

# The 100 Gram Oral Glucose Tolerance Test Results in Twin and Single Pregnancies After Art

YARDIMCI ÜREME TEKNİĞİ SONRASI, TEKİL VE İKİZ GEBELİKLERDEKİ 100 GRAM ORAL GLİKOZ TOLERANS TESTİNİN SONUÇLARI

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## Abstract

**Objective:** The aim of the study is to investigate if ART per se, and twinning in ART pregnancies have any effects on 100-g oral GTT results.

**Material and Methods:** One hundred singleton In Vitro Fertilization/IntraCytoplasmic Injection-Embryo Transfer (IVF/ICSI-ET) pregnancies (Group 1), 72 twin IVF/ICSI-ET pregnancies (Group 2), and 128 singleton spontaneous pregnancies (Group 3) were retrospectively compared with respect to the results of 100-g oral glucose tolerance test.

**Results:** Singleton IVF/ICSI-ET pregnancies and twin IVF/ICSI-ET pregnancies were similar regarding the results of 100-g oral glucose tolerance test, although first and second hour plasma glucose levels were higher in singleton IVF/ICSI-ET pregnancies than in singleton spontaneous pregnancies.

**Conclusion:** The present findings indicate that glucose tolerances in singleton and twin IVF/ICSI-ET pregnancies were similar, although singleton IVF/ICSI-ET pregnancies have a higher level of glucose intolerance than that of spontaneous singleton pregnancies.

**Key Words:** Twin pregnancy, singleton pregnancy, IVF, gestational diabetes mellitus

## Özet

**Amaç:** Bu araştırmanın amacı; yardımcı üreme tekniği ile elde edilen, tekil ve ikiz gebelerdeki 100 gr oral glikoz tolerans sonuçlarını karşılaştırmaktır.

**Gereç ve Yöntemler:** Yüz tekil in vitro fertilizasyon/intrastoplazmik injeksiyon- Embryo transferi gebeliği (IVF/İSİ-ET) (Grup 1), 72 ikiz IVF/İSİ-ET gebeliği (Grup 2) ve 128 tekil spontan gebelik (Grup 3), geriye dönük olarak 100 gr oral glikoz tolerans testi sonuçları için karşılaştırıldı.

**Bulgular:** İVF/İSİ-ET ile elde edilen tekil gebelerin birinci ve ikinci saatte elde edilen plazma glikoz düzeyleri, spontan tekil gebelerin sonuçlarından daha yüksek olmasına rağmen, İVF/İSİ-ET sonucu oluşan tekil ve ikiz gebelerin 100 g sonuçları benzerdi.

**Sonuç:** İVF/İSİ-ET sonucu meydana gelen tekil gebelerde, glikoz intoleransının düzeyi spontan tekil gebeliklerden elde edilen değerlere göre daha yüksek olmakla beraber, İVF/İSİ-ET sonucu elde edilen tekil ve ikiz gebeliklerin glikoz toleransları benzerdi.

**Anahtar Kelimeler:** İkiz gebelik, tekil gebelik, IVF, gestasyonel diabetes mellitus

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Gestational diabetes mellitus (GDM) is defined as carbohydrate intolerance of varying severity with onset or first recognition during pregnancy.<sup>1</sup> It is the most frequent metabolic disorder occurring during pregnancy and its prevalence may range from 1% to 16% of all

pregnancies depending on the type of population and the diagnostic criteria used.<sup>2</sup> A report by O'Sullivan et al.<sup>3</sup> demonstrated a fourfold increase in the perinatal mortality rate among untreated patients with gestational diabetes compared with that of controls.

