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COMPARISON OF THE ORAL GLUCOSE TOLERANCE TEST AND HOMA-IR IN SCREENING FOR GESTATIONAL DIABETES MELLITUS IN PREGNANT WOMEN

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ABSTRACT

Aim: The Oral Glucose Tolerance Test (OGTT) is used for the screening of Gestational Diabetes Mellitus (GDM) and is a difficult test for some patients to tolerate. Insulin resistance (IR) can also be checked in pregnant women by using the fasting glucose and fasting insulin values. In this study, we aimed to compare the effectiveness of OGTT and HOMA-IR for GDM screening in pregnant women.

Methods: This cross-sectional study was carried out on all pregnant women who underwent GDM screening at the Adana City Training and Research Hospital between April 1 and June 30, 2021. Sociodemographic data were recorded and anthropometric and blood pressure measurements were made. In addition to OGTT with 75g glucose, the HOMA-IR results were also recorded. The cut-off value for IR was 2.4.

Results: The mean age of the 107 participants was 29.2±5.7 years. According to the OGTT, 32 (29.9%) had GDM, and according to the HOMA-IR 27 (25.2%) had IR. Among the 32 women diagnosed with GDM according to the OGTT, 17 (53.1%) had no insulin resistance (HOMA-IR<2.39), while 15(46.9%) had insulin resistance (HOMA-IR>2.40), (p=0.002).In women with and without GDM, there was no significant difference in pre-pregnancy weight and BMI, and current weight and BMI. However, pre-pregnancy weight and BMI, and current weight and BMI were found to be significantly higher in pregnant women with IR compared to those without IR.

Conclusions: Detection of IR with HOMA-IR in pregnant women can be helpful in revealing additional findings when used together with OGTT and may be useful in patients who do not want or cannot tolerate the OGTT.

Keywords: Gestational diabetes, Glucose intolerance, Oral Glucose Tolerance Test, Insulin resistance

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INTRODUCTION

Gestational Diabetes Mellitus (GDM) is defined as carbohydrate intolerance that is detected for the first time during pregnancy or that begins during pregnancy [1]. The prevalence of GDM varies between 2 and 38% worldwide, in direct proportion to the prevalence of Type 2 DM, and has been reported to be approximately 6% in the United States [2- 4]. In our country, it is seen that the prevalence of GDM is between 2.6% and 27.9% according to studies conducted in different regions [5]. In the long term, GDM increases the risk of developing type 2 DM, metabolic syndrome, and cardiovascular disease in the mother [6]. The risk of developing Type 2 DM is approximately 10 times higher in women who were diagnosed with GDM during pregnancy compared to women who were not [7]. In babies born as a result of pregnancy of mothers diagnosed with GDM, the risks of developing childhood obesity and Type 2 DM in the long term are increased compared to other babies [8, 9].

Today, the Oral Glucose Tolerance Test (OGTT) is used as a screening test for the diagnosis of GDM, either by administering 50 g of glucose and repeating with 100 g of glucose if the result is positive, or by administering 75 g of oral glucose at once. Before each glucose load, blood is taken for fasting blood glucose, and then the blood glucose values are measured at the 1st and 2nd hours [10]. Since the OGTT is a long and gradual test, patients may experience difficulties in adapting. Some patients report nausea-vomiting and headache complaints during the OGTT [11]. It is known that insulin resistance (IR) caused by diabetogenic hormones secreted from the placenta during pregnancy plays a role in the pathophysiology of GDM [12]. The Hyperinsulinemic Euglycemic Clamp Technique is accepted as the gold standard method to measure IR, but it is not widely used because it is difficult to apply [13]. Cohen et al. compared the Hyperinsulinemic Euglycemic Clamp Technique with the Homeostatic Model Assessment for Insulin Resistance (HOMA-IR) method in a study they conducted on obese pregnant women with normal glucose tolerance in the 2nd and 3rd trimesters, and they found that the use of HOMA-IR was suitable in both trimesters [14].

