

## Effect of number of abnormal oral glucose tolerance test (OGTT) values on birthweight in women with gestational diabetes

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**Background & objectives:** To examine the effect of abnormal oral glucose loading (OGL) and number of abnormal oral glucose tolerance test (OGTT) values on foetal weight in Turkish pregnant women.

**Methods:** This retrospective study included 810 pregnant women between 24 and 28 wk of gestation who were screened for gestational diabetes mellitus (GDM). Women were grouped according to degree of glucose intolerance and compared for clinical, biochemical parameters. Women who delivered macrosomic infants were compared with those who delivered normal infants.

**Results:** GDM was detected in 70 (8.6%) women. Median age and infant birthweight of GDM cases were higher than the other groups. Infants of women with GDM weighted 200 g more than infants of non-GDM cases. No difference was found in terms of birthweight between diabetes cases with 2, 3 or 4 OGTT values abnormality.

**Interpretation & conclusions:** The number of abnormal OGTT values in GDM cases had no effect on foetal weight. Macrosomia was observed more in GDM cases than in non-GDM cases. Birthweight was significantly higher in women with GDM despite the therapy used for regulation of blood glucose. This may be related to ethnical, dietary, nutritional differences, and treatment compliance in our study population.

**Key words** Birthweight - gestational diabetes - glucose - macrosomia - oral glucose tolerance test

Gestational diabetes mellitus (GDM) is any degree of glucose intolerance with onset or first recognition during pregnancy<sup>1,2</sup>. It affects 1.2 to 14.3 per cent of the pregnant women population. Prevalence rates of GDM varies widely by ethnicity<sup>3-6</sup>. Asians have the highest reported prevalence rates of GDM<sup>6,7</sup>.

Macrosomia risk is increased in women with GDM<sup>8</sup>, and is associated with increased risk of maternal and neonatal complications during labour and/or perinatal period in addition to some long-term

complications<sup>9-11</sup>. Thus, it was advised by the American College of Obstetricians and Gynecologists (ACOG) and the American Diabetes Association (ADA) that all pregnant women should be screened for GDM<sup>12,13</sup>. Generally, the 50 g 1 h oral glucose loading test (OGL) is performed for screening which is followed by a 100 g 3 h oral glucose tolerance test (OGTT) for confirmation, if OGL is positive.

It has been shown before that the number of abnormal OGTT values in GDM was significantly

associated with increased birthweight<sup>14</sup>. If impact of ethnic factors is taken into consideration, whether having gestational diabetes or number of abnormal values are more important for development of macrosomia is not known. In this study the effect of number of abnormal OGTT values on foetal weight was examined in Turkish pregnant women.

### Material & Methods

This retrospective study was conducted in the Department of Obstetrics & Gynaecology, Fatih University, Faculty of Medicine, Ankara/Turkey, during January 2008 and December 2009. Power analysis was conducted for sample size calculation. Using an  $\alpha$  level of 0.05,  $\beta$  level of 0.20, a power of 80 per cent and effect size of 0.20, a sample size of 416 cases was needed for the study.

All consecutive pregnant women during study period screened for GDM and delivered at Fatih University were included. Approval for the study protocol was obtained from the Clinical Research Ethics Committee, Faculty of Medicine, Fatih University. All relevant data including demographic information, OGL and OGTT results were collected for further analysis. Age, gravida, parity, body mass index (BMI), obstetric history, family history for DM, gestational week of all women were obtained.

Screening test of GDM was performed in all pregnant women. Screening was performed between 24 and 28 wk of gestation using the 1 h 50 g OGL with a subsequent 3 h 100 g OGTT for confirmation if screened positive. The positive result was defined as plasma glucose of 130 mg/dl or greater. The glucose values obtained were analysed by the Carpenter and Coustan (C&C) criteria for the diagnosis of GDM and impaired glucose tolerance (IGT)<sup>15-17</sup>.

An abnormal 3 h OGTT is defined as two or more serum glucose values that meet or exceed the standards of C&C criteria (fasting >95, 1 h >180, 2 h >155 and 3 h >140 mg/dl). A fasting serum glucose >140 mg/dl was considered as diabetes and OGL was omitted. Serum glucose >200 mg/dl after OGL was also accepted as diabetes and 3 h OGTT was not performed. Treatment was based on diagnosis made on the C&C criteria. Serum glucose was determined from a peripheral venous sample by the hexokinase method (COBAS Integra 800, Roche, Germany).

