

Identifying the Risk Group for Insulin Therapy in Patients with Gestational Diabetes

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ABSTRACT

Aim: This study aims to determine the predictors of antenatal insulin therapy (AIT) in patients with gestational diabetes mellitus (GDM) who applied to the outpatient endocrine clinic of a tertiary hospital.

Material and Methods: The study included 619 patients with GDM. Oral glucose tolerance test (OGTT), HbA1c (%), lipid levels, and other biochemical measurements of two groups (patients with or without insulin use) were compared with Mann-Whitney U or Student t-test. Demographic characteristics, obesity, and diet adherence were compared with the Chi-Square test. OGTT-75 measurements between the three insulin groups (basal, bolus or both uses) were compared with ANOVA.

Results: In this study, 27.0% of the GDM patients needed insulin therapy. The insulin group had a significantly higher rate of obese, morbidly obese, and poor diet adherence patients than the MNT group and had significantly higher values measured in the 75-g OGTT (OGTT₋₇₅) for 0-h glucose, 2-h glucose, HbA1c (%), and triglyceride. In OGTT₋₇₅, all three measurement values (0-h, 1-h, 2-h glucose) above the cut-off were associated with insulin requirement. In OGTT₋₇₅, 2-h glucose value > 151.5 mg/dL (68.4% sensitivity and 60.0% specificity) predicted general need for insulin, and 0-h glucose value > 95.0 mg/dL (72.0% sensitivity and 69.0% specificity) predicted the need for basal AIT.

Conclusion: We suggest identifying the risky group for insulin therapy at the time of diagnosis in GDM. Closer follow-up is required for the patients found to be in the risk group for insulin therapy.

Keywords: Gestational diabetes mellitus, Oral glucose tolerance test, Insulin, Nutrition, Triglyceride, Glucose

Gestasyonel Diyabetli Hastalarda İnsülin Tedavisi İçin Riskli Grubun Belirlenmesi

ÖZ

Amaç: Bu çalışmanın amacı üçüncü basamak bir hastanenin endokrin polikliniğine başvuran gestasyonel diyabetes mellitus (GDM) tanılı hastaların antenatal insülin tedavisini (AIT) predikte eden değişkenleri tespit etmektir.

Gereç ve Yöntemler: Çalışmaya GDM tanılı 619 hasta dahil edildi. İnsülin kullanan ve kullanmayan iki grubun oral glukoz tolerans testi (OGTT), HbA1c, lipid düzeyleri ve diğer biyokimyasal ölçümleri Mann-Whitney U veya Student t-testi ile karşılaştırıldı. Bu gruplar arasındaki demografik özellikler, obezite, HbA1c (%) ve diyet uyum Ki Kare testi ile karşılaştırıldı. Üç insülin grubu (bazal, bolus veya her ikisini kullanan) arasındaki OGTT-75 ölçümleri ANOVA ile karşılaştırıldı.

Bulgular: Çalışmamıza dahil edilen GDM'li hastaların %27.0'sinde insülin ihtiyacı olmuştur. İnsülin grubunda; obez, morbid obez ve düşük diyet uyumu olan hasta oranı, ayrıca OGTT₋₇₅ 0-s glukoz, 2-s glukoz, HbA1c (%) ve trigliserid ölçümleri MNT grubuna göre anlamlı olarak yüksek bulundu. OGTT₋₇₅ 'de üç ölçüm değerinin birden kesme değer üstünde olması insülin ihtiyacı ile ilişkiliydi. OGTT₋₇₅ 2-s glukoz değeri > 151.5 mg/dL (% 68.4 sensivite, % 60.0 spesifite) olması insülin ihtiyacını genel olarak predikte ederken, 0-s glukoz değerinin > 95.0 mg/dL (% 72.0 sensivite, %69.0 spesifite) olması bazal AIT ihtiyacını predikte etti.

Sonuç: GDM'de tanı ile birlikte insülin tedavisi için riskli grubun belirlenmesini öneriyoruz. İnsülin tedavisi için risk grubunda bulunan hastalarda daha yakın takip gereklidir.

Anahtar Sözcükler: Gestasyonel diyabetes mellitus, Oral glukoz tolerans testi, İnsülin, Nutrisyon, Trigliserid, Glukoz

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INTRODUCTION

The prevalence of gestational diabetes mellitus (GDM) is around 17 percent (1). GDM is hyperglycemia that occurs and continues throughout pregnancy in the third trimester in pregnant women with no history of diagnosed diabetes (2). In cases where pregnancy occurs in a woman with already diagnosed diabetes, it is called “pregestational diabetes mellitus” (PGDM) (3). After the diagnosis of GDM, such patients are followed up along with the provision of counselling for medical nutrition therapy (MNT) and self-monitoring of blood glucose (SMBG) (4). In patients followed up with a diagnosis of GDM, the ideal range is < 95 mg/dl for fasting plasma glucose (FPG), < 140 mg/dl for PG at 1-h post-meal, and < 120 mg/dl for PG at 2-h post-meal, whereas the ideal A1C level is 6-6.5% (42-48 mmol/mol) (4). In GDM, if the targeted glucose values cannot be attained within 1-2 weeks or if blood glucose rises again under control, it is recommended to start insulin therapy (4-6).