HOMA-IR is calculated by the equation [(Fasting insulin (μU/ml) X Fasting glucose (mg/dL) / 405]. The result is directly proportional to IR, and the higher the result, the higher the IR [15, 16]. HOMA-IR values above 2.38 are accepted by the International Diabetes Federation (IDF) as increased insulin resistance for Metabolic Syndrome [17]. Insulin resistance (IR) (HOMA-IR>2.4) can give results parallel to OGTT and its use can be helpful in revealing additional findings when used together with OGTT and it may be beneficial especially in patients who do not want or cannot tolerate OGTT. In this study, we aimed to compare the effectiveness of OGTT and HOMA-IR in pregnant women.

METHODS

The population of this descriptive cross-sectional study consists of all the women with 24-

28 weeks of pregnancy who underwent GDM screening in our Obstetrics and Gynecology outpatient clinics between 01.04.2021 and 30.06.2021. The study was conducted with 107 pregnant women who agreed to participate and signed the voluntary consent form. The study was approved by the Ethics Committee with decision number 1335at the meeting numbered 77 on 24.03.2021, and the study complies with the Declaration of Helsinki Principles.

Sociodemographic data, and the anthropometric and blood pressure measurements of the participants were recorded. The Oral Glucose Tolerance Test (OGTT) is used routinely to determine insulin resistance in pregnant women. The patient is asked to drink a glucose drink and the blood glucose level is measured before and at intervals after the sugary drink is ingested. In addition to the routine OGTT, we calculated IR by using the HOMA-IR formula with fasting glucose and insulin values. The cut-off value for the presence of IR was determined as 2.4 [17].

Statistical Analysis

Data was analyzed by usingIBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp.Descriptive statistical methods (mean, standard deviation, median, frequency, ratio, minimum, maximum) were used for evaluating data. In addition, the Kolmogrov Smirnov test was used to evaluate the normality of the distribution.After the descriptive data were presented, the Chi-square test was used to compare nominal data. We used the independent *t-test* when the samples satisfied the conditions of normality and equal variance. In cases in which the probability distribution could not be defined, we used the Mann-Whitney U test to compare two groups of continuous variables. Spearman's Correlation analysis was used to investigate the connection between numerical and ordinal data or both of which are ordinal. A p value of <0.05 was considered significant.

RESULTS

The mean age of the 107 pregnant women who participated in the study was 29.27±5.76 years (the youngest was 18, the oldest 43 years). Among the participants, 47 (43.9%) had low education, 30 (28%) had secondary education, and 30 (28%) had high education level. Of the pregnant women, 81 (75.7%) were not working, 24 (22.4%) had low income, 42 (39.3%) had medium income, and 41 (38.3%) had high income levels. Of the participants, 86 (80.4%) had nuclear families and 21 (19.6%) had extended families. The mean height of the participants was 161.9±6.8 cm. The mean pre-pregnancy and current body weights of the participants were 69.3±14.1 kg and 77.7±13.8 kg, respectively. Mean blood glucose values measured at fasting, and the 1st hour and 2nd hour in the 75 g OGTT were 84.8±11.2 mg/dL, 142.5±38.1 mg/dL, and 113.8±35 mg/dL, respectively. According to the 75 g OGTT administered to the participants, GDM was detected in 32 women (29.9%). The mean fasting insulin level of the participants was 10.0±7.4 µU/ml. The mean HOMA-IR value, which was calculated using the fasting glucose and insulin

results was 2.1±1.8. According to the HOMA-IR calculation, there were 27 (25.2%) individuals with IR when the cut-off value was taken as 2.4. The number and rates of IR (according to HOMA-IR) in participants with GDM (according to OGTT) are given in Table1. The number and rates of GDM (according to OGTT) in participants with IR (according to HOMA-IR) are given in Table2.

