

Glucose Challenge Test and Association with Pregnancy Outcome

Enis ÖZKAYA¹, Burak KARADAĞ¹, Neslihan YEREBASMAZ¹, Oya ALDEMİR¹, Soner DÜZGÜNER¹

Evrin ÇAKIR², Salim ERKAYA¹

Ankara, Turkey

OBJECTIVE: We designed this study to evaluate the relationship between glucose intolerance and pregnancy outcome in terms of birth weight and cesarean (C/S) rates.

STUDY DESIGN: Two hundred fifty eight pregnancies were included in the study. After delivery birth weights and route of deliveries were recorded and oral glucose challenge tests with 50 grams were viewed from records.

RESULTS: Mean age, gravida, parity, glucose challenge test (GCT), birth and maternal weights were 25.6±5.3, 1.9±1.5, 0.6±0.9, 105.9±26.9 mg/dl, 3235±469 gr, 75.04±12 kg respectively. Correlation analysis revealed a significant positive correlation between GCT result with maternal age, gravida and maternal weight (95% CI, $r=0.334$, $p:0.001$, $r=0.300$, $p:0.001$, $r=0.201$, $p:0.003$ respectively). A significant negative correlation with birth weight was found. ($r=-0.167$, $p=0.007$). GCT level between 120-140 mg/dl was found to be significantly associated with low birth weight (LBW) and values of 120-160 mg/dl were positive confounder for higher C/S rates.

CONCLUSION: In this study GCT results between 120-140 mg/dl were found to be risk factor for LBW after adjustment of other confounders and this value and higher values up to 160 mg/dl were positive confounders for C/S rates.

Key Words: Birth weight, Glucose challenge test, Pregnancy outcome

Gynecol Obstet Reprod Med; (2011;17:7-11)

Introduction

The importance of gestational diabetes mellitus (GDM) has been questioned because of the lack of consistent evidence on its effects on pregnancy outcomes.^{1,2} In 1998, the World Health Organization (WHO) published diagnostic criteria for GDM³ and recommended treatment for both impaired glucose tolerance (IGT) and diabetes in pregnancy. The effect of IGT on pregnancy outcomes remains unknown. The Tianjin Study of Diabetes in Pregnancy (TSDP) introduced a universal screening of diabetes during pregnancy in December 1998 using a unique population of pregnant women.⁴ In the United States, low birthweight is a primary indicator of poor maternal and neonatal health.⁵ Despite the substantial proportion mothers who live in poverty and receive inadequate prenatal care,⁶

low birthweight is a rare outcome, especially among infants. This observation, which is cited as an example of the “Hispanic paradox,” has resulted in efforts to understand the apparently protective social and cultural factors that might explain this “good outcome.”^{7,8} Overt diabetes mellitus during pregnancy is associated with significantly increased risks of adverse perinatal outcomes. Whereas some data suggest that current diagnostic criteria for gestational diabetes mellitus are too restrictive and that lesser degrees of hyperglycemia also increase risk,^{9,10} risks associated with hyperglycemia that is less severe than that diagnostic of overt diabetes mellitus are uncertain for a number of reasons. First, there are no uniform international standards for the ascertainment and diagnosis of gestational diabetes mellitus.¹¹ In addition, the extent to which adverse outcomes associated with GDM may be explained by confounders (including obesity, advanced maternal age, or associated medical complications) is unclear.^{12,13}

We conducted this study to clarify the significance of IGT on pregnancy prognosis in terms of birth weight and route of delivery.

Material and Method

Two hundred fifty eight term pregnancies (>37 weeks) were included in the study. Study was conducted in Etlik Zübeyde Hanım Maternity & Women’s Health Teaching and

¹Department of Obstetrics and Gynecology Etlik Zübeyde Hanım Maternity & Women’s Health Teaching and Research Hospital, Ankara

²Department Endocrinology Dışkapı Yıldırım Beyazıt Training and Research Hospital, Ankara

Address of Correspondence: Enis Özkaya
Demetevler 10. Sok. 63/15 Yenimahalle
Ankara
enozkaya1979@gmail.com

Submitted for Publication: 01. 11. 2010

Accepted for Publication: 24. 03. 2011

Research Hospital, Department of Obstetrics and Gynecology between January 2008 -August 2009 in patients who were admitted to delivery room. After delivery birth weight and route of deliveries were recorded and GCT results were viewed from records that were collected prospectively. GCT was performed in all patients between 24-28 weeks of gestations with 50 grams of glucose and glucose levels were measured 1 hour after ingestion. Women were excluded if they had preexisting diabetes, an abnormal result on a glucose screening test before 24 weeks of gestation, prior gestational diabetes, a history of stillbirth, elective cesareans, multifetal gestation, asthma, or chronic hypertension; if they were taking corticosteroids, smoking cigarettes; if there was a known fetal anomaly; or if imminent or preterm delivery was likely because of maternal disease or fetal conditions. All the women who participated in the study provided written informed consent. The study was approved by the local ethics committee. Patients with GCT result over than threshold value (140 mg/dl) were ordered 100 gr oral glucose tolerance test and women with severe glucose impairment (at least 2 values higher than threshold) were not eligible for this trial. Threshold value for 100 gr OGTT were accepted according to American Diabetes Association (ADA) criterias. Birth weights lower than 2500 gr were accepted as low birth weight.