Problems of adherence to insulin therapy and treatment adherence in gestational diabetes have been reported (7,8). Insulin-treated women with GDM are reported to have more perinatal complications compared to diet-treated women (9,10). It has been reported that caloric restriction to avoid insulin therapy reduces the need for insulin but causes intrauterine growth retardation (11). We believe that evaluating the factors that predict and guide insulin therapy will positively contribute.

This study aims to determine the predictors of antenatal insulin therapy in patients with gestational diabetes mellitus (GDM) who applied to the outpatient endocrine clinic of a tertiary hospital. We retrospectively scanned the variables measured in these patients at the time of diagnosis and during the post-diagnostic period.

MATERIAL and METHODS

The records of 1199 patients admitted to Karadeniz Technical University Faculty of Medicine Department of Endocrinology and Metabolic Diseases, between 2017 and 2021, as outpatients and coded as “Strip used in gestational diabetes” (CODE: 53) were reviewed retrospectively.

The exclusion criteria included having the history of diabetes mellitus history or a diagnosis of diabetes mellitus during the first 24 weeks of gestation, history of gestational diabetes in a previous pregnancy, diagnosis of diabetes mellitus with 50 g or 100 g oral glucose tolerance test (OGTT), having fasting plasma glucose level of ≥ 126 mg/dL or HbA1C of $\geq 6.5\%$ at the time of diagnosis, and multiparity.

The records of patients whose gestational diabetes diagnoses were confirmed by OGTT-75, according to the guideline

were reviewed (confirmed by the presence of at least one of the diagnostic criteria, fasting plasma glucose ≥ 92 mg/dL, 1-h plasma glucose ≥ 180 mg/dL, and 2-h plasma glucose ≥ 153 mg/dL) (4). Subsequently, 619 patients initiated insulin therapy after at least one week of SMBG, following the MNT recommendation, or followed up with MNT were included in the study (the insulin group and the MNT group, respectively).

The patients' medical data included in the study and their results in the first biochemical measurements run after their admission to our outpatient clinic after the 24th gestational week were all recorded.

The body mass index (BMI) information of the patients includes the measurements at the time of their first admission to our outpatient clinic after the diagnosis of GDM; they have been grouped according to the WHO classification (12). After giving the MNT counselling, the patients with data on dietary adherence were classified in terms of their dietary adherence being good, average, or poor.

The assessment of dietary adherence was based on patients reports. We divided the patients receiving insulin into three groups as basal-only, bolus-only, and basal + bolus combination, and subsequently compared them. Patients in the groups using basal-only or bolus-only insulin included patients who were monitored following either of the therapies mentioned above until the end of pregnancy.

Biochemical Analysis

Glucose, creatinine, lipid parameters (total cholesterol, high-density lipoprotein cholesterol [HDLc], low-density lipoprotein cholesterol [LDLc], and triglyceride [TG] levels, were measured using the enzymatic colourimetric method with a Beckman Coulter AU5800 (Shizuoka, Japan) autoanalyzer with the manufacturer's original kits. Using a Cobas 6000 (Roche), the immunoturbidimetric method was used for HbA1c analysis. Normal ranges for glucose, creatinine, albumin, HbA1c, total cholesterol, HDL, LDL, TG levels were defined as 70-100 mg/dl, 0.51-0.95 mg/dl, 35-52 g/L, % 4.27-6.07, 120-200 mg/dl, 45-65 mg/dl, <160 mg/dl and 50-150 mg/dl respectively.

Statistical Analysis

All statistical analyses were performed with the SPSS 23.0 software package (SPSS, Inc., Chicago, Illinois). Descriptive statistics for the continuous variables were expressed as mean \pm SD or median (range), and categorical variables were noted as numerics and percent (%). The normal distribution of the results was checked by the Kolmogorov-Smirnov test. Student T-test was used to compare measurements with normal distribution in two independent

groups (patients with and without insulin use), ANOVA was used to compare measurements with normal distribution in three independent groups (patients with basal, bolus, and both insulin use), and Mann Whitney U (MWU) test was used to compare measurements that are not normally distributed in two independent groups (patients with and without insulin use). Chi-square was used to compare categorical variables between the groups.