Cases with GDM and impaired glucose tolerance (IGT) were seen by a dietician and received

dietary evaluation and diet therapy first to achieve normoglycaemia. Diet therapy was continued if fasting blood sugar (FBS) was <105 mg/dl, and 2 h post prandial <140 mg/dl, with home blood glucose monitoring continued once daily. In women with glucose values >200 mg/dl on initial OGTT, and those who showed FBS >105 and 2 h post prandial glucose >140 mg/dl for at least 2-3 values while on a dietary regimen, insulin therapy was commenced. All women were followed up to term and delivered in our hospital.

*Inclusion and exclusion criteria:* Pregnant women who screened for GDM and delivered at Fatih University hospital were included into the study. Those having systemic diseases, previous diabetes, smokers, having infectious disease during pregnancy, cases with polyhydramnios, foetal abnormality, multi-foetal pregnancies and delivery prior to 36 completed weeks of gestation were excluded from the study.

According to the OGTT results, women were grouped as normal, high OGL with normal OGTT (false positive OGL), IGT and GDM. These groups were compared with each other in terms of clinical, biochemical parameters, delivery route, birthweight and presence of macrosomia. Cases with GDM were compared with non-GDM women for the same parameters. GDM cases were further divided as women with 2, 3, or 4 abnormal value. These subgroups were also compared with each other.

Pregnant women with GDM were further classified according to their OGL results. Women with OGL >200 mg/dl and women with OGL <200 mg/dl were compared for infant birthweights. Another comparison was done between diabetic women who delivered macrosomic infant with those who did not. Women with GDM were grouped according to birthweight >4000 g or <4000 g. These two groups were compared for clinical, biochemical parameters and delivery route.

*Statistical analysis:* The statistical analyses were carried out using the SPSS 15.0 statistical software package (SPSS Inc., Chicago, IL, USA). Conformity of the measured values to normal distribution was examined graphically and using Shapiro-Wilks test<sup>18</sup>. In presenting descriptive statistics, numbers and percentages were used for categorical variables, and median (Interquartile range, IQR) values were used for the data. Mann Whitney test was used for comparison of two groups, Kruskal Wallis test and Bonferoni corrected Mann Whitney test were used in comparison of three or more groups. Categorical

variables were evaluated by Chi square test. Spearman correlation analysis and logistic regression were used for parameters that can effect birthweight.

### Results

A total of 810 pregnant women were included in the study. In 228 (28.1%) of them OGL value was over 130 mg/dl, so 100 g OGTT was done. GDM was detected in 70 (8.6%) cases. Forty six (5.7%) cases had IGT and 195 (24.1%) cases had normal OGTT result despite high OGL results. Median age of these women was 28 yr (IQR-7), birthweight 3300 g (300) , BMI 25.9 kg/m<sup>2</sup> (4.4), and OGL value 158 mg/dl (27). In women with GDM were considered, mean age was 30 yr (9), birthweight 3400 g (425), BMI 27 kg/m<sup>2</sup> (4.8), and OGL 165 mg/dl (41) (Table I).

Median age of GDM cases was significantly higher than the normal, false positive OGL and IGT groups ( $P<0.001$ ). Birthweight was significantly higher in GDM group ( $P=0.001$ ) compared to other groups. There were significant differences between the groups (normal, false positive OGL, IGT and GDM groups) in

terms of OGL and OGTT results ( $P<0.001$ ) (Tables I and II).

When GDM cases (n=70) were compared with the remaining 740 cases, age, birthweight, OGL and OGTT results were significantly higher in GDM than non-GDM group ( $P<0.001$ ). There was statistically significant difference between GDM and non-GDM cases in terms of macrosomia ( $P<0.001$ ) (Table II).

No difference was found in terms of birthweight between cases with 2, 3 or 4 values abnormality (Table III). Diabetes cases with OGL less than 200 mg/dl and over 200 mg/dl were also compared for birthweight and no difference was found (Table IV).

Another comparison was done between women with GDM according to birthweights as  $\geq 4000$  g or  $<4000$  g. Comparison of the groups for OGL and OGTT results revealed no difference between them (Table V).

