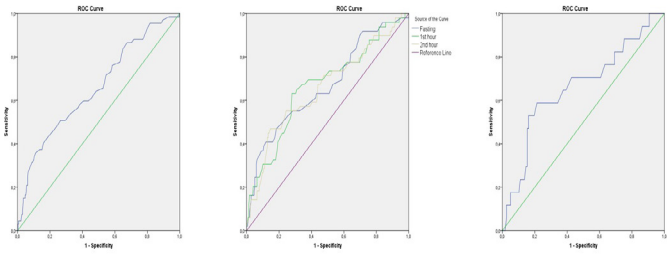

Figure 1. ROC curves of fasting, 1st hour and 2nd hour serum glucose levels to predict insulin requirements in patients diagnosed with gestational diabetes mellitus

ROC: Receiver operating characteristic

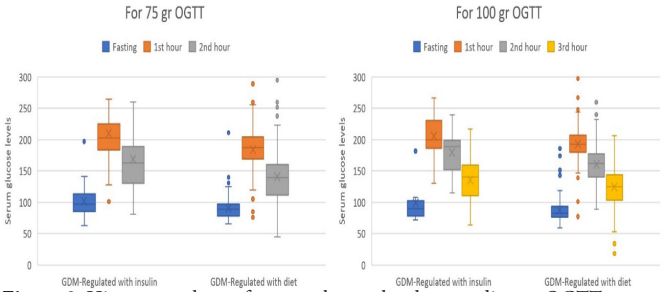

Figure 2. Histogram chart of serum glucose levels according to OGTT

OGTT: Oral glucose tolerance test

DISCUSSION

The primary conclusions of our study indicate that glucose measurements and HbA1c levels derived from a 75 g OGTT can effectively predict the necessity for insulin in pregnancies diagnosed with GDM. The data in the 100 g OGTT results lack statistical significance in forecasting insulin utilization. Despite the elevated incidence of preterm delivery in the insulin-treated cohort suggesting worse prenatal outcomes, dismal neonatal outcomes did not exhibit a statistically significant difference in this group. Maternal age, familial diabetes history, and specific hematological and biochemical indicators can predict insulin utilization.

In the demographic data of our investigation, contrary to existing literature, maternal age was lower and the nulliparity rate was considerably elevated among insulin users, specifically within the group diagnosed with the 75 g OGTT. Certain research have identified a correlation between youth, nulliparity, and gestational diabetes. This study contradicts the prevailing trend in the literature and indicates that several factors may influence the onset of gestational diabetes. Genetic predisposition, lifestyle, and environmental variables may elevate the risk of gestational diabetes in young

Table 8. Evaluation of HgbA1c to predict insulin requirements in patients diagnosed with GDM by 75 g OGTT using ROC analysis

	LR+	LR-	Cut-off*	Sensitivity	Specificity	AUC	95% CI	p-value
HgbA1c	1.87	0.65	>5.25	53.5%	71.4%	0.633	0.53-0.74	0.009

*Cut-off values were found according to Youden Index, HgbA1c: Hemoglobin A1c, GDM: Gestational diabetes mellitus, OGTT: Oral glucose tolerance test, ROC: Receiver operating characteristic, LR+: Positive likelihood ratio, LR-: Negative likelihood ratio, AUC: Area under the curve, CI: Confidence interval

Table 9. Evaluation of HgbA1c to predict composite adverse perinatal outcome in patients diagnosed with GDM by 75 g OGTT using ROC analysis

	LR+	LR-	Cut-off*	Sensitivity	Specificity	AUC	95% CI	p-value
HgbA1c	1.76	0.68	>5.25	52.8%	69.9%	0.662	0.57-0.76	0.003

*Cut-off values were found according to Youden Index, HgbA1c: Hemoglobin A1c, GDM: Gestational diabetes mellitus, OGTT: Oral glucose tolerance test, ROC: Receiver operating characteristic, LR+: Positive likelihood ratio, LR-: Negative likelihood ratio, AUC: Area under the curve, CI: Confidence interval

nulliparous women. Consequently, it is essential to evaluate individual risk factors instead of concentrating exclusively on demographic variables like age and parity in the assessment of gestational diabetes risk. Every pregnant woman must undergo an assessment of her individual and familial medical history, lifestyle, and other possible risk factors.[22,23]

Research indicates that elevated levels of white blood cells, platelets, and hematocrit are prevalent among non-pregnant individuals with diabetes who experience high complication rates, suggesting a potential correlation with the chronic inflammatory processes associated with diabetes.[24,25] Jindal et al.[26] indicated in their research that elevated platelet counts may correlate with microvascular problems. Consistent with these findings, HgbA1c levels were markedly elevated in diabetes patients with problems and in those utilizing insulin. Research on GDM mostly focused on predicting hematological markers only. Markovic et al.[27] assessed various hematological and biochemical markers in women with GDM compared to control groups. Alanine aminotransferase (ALT), fibrinogen, sedimentation rate, granulocyte count, and leukocyte count were correlated with adverse neonatal outcomes in patients with GDM. Another study revealed that HgbA1c and platelet distribution width were considerably elevated in GDM.[28] These investigations indicate that certain hematological and biochemical markers may forecast GDM, although they are not pertinent for anticipating insulin requires. In our investigation, women who took a 75 g OGTT and required insulin exhibited significantly elevated lymphocyte count, platelet count, albumin levels, and HbA1c levels. Consequently, to our knowledge, this study is the inaugural investigation in the literature that substantiates the potential of hematological and biochemical markers to predict insulin utilization, warranting further extensive studies on this topic.