Cohen's *d* was calculated to estimate the effect size for each of the *t*-tests, Pearson's *r* was calculated to estimate the effect size for each of the MWU tests, and Cohen's *f* was calculated to estimate the effect size for each of the ANOVA tests (Cohen's *d* = 0.2- < 0.5 small effect size; 0.5- < 0.8 medium effect size; ≥ 0.8 large effect size. Pearson's *r* = 0.10- < 0.30 small effect size; 0.3- < 0.5 medium effect size; ≥ 0.5 large effect size. Cohen's *f* = 0.10- < 0.25 small effect size; 0.25- < 0.40 medium effect size; ≥ 0.40 large effect size) (13).

The marking features about OGTT-75 glucose (0-h, 1-h, 2-h), HbA1C, triglyceride serum levels in predicting insulin use were assessed by Receiver Operating Characteristics (ROC) curve analysis. In evaluating the area under the curve (AUC), cases with Type-1 error levels below 5% were interpreted as the diagnostic value of the test was statistically significant. *p* < 0.05 was considered as statistically significant.

RESULTS

In our study, 73.0% (*n* = 452) of the 619 patients included were followed up with MNT alone, whereas 27.0% (*n* = 167) required antenatal insulin therapy. According to the BMIs calculated for the patients, 7.4% (*n* = 46) were normal-weighted, 36.1% (*n* = 223) were overweight, 49.6% (*n* = 307) were obese, and 6.9% (*n* = 43) were morbidly obese. There was no difference between the groups of MNT and insulin therapy that included patients with normal weight (*p* = 0.128). The rate of obese and morbidly obese patients was higher in insulin patients (*p* = 0.027, *p* = 0.008, respectively). In patients who were followed up with only MNT, the rate of overweight patients was higher (*p* = 0.004). The median maternal age of the normal and overweight patients was 31 years (19-45), whereas the median maternal age of the obese and morbidly obese patients was 33 years (18-45). 65.8% (*n* = 407) of the patients were multiparous and 34.2% (*n* = 212) were primiparous.

In OGTT-75 testing of all included patients included, the median plasma glucose value was 94 mg/dl (68-124) at the hour 0, 182 mg/dl (105-277) at hour 1, and 148 mg/dl (61-275) at hour 2. The OGTT-75 0-h, 1-h, and 2-h glucose measurements were higher in the insulin group than in the MNT group (*p* < 0.001, *p* < 0.001, *p* < 0.001, respectively). According to the OGTT-75 results obtained in all patients,

48.9% (*n* = 303) demonstrated elevation in one, 33.5% (*n* = 207) in two, and 17.6% (*n* = 109) in three measurements. The number of patients with elevation in three measurements was higher in the insulin group, whereas the number of patients with elevation in one measurement was higher in the MNT group (*p* < 0.001, *p* < 0.001, respectively). According to measurements of all patients at the time of the first visit following the diagnosis in the third trimester, the median level of glucose (mg/dl) was 87 (63-121), whereas the median level of HbA1C (%) was 5.2 (4.0-6.3), creatinine (mg/dl) was 0.46 (0.27-1.10), albumin (g/L) was 35.0 (23.0-44.0), and hemoglobin was (mg/dl) 11.80 (8.90-14.50). The levels of glucose and HbA1C (%) were found to be higher in the group of patients receiving insulin (*p* < 0.001, *p* < 0.001, respectively). No significant difference was found between the values measured for albumin and hemoglobin (Table 1).

Of the 220 patients who had lipid measurements, the group of patients who needed insulin was found to have higher TG levels and higher TG/HDL ratios than the MNT group (*p* = 0.049, *p* = 0.047, respectively); however, the levels of LDL-cholesterol, total cholesterol, and HDL cholesterol measured here did not differ (Table 2). Of all patients receiving insulin therapy (*n* = 167), the group of patients on basal-only therapy accounted for 36.5% (*n* = 61) and those on bolus-only therapy accounted for 34.7% (*n* = 58), whereas the group of patients receiving basal + bolus insulin therapy accounted for 28.7% (*n* = 48). When the OGTT-75 glucose measurement results of the patients using insulin were compared among themselves, a difference was detected between the hour 0 and hour 2 measurements (*p* < 0.001, *p* < 0.001, respectively) (Table 3).