The underlying cause of diabetic fetopathy was described by Pedersen<sup>4</sup> as, exaggerated fetal insulin response led by fetal hyperglycemia which was the consequence of maternal hyperglycemia quickly transmitted to the fetus. Fetal hyperinsulinemia may cause macrosomia, decreased fetal surfactant production, and neonatal hypoglycemia

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which may result in increased perinatal morbidity and mortality, complications during pregnancy and delivery, and a greater frequency of long-term complications in both mother and child.<sup>1,2</sup> These consequences justify the proper diagnosis and management of GDM. The most widely used screening method for GDM is the 50-g oral glucose challenge test (GCT), and determination of glycemia one hour later. The most often used threshold value is 140 mg/ dl. There is insufficient evidence to recommend for or against routine screening for GDM,<sup>5</sup> and this subject continues to create debate at present.<sup>6-9</sup> WHO recommends the universal screening of pregnant women.<sup>10</sup> Screen positive pregnant women are subject to 100-g oral glucose tolerance test (OGTT) for the diagnosis of GDM.

In a study blinded to health care providers, Sermer et al.<sup>11</sup> performed 100-g oral GTT on 3.836 gravidas, 3.637 of whom did not meet the predetermined criteria for GDM. There was a direct and continuous relationship between the OGTT results and macrosomia, cesarean section rates, and pre-eclampsia. The OGTT result predicted these outcomes independent of potential confounders such as maternal obesity, parity, age, and race.<sup>1</sup>

The frequency of GDM in twin pregnancies may be influenced by the the increased levels of hormones with insulin antagonistic effects such as human placental lactogen, estrogen and progesterone.<sup>12</sup> Although there is limited and conflicting information in the literature regarding the effect of twin pregnancy on GDM,<sup>12-14</sup> the higher risks of perinatal loss associated with twin pregnancies may thereby be further increased by adverse effects of superimposed GDM.<sup>12</sup>

Polycystic ovary syndrome (PCOS) is an extremely common disorder with a prevalence rate of 3-7% in the general population<sup>15,16</sup> and as high as 20% in the infertile population.<sup>17</sup> However, there is a debate about the pregnancy complication such as gestational diabetes mellitus, especially in whom differences in age and weight between PCOS patients and controls are negligible.<sup>18,19</sup>

In the present study we investigated whether Assisted Reproductive Technology (ART) per se or

twinning in ART pregnancies have any effects on 100-g oral OGTT results and the frequency of GDM in this group. We also compared singleton In Vitro Fertilization/IntraCytoplasmic Injection-Embryo Transfer (ICSI-ET) pregnancies with singleton spontaneous pregnancies, and singleton ICSI-ET pregnancies with twin ICSI-ET pregnancies.

### Material and Methods

The study comprised of 172 of our IVF/ICSI-ET pregnancies who were under our surveillance during January 2001 - December 2003 at Özel Ege Tüp Bebek Merkezi as well as 128 singleton spontaneous pregnancies who were under our surveillance during January 2002-December 2003 at Kahramanmaraş Sütçü İmam University, Faculty of Medicine, Department of Obstetrics & Gynecology. The test results were present in our special ART center databases. The records were retrospectively evaluated. Local Ethical Committee stated that ethical approval is no necessary for the publication of retrospective studies.

All pregnant women were subject to 50-g oral GCT between the 26<sup>th</sup> and 28<sup>th</sup> weeks of their pregnancies, and if the result of 50-g oral GCT is positive, 100-g oral OGTT was also performed. GCT was performed by 50 g glucose taken orally and determining the plasma glucose level one hour later. The results exceeding 140 mg/ dl were considered positive for screening. After having 3 days of unrestricted diet containing at least 150 g of carbohydrates per day, the screen positive pregnant women were also subject to 100-g oral OGTT for the diagnosis of GDM. After determining the fasting plasma glucose level, pregnant women were given 100-g glucose orally and the plasma glucose levels on the 1<sup>st</sup>, 2<sup>nd</sup>, and 3<sup>rd</sup> hours were also determined. Fasting, 1<sup>st</sup> hour, 2<sup>nd</sup> hour, and 3<sup>rd</sup> hour plasma glucose levels were considered normal if they did not exceed 95 mg/dl, 180 mg/dl, 155 mg/dl, and 140 mg/dl, respectively. Plasma glucose levels were determined using glucose oxidase method, in all pregnant women.