Table1. The number and rates of IR (according to HOMA-IR) in participants with GDM (according to OGTT).

n=107	IR (n=27), (n, %)	No IR (n= 80), (n, %)	X^{2*}	p
GDM (n=32)	15 (46.9)	17 (53.1)	9.756	**0.002**
No GDM (n=75)	12 (16.0)	63 (84.0)		

Chi-Square test is used.* ***GDM:* *Gestational Diabetes Mellitus,* ***HOMA-IR:*** *Homeostatic Model Assessment for Insulin Resistance.*

Table2. The number and rates of GDM (according to OGTT) in participants with IR (according to HOMA-IR)

n=107	GDM present (n=32) (n, %)	GDM absent (n=75) (n, %)	X^{2*}	p-value
IR(n=27)	15 (55.6)	12 (44.4)	11.333	**0.001**
No IR (n= 80)	17 (21.2)	63 (78.8)		

The Chi-Square test is used.* ***GDM:* *Gestational Diabetes Mellitus,* ***HOMA-IR****: Homeostatic Model Assessment for Insulin Resistance.*

Mean and standard deviation of laboratory values for GDM and IR was given in Table3.

Comparison of the average of the ranks for laboratory values within GDM and IR groups were given in Table4.

Table3. Mean and standard deviation of laboratory values for GDM and IR.

	GDM (n=32) Mean±SD	IR (n=27) Mean±SD
Fasting blood glucose (mg/dL)	96±12.7	91.6±13.2
1st hour blood glucose (mg/dL)	**183.2±29.9**	**163.0±39.0**
2nd hour blood glucose (mg/dL)	143.6±43.8	129.1±39.9
Fasting insulin level (µU/ml)	**13.6±11.2**	**18.2±10.5**
HOMA-IR	**3.2±2.8**	**4.1±2.7**

GDM: *Gestational Diabetes Mellitus,* ***IR:*** *Insulin resistance.* ***HOMA-IR****: Homeostatic Model Assessment for Insulin Resistance.****SD:*** *Standard deviation.*

Table4. Comparison of the average of the ranks for laboratory values within GDM and IR groups.

	GDM (n=32) Mean Rank	IR (n=27) Mean Rank	Z*	p
Fasting blood glucose (mg/dL)	32.3	27,2	-1.135	0.256
1st hour blood glucose (mg/dL)	**34.7**	**24.3**	**-2.330**	**0.020**
2nd hour blood glucose (mg/dL)	33.1	26.3	-1.514	0.130
Fasting insulin level (µU/ml)	**23.6**	**37.5**	**-3.112**	**0.002**
HOMA-IR	**24.1**	**36.9**	**-2.869**	**0.004**

The Mann-Whitney U test is used.* ***GDM:* *Gestational Diabetes Mellitus,* ***IR:*** *Insulin resistance.* ***HOMA-IR****: Homeostatic Model Assessment for Insulin Resistance.*

The comparison of anthropometric measurements and blood pressure values according to the presence of GDM in the participants is given in Table5.

Table5. Comparison of anthropometric measurements and blood pressure values according to the presence of GDM.

n=107	No GDM (n=75) Mean±SD	GDM (n=32) Mean±SD	t*	p
Pre-pregnancy weight (kg)	68.6±13.8	70.9±14.8	-0.773	0.441
Pre-pregnancy BMI (kg/m²)	26.0±5.3	27.4±5.2	-1.246	0.216
Current weight (kg)	76.7±13.4	79.8±14.8	-1.044	0.299
Current BMI (kg/m²)	29.1±5.0	30.9±5.2	-1.653	0.101
Height (cm)	162.4±6.5	160.6±7.4	1.236	0.219
Weight change during pregnancy (kg)	8.1±4.5	8.8±5.7	-0.714	0.477
Systolic blood pressure (mmHg)	**116.9±13.0**	**124.2±13.2**	**-2.638**	**0.010**
Diastolic blood pressure (mmHg)	70.1±8.4	73.4±11.4	-1.651	0.102

The Independent samples t test is used.**BMI:*** *Body Mass Index,* ***GDM:*** *Gestational Diabetes Mellitus,* ***SD:*** *Standard deviation.*

Mean and standard deviation of anthropometric measurements for No IR and IR groups was given in Table6. Comparison of the average of the ranks for anthropometric measurements within No IR and IR groups were given in Table7.