The basal only group and the basal + bolus insulin group were significantly higher glucose levels at the 0-h measurement. The 0-h glucose levels were higher in the basal only and basal + bolus groups than the bolus only group of (*p* < 0.001, *p* < 0.001, respectively). However, there was no difference between the basal-only group and basal + bolus insulin group in terms of the glucose levels measured at hour 0 (*p* = 0.985). The group of basal-only therapy had a lower glucose level measured at hour 2 than the bolus only and group of basal + bolus insulin groups (*p* < 0.001, *p* = 0.003, respectively). There was no difference between the bolus-only group and the basal + bolus insulin group regarding the glucose levels measured at hour 2 (*p* = 0.816). The OGTT-75 glucose (0-h, 1-h, and 2-h), HbA1C, and triglyceride were significant variables for predicting the use of insulin, according to the ROC analysis result (Table 4).

The OGTT-75 2-h glucose values that can predict AIT were identified to be > 151.5 mg/dL, with 68.4% sensitivity and

Table 1: Comparison of patients with gestational diabetes receiving insulin therapy with those who can be managed with MNT.

Parameters	All patients (n=619)	MNT group (n =452)	Insulin group (n=167)	<i>p</i>
Age (years) ^a	32 (18-45)	32 (18-45)	33 (19-45)	0.011^c
BMI (kg/m ²)				
< 24.99 ^b	46 (7.4)	38 (8.4)	8 (4.8)	0.128 ^d
25-29.99 ^b	223 (36.1)	178 (39.4)	45 (26.9)	0.004^d
30-39.99 ^b	307 (49.6)	212 (46.9)	95 (56.9)	0.027^d
> 40.0 ^b	43 (6.9)	24 (5.3)	19 (11.4)	0.008^d
Parity				
Multipar ^b	407 (65.8)	289 (63.9)	118 (70.7)	0.118 ^d
Primipar ^b	212 (34.2)	163 (36.1)	49 (29.3)	
OGTT				
0-h plasma glucose ^a	94 (68-124)	94 (68-124)	98 (74-123)	< 0.001^c
1 h plasma glucose ^a	182 (105-277)	180 (105-249)	195 (120-277)	< 0.001^c
2 h plasma glucose ^a	148 (61-275)	144 (61-212)	164 (70-275)	< 0.001^c
Abnormal values in OGTT-75				
1 ^b	303 (48.9)	258 (57.1)	45 (26.9)	< 0.001^c
2 ^b	207 (33.5)	148 (32.7)	59 (35.3)	0.545 ^c
3 ^b	109 (17.6)	46 (10.2)	63 (37.7)	< 0.001^c
Glucose (mg/dl) ^a	87 (63-121)	85 (63-118)	91 (63-121)	< 0.001^c
Hba1C (%) ^a	5.2 (4.0-6.3)	5.2 (4.0-6.3)	5.4 (4.3-6.3)	< 0.001^c
Creatinine (mg/dl) ^a	0.46 (0.27-1.10)	0.46 (0.28-1.10)	0.46 (0.27-1.02)	0.474 ^c
Albumin (g/L) ^a	35.0 (23.0-44.0)	35.0 (23.0-44.0)	35.0 (30.0-43.0)	0.805 ^c
Hemoglobin (mg/dl) ^a	11.80 (8.90-14.50)	11.75 (8.90-14.50)	11.90 (9.20-13.70)	0.539 ^c

^a median (minimum-maximum), ^b n (%), ^c Mann-Whitney U test, ^d chi-square test, MNT: Medical nutrition therapy, BMI: Body mass index, OGTT: Oral glucose tolerance test, LDL: Low-density lipoprotein, HDL: High-density lipoprotein, *p*-values in bold are significant values.

Table 2: Comparison of the lipid levels in patients receiving insulin therapy and those who can be managed with MNT.

Parameters	All patients (n=220)	MNT group (n =162)	Insulin group (n=58)	<i>p</i>	<i>d /r</i>
TG (mg/dl) ^a	226.90 ± 100.77	218.90 ± 96.93	249.27 ± 108.57	0.049^c	0.295
LDL cholesterol (mg/dl) ^a	134.03 ± 40.54	135.61 ± 41.36	129.62 ± 38.16	0.335 ^c	0.150
Total cholesterol (mg/dl) ^a	240.78 ± 50.66	242.80 ± 52.39	235.13 ± 45.44	0.324 ^c	0.156
HDL cholesterol (mg/dl) ^a	65.18 ± 15.24	66.14 ± 16.37	62.50 ± 11.20	0.064 ^c	0.260
TG/ HDL cholesterol ^b	3.21 (0.91-12.50)	3.08 (0.91-10.61)	3.80 (1.64-12.50)	0.047^d	0.133

^a mean ± standard deviation, ^b median (minimum-maximum), ^c Student t-test, ^d Mann Whitney U test, MNT: Medical nutrition therapy, TG: Triglyceride, LDL: Low-density lipoprotein, HDL: High-density lipoprotein, *p*-values in bold are significant values,

Table 3: Comparison of the type of antenatal insulin therapy in reference to OGTT-75 results.