We compared singleton IVF/ICSI-ET pregnancies with twin IVF/ICSI-ET pregnancies, and singleton IVF/ICSI-ET pregnancies with singleton spontaneous pregnancies. We were not interested in the comparison of twin IVF/ICSI-ET pregnancies with singleton spontaneous pregnancies, since we could not make any reasonable conclusions. Therefore, we did not use 'Analysis of Variance' or 'Kruskal-Wallis Analysis of Variance' tests. Instead, we used *t*-test and Mann-Whitney U test to compare the groups as can be seen in Table 1 and 2. In order to prevent significance inflation, the difference between the groups was accepted statistically significant if  $p < 0.025$ . We made this correction by dividing ( $\alpha = 0.05$ ) by 2, since we used 2 matches (singleton ICSI-ET pregnancies with twin ICSI-ET pregnancies and singleton ICSI-ET pregnancies with singleton spontaneous pregnancies) to compare the three groups.

### Results

Singleton IVF/ICSI-ET pregnancies (Group 1,  $n = 100$ ), twin IVF/ICSI-ET pregnancies (Group 2,  $n = 72$ ), and singleton spontaneous pregnancies (Group 3,  $n = 128$ ) were compared, using *t*-test and the results are shown in Table 1. IVF procedures were performed in 172 cases due to the causes belonging to male (41%), unexplained (18%), tubal factor (20%), ovarian problems (21%). Polycystic ovary syndrome was observed in 10% ( $n = 10$ ) singleton IVF/ICSI-ET, 12% ( $n = 9$ ) twin IVF/ICSI-ET pregnancies prior to pregnancy. 50-g oral GCT positive patients in Group 1, Group 2 and Group 3 were assigned in Group 1a ( $n = 31$ ), Group 2a ( $n = 27$ ) and Group 3a ( $n = 38$ ) respectively. Group 1a, Group 2a, and Group 3a were compared using

Mann-Whitney U and *t*-tests, and the results are shown in Table 2.

### Discussion

GDM is the carbohydrate intolerance of pregnant women. Decrease in insulin sensitivity in pregnancy and the inability of beta cells to respond and to secrete insulin to offset the insulin resistance cause hyperglycemia in pregnant women with GDM.<sup>20</sup> The resultant fetal hyperglycemia is the underlying pathophysiology of the adverse effects of GDM on perinatal outcome. The second mechanism is through the effects of resultant fetal hyperinsulinemia which may lead to increased oxygen demand and following fetal hypoxia and acidemia.<sup>12</sup>

Higher risks of perinatal morbidity and mortality in twin gestations may be further increased by superimposed GDM. However there is limited and conflicting information in the literature regarding the effects of twin pregnancy on GDM. Schwartz et al.<sup>12</sup> reported the results of their study investigating metabolic and blood glucose parameters in singleton and twin pregnancies. Their results comprised the greater frequency of GDM as well as the greater 3<sup>rd</sup> hour blood glucose level of 100-g oral OGTT in twin gestations than in singletons, all other values of OGTT in singleton and twin pregnancies were not significantly different. This evidence suggested a greater disturbance of carbohydrate intolerance in twin gestations. They concluded that the potential for hypoxemia and acidemia caused by metabolic effects of hyperinsulinemia might be of significance if superimposed on twin pregnancies associated with either intrauterine growth restriction or discordance resulting

**Table 1.** Age, body mass index, and plasma glucose level in glucose challenge test.

	Group 1 (n=100)	Group 2 (n=72)	Group 3 (n=128)	P value (Group1and 2)	P value (Group1and 3)
Age	30.1 ± 5.4	29.3 ± 4.6	26.9 ± 4.6	NS	<0.001
GCT result (mg/dl)	130.2 ± 31.5	131.6 ± 31.9	124.1 ± 32.3	NS	NS
BMI (kg/m <sup>2</sup> )	25.0 ± 4.8	25.6 ± 4.6	25.9 ± 3.8	NS	NS

**GCT:** Glucose challenge test, **BMI:** Pre-pregnancy body mass index of the patients, **NS:** Not significant

**Table 2.** Age, body mass index, plasma glucose levels, and number of abnormal values in patients undergoing 100-g OGTT.