Table6. Mean and standard deviation of anthropometric measurements for no IR and IR groups.

n=107	No IR (n=80) Mean±SD	IR (n=27) Mean±SD
Pre-pregnancy weight (kg)	**67.31±14.56**	**75.37±11.02**
Pre-pregnancy BMI (kg/m²)	**25.47±5.15**	**29.53±4.69**
Current weight (kg)	**75.76±13.85**	**83.44±12.49**
Current BMI (kg/m²)	**28.67±4.78**	**32.71±5.16**
Height (cm)	162.55±7.01	160.00±6.08
Weight change during pregnancy (kg)	8.45±4.63	8.07±5.72
Systolic blood pressure (mmHg)	**117.30±13.45**	**124.59±12.1**
Diastolic blood pressure (mmHg)	70.39±9.33	73.37±9.7

BMI: *Body Mass Index,* ***IR:*** *Insulin resistance,* ***SD:*** *Standard deviation.*

Table7. Comparison the average of the ranks for anthropometric measurements within no IR and IR groups.

n=107	No IR (n=80) Mean Rank	IR (n=27) Mean Rank	Z*	p
Pre-pregnancy weight (kg)	**48.4**	**70.5**	**-3.209**	**0.001**
Pre-pregnancy BMI (kg/m²)	**47.5**	**73.2**	**-3.730**	**0.000**
Current weight (kg)	**49.0**	**68.6**	**-2.846**	**0.004**
Current BMI (kg/m²)	**47.9**	**71.8**	**-3.454**	**0.001**
Height (cm)	54.8	51.4	-1.749	0.080
Weight change during pregnancy (kg)	57.0	44.9	-0.504	0.614
Systolic blood pressure (mmHg)	**49.7**	**66.6**	**-2.467**	**0.014**
Diastolic blood pressure (mmHg)	52.4	58.5	-0.884	0.377

** The Mann-Whitney U test is used.* ***BMI:*** *Body Mass Index,* ***IR:*** *Insulin resistance.*

Correlation of the presence of GDM and IR with laboratory values, anthropometric measurements, and blood pressure values is given in Table8.

Table8. Correlation of the presence of GDM and IR with laboratory values, anthropometric measurements, and blood pressure values.

n=107		GDM presence	IR presence
Fasting blood glucose(mg/dL)	r_s	**0.577****	**0.345****
	p	<0.001	<0.001
1st hour blood glucose(mg/dL)	r_s	**0.685****	**0.287****
	p	<0.001	0.003
2nd hour blood glucose(mg/dL)	r_s	**0.546****	**0.277****
	p	<0.001	0.004
Fasting insulin level (µU/ml)	r_s	**0.277****	**0.719****
	p	0.004	<0.001
HOMA-IR	r_s	**0.396****	**0.752****
	p	<0.001	<0.001
Pre-pregnancy weight (kg)	r_s	0.056	**0.312****
	p	0.570	0.001
Pre-pregnancy BMI (kg/m²)	r_s	0.129	**0.362****
	p	0.187	<0.001
Current weight (kg)	r_s	0.087	**0.276****
	p	0.373	0.004
Current BMI (kg/m²)	r_s	0.170	**0.335****
	p	0.080	<0.001
Weight change during pregnancy (kg)	r_s	0.042	-0.049
	p	0.669	0.617
Height (cm)	r_s	-0.110	-0.170
	p	0.260	0.080
Systolic blood pressure (mmHg)	r_s	**0.282****	**0.240***
	p	0.003	0.013
Diastolic blood pressure (mmHg)	r_s	0.148	0.086
	p	0.129	0.379

r_s: Spearman's Correlation Coefficient, ***GDM:*** *Gestational Diabetes Mellitus,* ***IR:*** *insulin resistance,* ***HOMA-IR:*** *Homeostatic Model Assessment For Insulin Resistance.* ***BMI:*** *Body Mass Index, *Correlation is significant at the 0.05 level (2-tailed), **Correlation is significant at the 0.01 level (2-tailed).*