OGTT-75, Glucose levels ^a	Basal-only (n=61)	Bolus -only (n=58)	Basal + bolus insulin (n=48)	<i>p</i>	<i>f</i>
0-h glucose (mg/dl) ^a	101 (84-121)	92.5 (74-121)	99.5 (80-123)	< 0.001^b	0.468
1-h glucose (mg/dl) ^a	194 (120-253)	195.5 (152-277)	195.5 (134-273)	0.287 ^b	0.123
2-h glucose (mg/dl) ^a	149.5 (70-231)	174 (98-242)	165 (115-275)	< 0.001^b	0.345

^a median (minimum-maximum), ^b ANOVA, OGTT: oral glucose tolerance test, *p*-values in bold are significant values

Table 4: ROC analysis to evaluate OGTT, HbA1C, and Triglyceride results in reference to the need for antenatal insulin therapy.

Parameters	AUC	<i>p</i>	95% confidence interval	
			Lower	Upper
OGTT-75				
0-h glucose (mg/dl)	0.625	0.006	0.533	0.717
2-h glucose (mg/dl)	0.716	<0.001	0.641	0.790
HbA1c (%)	0.622	0.007	0.537	0.706
Triglycerides (mg/dl)	0.593	0.040	0.505	0.681

OGTT: Oral glucose tolerance test, AUC: Area Under the Curve, *p*-values in bold are significant values

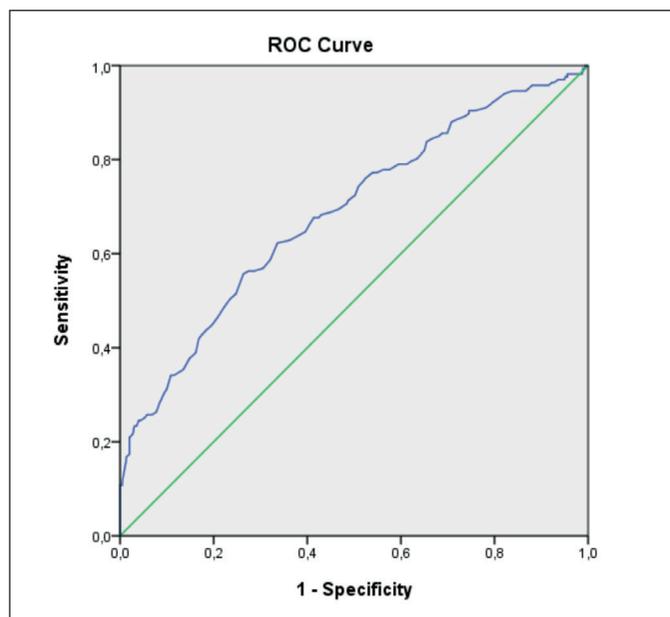


Figure 1: ROC exhibiting 2-h OGTT-75 plasma glucose for prediction of insulin requirement (AUC 0.716, arrow shows cut off of > 151.5 mg/dL, corresponding to a sensitivity of 68.4% and specificity of 60.0%).

60.0% specificity ($p < 0.001$). Its positive predictive value was 38.9%, whereas its negative predictive value was 83.9% ($p < 0.001$; Figure 1). The OGTT-75 0-h glucose values that can predict basal AIT were identified to be > 95.0 mg/dL, with 72.0% sensitivity and 69.0% specificity ($p < 0.001$; Figure 2). Its positive predictive value was 33.7%, whereas its negative predictive value was 91.8% ($p < 0.001$). Of all patients who were evaluated for dietary adherence ($n = 239$), the dietary adherence in patients receiving insulin therapy ($n = 63$) was found to be poor in 20.6% ($n = 13$), average in 55.6% ($n = 35$), and good in 23.8% ($n = 15$) good, whereas the dietary adherence in patients followed up with MNT ($n = 176$) was found to be poor in 2.3% ($n = 4$), average in 47.2% ($n = 83$), and good in 50.5% ($n = 89$) ($p < 0.001$, $p < 0.001$, $p = 0.253$, respectively).