	Group 1a (n=31)	Group 2a (n=27)	Group 3a (n=38)	P value (Group1a and 2a)	P value (Group1a and 3a)
Age	32.0 ± 4.0	30.6 ± 4.4	28.6 ± 5.1	NS	<0.01
BMI (kg/m <sup>2</sup> )	25.3 ± 4.5	26.2 ± 5.4	26.3 ± 3.6	NS	NS
OGTT(fasting mg/dl)	90.3 ± 13.8	89.8 ± 9.7	85.7 ± 12.5	NS	NS
OGTT (1 <sup>st</sup> hour mg/dl)	188.9 ± 37.8	181.0 ± 27.6	165.2 ± 34.1	NS	<0.01
OGTT (2 <sup>nd</sup> hour mg/dl)	165.9 ± 40.0	156.4 ± 25.6	138.4 ± 37.7	NS	<0.01
OGTT (3 <sup>rd</sup> hour mg/dl)	111.6 ± 22.0	118.2 ± 25.0	106.3 ± 32.9	NS	NS
OGTT (n of abnormal values)	1.6 ± 1.1	1.4 ± 1.2	1.0 ± 1.2	NS	NS

**OGTT:** Oral glucose tolerance test, **BMI:** Pre-pregnancy body mass index of the patients, **NS:** Not significant

from placental insufficiency of vascular origin or both.

Ihara et al.<sup>13</sup> found lower fasting and 30 minutes plasma glucose concentrations in twin gestations than in singletons, in 75-g OGTT, but their study comprised no pregnant women with GDM. Wein et al.<sup>14</sup> reported higher prevalence of GDM in twin pregnancies in the period 1971-1980, although they could not demonstrate a significant difference between the prevalences of GDM in twin and singleton pregnancies in the period 1981-1991.

In our study, fasting, 1<sup>st</sup>, 2<sup>nd</sup>, and 3<sup>rd</sup> hour plasma glucose values of OGTT in Group 1a were similar to the corresponding values in Group 2a. Fasting and the 3<sup>rd</sup> hour plasma glucose values were similar in Group 1a and Group 3a, although the 1<sup>st</sup> and 2<sup>nd</sup> hour plasma glucose values in Group 1a were higher than the corresponding values in Group 3a.

There is an evolving body of evidence from the last decade presenting similarities between gestational diabetes and the metabolic (insulin resistance) syndrome. These new observations suggest that GDM might be an early manifestation of the metabolic syndrome.<sup>21</sup> Higher frequency of insulin resistance in the infertile population may account for the higher 1<sup>st</sup> and 2<sup>nd</sup> hour plasma glucose levels of OGTT in Group 1a than in Group 3a. These differences might be related to the patients with PCOS.<sup>19</sup> As we determined the sponta-

neous single pregnant women with advancing pregnancy, we were not aware about pre-pregnancy ovary state of the cases. So, we were not able to compare the effect of polycystic ovary syndrome on pregnancy between IVF and spontaneous pregnancies.

There are a number predisposing factors leading to glucose intolerance such as obesity, age, family history etc. Although there is statistically difference for age between the Group 1 and 3, we did not contemplate this creates the IGT for the groups.<sup>1</sup>

In conclusion, our results indicate that glucose tolerances in singleton and twin IVF/ICSI-ET pregnancies are similar, although singleton IVF/ICSI-ET pregnancies have a higher level of glucose intolerance than that of spontaneous singleton pregnancies.

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