Numerous studies have examined factors that retroactively predict diagnosis in GDM patients identified using the 100 g and 75 g OGTTs. These studies corroborate that the risk factors for GDM are identical for both screening techniques.[16,29,30] Helseth et al.[31] conducted a study indicating that the diagnosis of GDM is more prevalent with the 75 g OGTT, and that the risk variables differ between the two diagnoses. The primary risk variables found were maternal age, BMI prior to and during pregnancy, familial history of type 2 diabetes, and weight gain during pregnancy. Nevertheless, the quantity of studies aimed at predicting insulin requirements or identifying risk factors for insulin utilization in patients with GDM is very restricted. Research is mostly focused on identifying risk factors for GDM to facilitate the use of screening tests. Tamagawa et al. assessed the predictive factors for insulin utilization by comparing the insulin requirement risk factors in pregnant women diagnosed with early GDM based on positive OGTT in the first trimester, and those identified with late GDM based on positive OGTT in the second trimester. It was determined that blood sugar measurements during the 1st and 2nd hours, excluding fasting blood sugar, were considerably elevated in the insulin-dependent group. They also indicated that among pregnant women with early GDM, a pre-pregnancy BMI of ≥25 kg/m^2, a family history of diabetes, and 75 g OGTT scores were all significantly elevated in those requiring insulin. The evaluation of unfavorable neonatal outcomes between the two groups revealed no statistically significant difference between the insulin-using group and the non-using group. Furthermore, this study found no statistically significant difference in HbA1c values between the insulin-administering group and the non-insulin-administering group.[13] Consistent with these observations, prior research indicate that insulin requirements in pregnant women identified with 75 g OGTT correlate with elevated BMI and a familial history of diabetes.[32,33] Our investigation revealed that insulin utilization in patients diagnosed via the 75 g OGTT correlated with maternal age, elevated HbA1c levels, and a familial history of diabetes; however, its association with BMI was not statistically significant. In individuals diagnosed with 100 g OGTT, only a family history of diabetes was correlated with the insulin-using cohort. The Hyperglycemia and Adverse Pregnancy Outcome (HAPO) project is among the greatest investigations on hyperglycemia and negative neonatal outcomes. This study unequivocally shown that maternal hyperglycemia is directly linked to negative neonatal outcomes.[15,34] Moreover, given that GDM is predominantly diagnosed using the 75 g OGTT, our study, alongside other research, suggests that predictive factors for insulin therapy may assist clinicians in managing hyperglycemia. This can be achieved by enhancing lifestyle modifications, such as dietary adjustments and physical activity, or by assessing the patient for the early initiation of insulin treatment.

In our investigation, individuals who received a 75 g OGTT had significantly elevated mean fasting, 1st hour, and 2nd hour blood sugar levels in the insulin-dependent group. In the 100 g OGTT, only the blood glucose level recorded at the second hour was substantially elevated in the insulin-using group. The primary findings of our investigation indicated that additional parameters could predict insulin utilization with the 75 g OGTT. The two-step diagnostic test may be less advantageous than the single-step diagnostic test for application and cost, and prior research have assessed the suggestion of the single-step method.[35,36] Furthermore, numerous studies have indicated that the treatment of GDM yields superior newborn outcomes relative to the expectant management method, underscoring the significance of hyperglycemia regulation.[13,34,37] We contend that our research could assist doctors in implementing OGTT during the initial weeks of pregnancy, with a preference for a single-step diagnosis approach, particularly for patients exhibiting risk indicators for GDM.

Limitations

A principal strength of this study is its thorough retrospective analysis of a substantial cohort of patients, facilitating an in-depth assessment of several OGTT methods and their predictive significance for insulin requirements in GDM. The research offers significant insights into the practical applicability of diverse diagnostic techniques and prospective biomarkers for informing early intervention tactics. Nevertheless, specific limits must also be recognized. The retrospective methodology obviously poses a risk of selection and information bias, as data were sourced from existing medical records, potentially resulting in incomplete or

absent information. The study is conducted on a single-center population, perhaps restricting the generalizability of the findings to wider, more heterogeneous populations. Future prospective, multi-center research employing standardized data collection methods would be advantageous for validating and reinforcing these findings.

CONCLUSION

This study assessed the impact of several OGTT procedures on the diagnosis and management of GDM and analyzed the factors influencing insulin need. The results indicate that the selection of OGTT procedures may influence clinical outcomes and that specific criteria should be considered when predicting the necessity for insulin therapy. In the management of GDM, it may be possible to predict insulin requirements using glucose levels based on the 75 g OGTT and this could support early interventions. The advancement of personalized strategies for managing gestational diabetes may enhance mother and newborn health.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was carried out with the permission of the Ankara Etlik City Hospital Scientific Researches Evaluation and Ethics Committee (Date: 25.12.2024, Decision No: AEŞH-BADEK–2024-1199).

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.

Financial Disclosure

The authors declared that this study has received no financial support.

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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