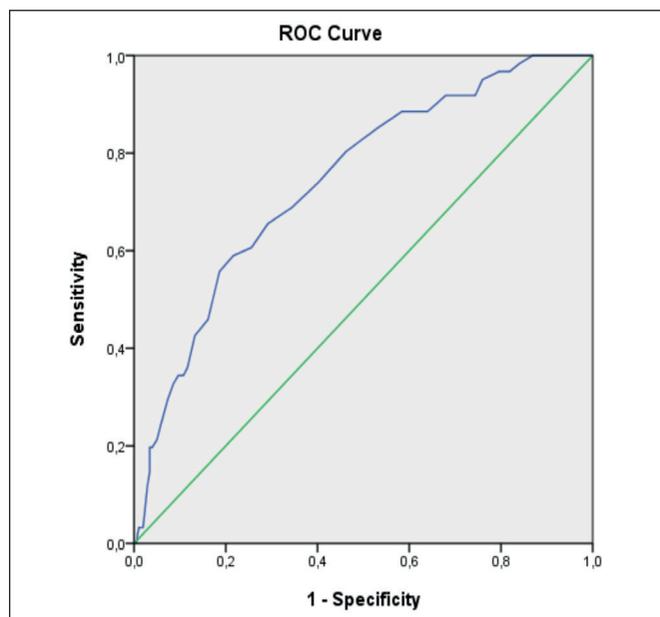


Figure 2: ROC exhibiting 0-h OGTT-75 plasma glucose for prediction of basal insulin requirement (AUC 0.754, arrow shows cut off of > 95.0 mg/dL, corresponding to sensitivity of 72.0% and specificity of 69.0%).

DISCUSSION

Most of the patients with GDM attain the desired level of blood glucose with only MNT, but 15-30% need antenatal insulin therapy (9,14,15). The rate of patients needing antenatal insulin therapy was higher in several studies (10,16). In our study, the rate of patients who needed antenatal insulin therapy was 27.0%, similar to the literature. Additionally, maternal age was higher in patients who needed insulin. The relationship between maternal age and insulin use is yet to be clarified in the literature, and the results are contradictory to each other (17-19). Our analysis found that obese and morbidly obese patients had a higher maternal age than the standard weight and overweight patients. This result suggests that advanced maternal age is related to insulin use because of the weight gain accompanying increasing

maternal age. In our study, more than half of the patients fell under the obesity range, and the obesity rate was much higher in patients using insulin. However, the rate of overweight patients was significantly higher in the MNT group, whereas the rate of obese and morbidly obese patients was significantly higher in the insulin group. In many studies, patients with insulin needs were found to have higher BMIs and demonstrated a higher rate of obesity and morbid obesity (10,18,20). Due to the retrospective design of our study, we do not have information about BMI at the onset of pregnancy. Therefore, we suggest that comprehensive examination of and counselling for overweight and obese women would positively reduce the need for insulin in planned pregnancies.

Our study showed that 0-h and 2-h glucose values measured in OGTT-75 were significantly higher in the group that needed antenatal insulin. The rate of patients with only one value elevated in the MNT group was significantly higher, whereas the rate of patients with all three values elevated was significantly higher in the group that needed antenatal insulin. Additionally, fasting plasma glucose and HbA1C values measured in the group that needed antenatal insulin were also significantly higher. Our results support other studies in the literature (9,10,15,17,21). It has been shown that the amount of abnormal glucose values in the OGTT is associated with an increased risk of fetal and maternal complications and that good glucose control reduces this risk (22-24). Our study did not present any data on maternal and fetal outcomes in pregnancy. However, our analyses for OGTT and HbA1C are consistent with the literature and believe that it will be useful in predicting patients who might need antenatal insulin.

The meta-analysis results show that TGs are significantly higher in women with GDM compared with other pregnant women (25). It has also been reported that women with GDM have higher total cholesterol, TG, LDL-cholesterol, and lower HDL-cholesterol (26). Our study presented that the TG level and the TG/HDL ratio were significantly higher in the group of patients who needed insulin therapy than in those patients who followed up with MNT. To the best of our knowledge, this is the first study that evaluates the relation by comparing patients who need antenatal insulin and those who do not.

The second significant result of our study was the relationship between the type of insulin therapy and OGTT, which is also reported for the first time in the literature. We found that patients who needed basal insulin had a different character than other insulin therapy groups and had higher 0-h

glucose values and lower 2-h glucose values. In other words, we thought that it would be helpful to evaluate the OGTT results separately in patients who need basal insulin. This result also confirms that an elevated level of 0-h glucose in OGTT is associated with the deterioration of the basal insulin secretion capacity (27). Therefore, we studied insulin use in two separate categories when evaluating the ROC analysis: general insulin use and basal insulin use. As a result of our ROC analysis, we found the area under the curve to be the highest for the 2-h glucose value for the whole group of patients using insulin. Additionally, we found that a 2-h glucose level over 151.5 mg/dL is the most specific and predictive value for insulin use. When we evaluated the ROC analysis for basal insulin need, we revealed that 0-h glucose above 95.0 mg/dl is the most specific and predictive value for basal insulin use. The low positive predictive value between insulin therapy and the variables is the relatively low need for insulin therapy during pregnancy. Therefore, our negative predictive value is high since the patients followed up with MNT are in the majority.