Correlation analysis was done for parameters that can effect birthweight (Table VI). A positive correlation

**Table I.** Demographic and clinical data of women according to oral glucose loading (OGL) and oral glucose tolerance test (OGTT) results

	Normal (n=499)	FP-OGL (n=195)	IGT (n=46)	GDM (n=70)	P value
Age (yr)	27 (8)	29 (8)	29 (7)	30 (9)	<0.001*
Gravida (n)	2 (2)	2 (2)	2 (3)	2 (2)	0.007†
Parity (n)	1 (1)	1 (2)	1 (2)	1 (2)	0.077
BMI (kg/m <sup>2</sup> )	25.9 (4.4)	25.6 (4.1)	25.2 (3.9)	27.0 (4.8)	0.177
Birthweight (g)	3200 (400)	3200 (375)	3200 (650)	3400 (425)	0.001£
Gender (n, %)					
Female	266, 53.4	110, 56.3	29, 64.3	45, 64.3	0.232
Male	233, 46.6	85, 43.7	17, 35.7	25, 35.7	
Labour (n, %)					
Normal	218, 43.7	81, 41.7	24, 51.7	22, 31.4	0.131
C/S	281, 56.3	114, 58.3	22, 48.3	48, 68.6	
OGL (mg/dl)	109 (19)	144.5 (22)	159 (23)	165 (41)	<0.001¶
OGTT 0 h		81 (12)	87.5 (18)	95 (18)	<0.001Ψ
(mg/dl) 1 h		147 (25)	170 (49)	194 (33)	<0.001‡
2 h		126 (25)	143.5 (34)	171 (18)	<0.001‡
3 h		98 (33)	112 (42)	140 (51)	<0.001£

\*Normal versus FP-OGL and normal versus GDM; †normal versus FP-OGL; £GDM versus normal, FP-OGL and IGT; ¶statistically significant difference between all groups; ΨFP-OGL versus IGT and GDM; ‡all groups except normal [statistically difference between SDM, IGT and FP-OGL groups]

Values are given as median (Interquartile range, IQR)  
FP-OGL, false positive OGL

**Table II.** Demographic and clinical data of GDM and non GDM women

	GDM (-) (n=740)	GDM (+) (n=70)	P value
Age (yr)	28 (8)	30 (9)	<0.001
Gravida (n)	2 (2)	2 (2)	0.987
Parity (n)	1 (1)	1 (2)	0.413
BMI (kg/m <sup>2</sup> )	26.7 (4.4)	27.0 (4.8)	0.060
Birthweight (g)	3200 (400)	3400 (425)	0.001
Macrosomia (n, %)	20, 2.7	11, 15.7	<0.001
Gender (n, %)			
Female	405, 54.7	45, 64.3	0.124
Male	335, 45.3	25, 35.7	
Labor (n, %)			
Normal	323, 43.5	22, 31.4	0.048
C/S	417, 56.5	48, 68.6	
OGL (mg/dl)	117 (33)	165 (41)	<0.001
OGTT 0 h	82 (11)	95 (18)	<0.001
(mg/dl) 1 h	152 (32)	194 (33)	<0.001
2 h	130 (28)	171 (18)	<0.001
3 h	102 (37)	140 (51)	<0.001

Values are given as median (Interquartile range, IQR)

was found between birthweight versus OGL and BMI (Rho=0.101;  $P=0.025$ , Rho=0.159;  $P<0.001$ ). No correlation was found between 100 g OGTT values and birthweight.

Ten step constant logistic regression analysis was done to find relation of some parameters with presence of macrosomia. It revealed borderline significance between macrosomia and 2 h, 3 h OGTT values ( $P=0.047$ ;  $P=0.048$ ). There was no relation between other factors and the presence of macrosomia.

### Discussion

GDM occurs in 1.2 to 14.3 per cent of all pregnancies and is associated with increased risk of important maternal and perinatal complications<sup>1,2</sup> such as increased risk for cesarean delivery, labour abnormalities and birth injuries such as shoulder dystocia, bone fractures and nerve palsies as well as adverse neonatal outcomes<sup>8</sup>. The most common neonatal complication associated with GDM that is responsible for most of the maternal and perinatal complications is macrosomia.

Foetal overgrowth in women with GDM suggests that macrosomia is directly related to maternal blood

glucose levels which leads to foetal hyperinsulinaemia<sup>19</sup>. Although treatment of GDM reduces foetal macrosomia risk by more than 50 per cent and, conversely, not treating GDM has a two- to four-fold increase in macrosomia risk<sup>19-22</sup>.