DISCUSSION

Timely diagnosis of GDM, which develops with glucose intolerance that occurs with increased IR during pregnancy, is very important for the protection of the health of the mother and baby. In a study by Trujillo et al. in which they screened 4926 pregnant women with 75 g OGTT in Brazil, the number of people with GDM was found to be 883 (18.0%) [18].In a study by Tai et al. in Taiwan between 2013 and 2018 on 512 pregnant patients using 75 g OGTT, they found GDM in 75 (14.6%) individuals [19]. A study conducted by İsmail et al. on 279 pregnant patients in Malaysia between 2010 and 2011found GDM in 63 patients (22.5%) with 75 g OGTT. By using a HOMA-IR cutoff value of 2.92 for these 63 patients, 40 (63.4%) patients were found to have IR [20]. In a study conducted by Özçimen et al. in Konya with 100 g OGTT on 253 pregnant women, HOMA-IR values were found to be higher in women with GDM. The cut-off value for IR with HOMA-IR was >2.38. Accordingly, IR was not found in only two of the patients with GDM, and IR (>2.38) was found in the remaining 18 pregnant women [21]. In a study by Alptekin et al. in which they screened 227 pregnant patients with 100-g OGTT, the cutoff value for HOMA-IR was 2.08, and according to this cut-off value61.4% of those without GDM had no IR, while 90% of those with GDM had IR [22]. A study by Derin et al. on 41 healthy pregnant women and 34 pregnant women with GDM found IR in 22 (64.7%) of GDM patients [23]. The rate of GDM (29.9%) in our study was found to be slightly higher than the existing literature data while the IR rate (46.9%) in patients with GDM was slightly lower than the literature data.

A study by Alanbay et al. on 79 pregnant women with 50 g OGTT found fasting glucose and HOMA-IR values to be significantly higher in the group with GDM. No significant difference was reported in terms of pre-pregnancy BMI, current BMI, and weight gain during pregnancy, and fasting insulin values between those who were diagnosed with GDM and those who were not [24]. In a study conducted by Tai et al. with 75 g OGTT on 512 pregnant patients in Taiwan, the fasting glucose, 1st hour blood glucose and 2nd hour blood glucose values, and the prenatal weight and prenatal BMI were found to be significantly higher in patients with GDM compared to those without GDM [19]. A study conducted by İsmail et al. on 279 pregnant patients found that the fasting insulin, fasting glucose, and 2nd hour glucose levels, and the HOMA-IR values and current weight were significantly higher in those diagnosed with GDM with the75 g OGTT [20]. A study conducted by Wei et al. in China with 75 g OGTT on 336 pregnant patients found the HOMA-IR values, mean systolic-diastolic blood pressure, and pre-pregnancy BMI to be significantly higher in the group diagnosed with GDM [25]. Özçimen et al., administering the 100 g OGTT to 253 pregnant patients, found the cut-off value of HOMA-IR for the presence of IR to be 2.38. According to the results they obtained, the mean value of fasting insulin, fasting plasma glucose, 1st hour plasma glucose, and the current BMI were significantly higher in those with IR than in those without IR [21]. Similarly, we found that the fasting blood glucose, 1st hour blood glucose, 2nd hour blood glucose, fasting insulin, and HOMA-IR values were significantly higher in patients with GDM (according to the 75 g OGTT) and IR

(according to HOMA-IR) compared to those without GDM and without IR in our study. There was no significant difference between those with and without GDM in terms of the pre-pregnancy weight, pre-pregnancy BMI, current weight, and current BMI. The mean systolic blood pressure value in those with GDM was significantly higher than in those without GDM. On the other hand, the mean pre-pregnancy weight, pre-pregnancy BMI, current weight, current BMI, and mean systolic blood pressure values were found to be significantly higher in those with IR compared to those without IR according to the HOMA-IR result. GDM is a condition that poses significant risks for the pregnant woman and the baby, and timely diagnosis is very important.

According to the results obtained from our small and well-defined sample group, the detection of IR with HOMA-IR in pregnant women can be helpful in revealing additional findings when used together with OGTT, and may be useful in patients who do not want or cannot tolerate OGTT. Further studies with larger sample sizes are needed to confirm the findings of this preliminary study.

Conflicts of interest: The authors have nothing to disclose.

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