In many studies, a history of gestational diabetes was associated with the need for antenatal insulin therapy (9,28). We excluded this group of patients in our study because this group did not have data on the chronicity of diabetes diagnosed during their previous pregnancy, and it is possible to overlook the diagnosis of PGDM in such patients.

The main limitations of our study include its retrospective design and the investigation where only the data of pregnant women admitted to the university hospital were studied. In addition, single-centered design of the study makes it difficult to generalize the study results. Multicenter studies with large samples should support the results. Other limitations were the lack of data concerning the family history, the outcome of the pregnancy and the fetal-maternal complications of the patients.

In conclusion, this is the first study investigating the relationship between lipid levels and insulin use and the relation between the type of insulin therapy and OGTT-75 results in patients with GDM. In addition, the number of patients included to the study was also higher than that of similar studies. The data of our study will help predict individuals at risk of insulin therapy in the population of GDM patients. The need for insulin therapy in GDM patients is associated with a poor metabolic profile. Identifying individuals at risk and providing counselling on this issue can help regulate blood glucose. The detection of risky individuals will help identify patients who should not be overlooked during follow-up.

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None

Author Contributions

Idea/Concept: **Muhammet Cuneyt Bilginer**, Design: **Muhammet Cuneyt Bilginer, Damla Tufekci, Yasemin Emur Gunay**, Control/Supervision: **Mustafa Kocak, Irfan Nuhoglu, Hulya Coskun, Ozge Ucuncu**, Data Collection and/or Processing: **Muhammet Cuneyt Bilginer, Damla Tufekci, Yasemin Emur Gunay**, Analysis and/or Interpretation: **Muhammet Cuneyt Bilginer**, Literature Review: **Muhammet Cuneyt Bilginer**, Writing: **Muhammet Cuneyt Bilginer**, Critical Review: **Muhammet Cuneyt Bilginer**, References and Fundings: **Muhammet Cuneyt Bilginer**, Materials: **Muhammet Cuneyt Bilginer, Damla Tufekci, Yasemin Emur Gunay, Mustafa Kocak, Irfan Nuhoglu, Hulya Coşkun, Ozge Ucuncu**.

Conflict of Interest

No conflicts of interest between the authors and/or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Financial Disclosure

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Ethical Approval

This study has been approved by The Clinical Researches Ethical Committee of Karadeniz Technical University (Number 2021/248). The declaration of Helsinki was followed in this study design and report.

Peer-Review Process

Extremely peer reviewed and accepted.