In a study by Pettitt *et al*<sup>23</sup>, the prevalence of infant macrosomia (birthweight >90<sup>th</sup> percentile for gestational age) was found much higher among women with GDM compared with women with normal glucose tolerance (44.4% versus 17.4%). Another study<sup>24</sup> reported that infants of women with GDM weighed 149 g more, on an average, than infants of non-GDM women. In our study, infant macrosomia was found in 15.7 and 2.7 per cent cases in GDM and non-GDM women, respectively. Despite fairly good glycaemic control, macrosomia was seen more in GDM cases. This might be due to some factors other than hyperglycaemia or there might be unrecognized hyperinsulinaemia or short term hyperglycaemia periods in some patients despite good glycaemic control.

**Table III.** Demographic and clinical data of women according to number of abnormal OGTT results

	Number of abnormal value		
	2 values (n=41)	3 values (n=13)	4 values (n=16)
Age (yr)	28 (6)	31 (12)	24 (13)
Gravida (n)	2 (2)	3 (2)	1 (2)
Parity (n)	1 (1)	1 (2)	0 (2)
BMI (kg/m <sup>2</sup> )	28.1 (4.6)	25.9 (3.2)	26.1 (5.0)
Birthweight (g)	3400 (650)	3300 (325)	3400 (1175)
Gender (n, %)			
Female	27, 65.9	10, 76.9	8, 50.0
Male	14, 34.1	3, 23.1	8, 50.0
Labor (n, %)			
Normal	11, 26.8	5, 38.5	6, 37.5
C/S	30, 73.2	8, 61.5	10, 62.5
OGL (mg/dl)	179 (46)	204 (28)	162 (92)
OGTT 0 h	84 (20)*	98 (11)	101.5 (36)
(mg/dl) 1 h	191 (41)	201 (74)	209 (21)
2 h	165 (40)*	184 (41)	184 (25)
3 h	112 (43)	136 (33) <sup>+</sup>	154.5 (43)

Values are given as median (Interquartile range, IQR)  
\* $P<0.001$  compared to 3- and 4- values; <sup>+</sup> $P<0.001$  compared to 4 values

**Table IV.** Demographic and clinical data of women with GDM according to OGL results

OGL (mg/dl)	<200 (n=55)	≥200 (n=15)
Age (yr)	31 (9)	28 (13)
Gravida (n)	2 (2)	2 (2)
Parity (n)	1 (2)	1 (2)
Birthweight (g)	3400 (425)	3400 (1138)
BMI (kg/m <sup>2</sup> )	27.8 (4.8)	26.5 (7.7)
Gender (n, %)		
Female	35, 63.6	10, 66.7
Male	20, 36.4	5, 33.3
Labor (n, %)		
Normal	19, 34.5	3, 16.7
C/S	36, 65.5	12, 83.3
OGL (mg/dl)	158 (26)*	212 (22)
OGTT 0 h	95 (18)	98 (5)
(mg/dl) 1 h	196 (29)	176 (35)
2 h	172 (19)	167 (36)
3 h	141 (51)	136 (39)

Values are given as median (Interquartile range, IQR)  
\*P<0.001 compared to OGL ≥200 mg/dl

The complications of GDM increased as number of abnormal OGTT values increased. Saldana *et al*<sup>14</sup> concluded that the highest frequency for all significantly associated complications including macrosomia was exhibited with four abnormal OGTT values. We could not find any difference in terms of birthweight between GDM cases with 2, 3 or 4 values abnormality. Regular follow up and precise treatment in our cases might have affected the outcomes and birthweight.

Ferrara and colleagues evaluated 45,245 women and found that both maternal fasting and 1 h, but not 2 or 3 h, OGTT glucose levels were independent predictors of macrosomia risk<sup>25</sup>. Caulfield *et al*<sup>26</sup> evaluated risk of macrosomia according to abnormal glucose results and found that the risk for infant macrosomia was higher among women with GDM only if they had fasting hyperglycaemia. Our findings were different from these studies. We found that 2 and 3 h glucose levels were the most important predictors of the offspring overweight at birth. Cause of the relation between 2 and 3 h glucose levels and macrosomia is unknown, but this may be used for prediction of offspring overweight at birth.

In a study it was found that 75 per cent macrosomic infants among the GDM women were born from mothers with insulin-treated GDM<sup>27</sup>. GDM women needing insulin showed a significantly higher incidence of foetal macrosomia than the diet-treated GDM women. In our study, no difference was observed between cases with OGL results over 200 or below 200 mg/dl in terms of presence of macrosomia.

In conclusion, GDM was seen in 8.6 per cent pregnant women in this study. Infant birthweight of cases with GDM was significantly higher than the control group. Correlation analysis revealed mild positive correlation between birthweight versus OGL and BMI. We found that the number of abnormal values in GDM women had no effect on foetal weight in terms of macrosomia (over 4000 g) or low birthweight (lower than 2500 g). This may be related to ethnical, dietary, nutritional differences and having lesser obesity problem in Turkish population<sup>28</sup>. Another explanation may be treatment compliance. In most of the cases, dietary therapy was enough for regulation

**Table V.** Demographic and clinical data of women with GDM according to presence of infant macrosomia

	Birth weight (g)	
	≥4000 (n=57)	≥4000 (n=13)
Age (yr)	27 (12)	32 (6)
Gravida (n)	2 (2)	2 (3)
Parity (n)	0 (1)	1 (1)
Gestational age (wk)	26 (3)	26 (2)
BMI (kg/m <sup>2</sup> )	27.0 (4.4)	30.7 (8.7)
Birthweight (g)	3400 (400)	4000 (200)*
Gender (n, %)		
Female	37, 64.9	8, 61.5
Male	20, 35.1	5, 38.5
Labour (n, %)		
Normal	22, 38.6	0, 0.0
C/S	35, 61.4	13, 100.0
OGL (mg/dl)	179 (47)	212 (39)
OGTT 0 h	96 (23)	86 (12)
(mg/dl) 1 h	201 (47)	176 (61)
2 h	178 (53)	170 (60)
3 h	136 (52)	112 (50)

Values are given as median (Interquartile range, IQR)  
C/S, cesarean section; \*P<0.001 compared to birthweight <4000 g



**Table VI.** Correlation analysis of parameters that can effect birthweight

		OGI	Age	Gravida	Parity	OGTT 0	OGTT 1	OGTT 2	OGTT 3	Birthweight	BMI
OGI	Rho		0.196*	0.161*	0.130*	0.156*	0.150*	0.185*	0.117	0.101*	0.074
	P value		<0.001	<0.001	<0.001	0.019	0.024	0.005	0.077	0.025	0.100
Age	Rho	0.196*		0.540*	0.540*	0.092	0.203*	0.223*	0.134*	0.020	0.197*
	P value	<0.001		<0.001	<0.001	0.168	0.002	0.001	0.043	0.663	<0.001
Gravida	Rho	0.161*	0.540*		0.876*	-0.075	-0.004	-0.012	-0.051	0.046	0.184*
	P value	<0.001	<0.001		<0.001	0.279	0.958	0.857	0.462	0.310	<0.001
Parity	Rho	0.130*	0.540*	0.876*		-0.055	0.083	0.007	-0.039	0.062	0.209*
	P value	<0.001	<0.001	<0.001		0.430	0.232	0.914	0.573	0.172	<0.001
OGTT 0	Rho	0.156*	0.092	-0.075	-0.055		0.311*	0.358*	0.310*	-0.079	-0.042
	P value	0.019	0.168	0.279	0.430		<0.001	<0.001	<0.001	0.374	0.635
OGTT 1	Rho	0.150*	0.203*	-0.004	0.083	0.311*		0.635*	0.287*	0.106	0.329*
	P value	0.024	0.002	0.958	0.232	<0.001		<0.001	<0.001	0.235	<0.001
OGTT 2	Rho	0.185*	0.223*	-0.012	0.007	0.358*	0.635*		0.515*	0.052	0.215*
	P value	0.005	0.001	0.857	0.914	<0.001	<0.001		<0.001	0.557	0.013
OGTT 3	Rho	0.117	0.134*	-0.051	-0.039	0.310*	0.287*	0.515*		-0.070	0.092
	P value	0.077	0.043	0.462	0.573	<0.001	<0.001	<0.001		0.431	0.298
Birthweight	Rho	0.101*	0.020	0.046	0.062	-0.079	0.106	0.052	-0.070		0.159*
	P value	0.025	0.663	0.310	0.172	0.374	0.235	0.557	0.431		<0.001
BMI	Rho	0.074	0.197*	0.184*	0.209*	-0.042	0.329*	0.215*	0.092	0.159*	
	P value	0.100	<0.001	0.001	<0.001	0.635	<0.001	0.013	0.298	<0.001	

\*Correlation is significant at the 0.05 level

of blood glucose, but in some insulin treatment was used. Further studies with larger sample are needed to determinate the significance of these parameters on foetal weight and related complications.

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