REFERENCES

- Guariguata L, Linnenkamp U, Beagley J, Whiting DR, Cho NH. Global estimates of the prevalence of hyperglycaemia in pregnancy. *Diabetes Res Clin Pract.* 2014;103(2):176-185.
- ACOG Practice Bulletin No. 190: Gestational Diabetes Mellitus. *Obstet Gynecol.* 2018;131(2):e49-e64.
- ACOG Practice Bulletin No. 201: Pregestational Diabetes Mellitus. *Obstet Gynecol.* 2018;132:e228-e248.
- American Diabetes Association. 14. Management of Diabetes in Pregnancy: Standards of Medical Care in Diabetes-2021. *Diabetes Care.* 2021;44(Suppl 1):S200-S210.
- The Society of Endocrinology and Metabolism of Turkey. Clinical Practice Guideline for Diagnosis, Treatment and Follow-up of Diabetes Mellitus and Its Complications - 2019. 178-183(12th Edition)
- Harrison RK, Cruz M, Wong A, Davitt C, Palatnik A. The timing of initiation of pharmacotherapy for women with gestational diabetes mellitus. *BMC Pregnancy Childbirth.* 2020;20(1):773.
- Asiedu-Danso M, Kretchy IA, Sekyi JK, Koduah A. Adherence to antidiabetic medications among women with gestational diabetes. *J Diabetes Res.* 2021;2021:9941538.
- Sarbacker GB, Urteaga EM. Adherence to insulin therapy. *Diabetes Spectr.* 2016;29(3):166-170.
- Benhalima K, Robyns K, Van Crombrugge P, Deprez N, Seynhave B, Devlieger R, Verhaeghe J, Mathieu C, Nobels F. Differences in pregnancy outcomes and characteristics between insulin- and diet-treated women with gestational diabetes. *BMC Pregnancy Childbirth.* 2015;15:271.
- Bakiner O, Bozkirli E, Ozsahin K, Sariturk C, Ertorer E. Risk factors that can predict antenatal insulin need in gestational diabetes. *J Clin Med Res.* 2013;5:381-388.
- Cheng YW, Chung JH, Kurbisch-Block I, Inturrisi M, Shafer S, Caughey AB. Gestational weight gain and gestational diabetes mellitus: Perinatal outcomes. *Obstet Gynecol.* 2008;112(5):1015-1022.
- World Health Organization. WHO fact sheet on overweight and obesity. Updated October 2017. (Accessed December 8, 2017, at <http://www.who.int/mediacentre/factsheets/fs311/en/>)
- Cohen J. Statistical power analysis for the behavioral sciences, 2th Edition, New York, Routledge, 1998.
- Society of Maternal-Fetal Medicine (SMFM) Publications Committee. Electronic address: pubs@smfm.org. SMFM Statement: Pharmacological treatment of gestational diabetes. *Am J Obstet Gynecol.* 2018;218(5):B2-B4.
- Mitra S, Nayak PK, Sahoo J, Mathew A, Padma A, Kamalanathan S, Agrawal S. Predictors for antenatal insulin requirements in gestational diabetes. *Gynecol Endocrinol.* 2014;30:565-568.
- Juutinen J, Hartikainen AL, Bloigu R, Tapanainen JS. A retrospective study on 435 women with gestational diabetes: Fasting plasma glucose is not sensitive enough for screening but predicts a need for insulin treatment. *Diabetes Care.* 2000;23:1858-1859.
- Zhang Y, Shao J, Li F, Xu X. Factors in gestational diabetes mellitus predicting the needs for insulin therapy. *Int J Endocrinol.* 2016;2016:4858976.
- Eleftheriades M, Chatzakis C, Papachatzopoulou E, Papadopoulos V, Lambrinouadaki I, Dinas K, Chrousos G, Sotiiriadis A. Prediction of insulin treatment in women with gestational diabetes mellitus. *Nutr Diabetes.* 2021;11(1):30.
- Yanagisawa K, Muraoka M, Takagi K, Ichimura Y, Kambara M, Sato A, Sakura H, Uchigata Y. Assessment of predictors of insulin therapy in patients with gestational diabetes diagnosed according to the IADPSG criteria. *Diabetol Int.* 2016;7(4):440-446.

20. Weschenfelder F, Lohse K, Lehmann T, Schleußner E, Groten T. Predictors of treatment requirements in women with gestational diabetes: A retrospective analysis. *J Clin Med*. 2021;10(19):4421.
21. Tang L, Xu S, Li P, Li L. Predictors of insulin treatment during pregnancy and abnormal postpartum glucose metabolism in patients with gestational diabetes mellitus. *Diabetes Metab Syndr Obes*. 2019;12:2655-2665.
22. Gruendhammer M, Brezinka C, Lechleitner M. The number of abnormal plasma glucose values in the oral glucose tolerance test and the fetomaternal outcome of pregnancy. *Eur J Obstet Gynecol Reprod Biol*. 2003;108(2):131-136.
23. Crowther CA, Hiller JE, Moss JR, McPhee AJ, Jeffries WS, Robinson JS. Effect of treatment of gestational diabetes mellitus on pregnancy outcomes. *N Engl J Med*. 2005;352:2477-2486.
24. Hartling L, Dryden DM, Guthrie A, Muise M, Vandermeer B, Donovan L. Benefits and harms of treating gestational diabetes mellitus: A systematic review and meta-analysis for the U.S. Preventive Services Task Force and the National Institutes of Health Office of Medical Applications of Research. *Ann Intern Med*. 2013;159(2):123-129.
25. Ryckman KK, Spracklen CN, Smith CJ, Robinson JG, Saftlas AF. Maternal lipid levels during pregnancy and gestational diabetes: A systematic review and meta-analysis. *BJOG*. 2015;122(5):643-651.
26. Hu J, Gillies CL, Lin S, Stewart ZA, Melford SE, Abrams KR, Baker PN, Khunti K, Tan BK. Association of maternal lipid profile and gestational diabetes mellitus: A systematic review and meta-analysis of 292 studies and 97,880 women. *E Clinical Medicine*. 2021;34:100830.
27. Di Cianni G, Seghieri G, Lencioni C, Cuccuru I, Anichini R, De Bellis A, Ghio A, Tesi F, Volpe L, Del Prato S. Normal glucose tolerance and gestational diabetes mellitus: What is in between? *Diabetes Care*. 2007;30(7):1783-1788.
28. Wong VW, Jalaludin B. Gestational diabetes mellitus: Who requires insulin therapy? *Aust NZ J Obstet Gynaecol*. 2011;51:432-436.