Statistical Analysis

Data is entered to SPSS version 11. Descriptive analysis was used for mean value calculations. Correlation analysis was performed to show the effects of independent variables and ROC analysis was used to show cut offs and calculate sensitivity and specificity values. Regression analysis was used for statistical adjustment of multivariates. Chi square and Fisher's tests were used for group comparisons.

Result

Mean age, gravida, parity, GCT, birth and maternal weights were 25.6 ± 5.3 , 1.9 ± 1.5 , 0.6 ± 0.9 , 105.9 ± 26.9 mg/dl, 3235 ± 469 gr, 75.04 ± 12 kg respectively. Correlation analysis revealed a significant positive correlation between GCT result with maternal age, gravida and maternal weight (95% CI, $r=0.334$, $p=0.001$, $r=0.300$, $p=0.001$, $r=0.201$, $p=0.003$ respectively). A significant negative correlation was observed between GCT result with birth weight ($r=-0.167$, $p=0.007$). GCT level between 120-140 mg/dl was found to be significantly associated with LBW and higher C/S rates. In ROC analysis area under curve for GCT and birth weight below 2500 grams was 0.880 ($p=0.001$). Optimal sensitivity (75%) and specificity (85.9%) were obtained with threshold value 127 mg/dl. Same analysis were performed for route of delivery area under curve was 0.825 ($p=0.001$). Optimal sensitivity (91%) and specificity (83.5%) were calculated at a value of 121 mg/dl. GCT mean values in patients with birth weight lower than 2500 was 135.9 ± 16.3 mg/dl, on the other hand value in normal birth weights was 102 ± 25.9 mg/dl ($p=0.001$). GCT results were divided into 6: 1) <80 mg/dl, 2) 80-100 mg/dl, 3) 100-120 mg/dl, 4) 120-140 mg/dl, 5) 140-160 mg/dl, 6) >160 mg/dl, rates of cesarean and low birth weight were compared (Table 1.2). Statistical analysis performed also after GCT results were divided into different 6 groups: 1) 80-100 mg/dl and others, 2) 100-120 mg/dl and others, 3) 120-140 mg/dl and others, 4) 140-160 mg/dl and others, 5) 160-200 mg/dl and others, 6) Lower-higher than 140 mg/dl. In these six groups we have compared rate of low birth weight and route of delivery, results were shown in table 3,4.

Table1: Cesarean rates between groups

	Glucose Challenge Test Results						P
	<80 mg/dl n:48	80-100 mg/dl n:69	100-120 mg/dl n:69	120-140 mg/dl n:48	140-160 mg/dl n:12	>160 mg/dl n:12	
Vaginal delivery	45 (94%)	69 (100%)	69(100%)	22 (46%)	7(60%)	9 (75%)	0.001
C/S	3(6%)	0	0	26 (54%)	5(40%)	3 (25%)	

Table2: Low birth weight rates between groups

	Glucose Challenge Test Results						P
	<80 mg/dl n:48	80-100 mg/dl n:69	100-120 mg/dl n:69	120-140 mg/dl n:48	140-160 mg/dl n:12	>160 mg/dl n:12	
Normal birth weight	48(100%)	69(100%)	69(100%)	30(62%)	9(75%)	9(75%)	0.001
LBW	0	0	0	18(38%)	3(25%)	3(25%)	

Table 3: Route of delivery between groups

GCT Result	C/S	Vaginal Delivery	P (Fisher Test)
80-100 mg/dl (n:72)	0 (%0)	72 (%100)	0.001
Other (n:186)	37 (%20)	149 (%80)	
100-120mg/dl (n:72)	0 (%0)	72 (%0)	0.001
Other (n:186)	37 (%20)	149 (%80)	
120-140 mg/dl (n:54)	26 (%48)	28 (%52)	0.001
Other (n:204)	11 (%5.4)	193 (%94.6)	
140-160 mg/dl (n:15)	8 (%53)	7 (%47)	0.001
Other (n:243)	29 (%12)	214 (%88)	
<140 (n:234)	29 (%12)	205 (%88)	0.015
>140 (n:24)	8 (%33)	16 (%67)	
160-200 (n:12)	3 (%25)	9 (%75)	0.239
Other (n:246)	34 (%14)	212 (%86)	

Table4: LBW rates between groups

GCT Result	LBW	Normal birth weight	P (Fisher Test)
80-100 mg/dl(n:72)	0 (%0)	72 (%100)	0.001
Other(n:186)	24 (%13)	162 (%87)	
100-120mg/dl(n:72)	0 (%0)	72 (%100)	0.001
Other(n:186)	24 (%13)	162 (%87)	
120-140 mg/dl(n:54)	18 (%33)	36 (%67)	0.001
Other(n:204)	6 (%2.9)	198 (%97.1)	
140-160 mg/dl(n:15)	3 (%20)	12 (%80)	0.53
Other(n:243)	21 (%8.6)	222 (%91.4)	
<140(n:234)	18 (%7.6)	216 (%92.4)	0.015
>140(n:24)	6 (%25)	18 (%75)	
160-200(n:12)	3 (%25)	9 (%75)	0.089
Other(n:246)	21 (%8.5)	225 (%91.5)	

Adjusted Odds ratio for LBW in group 3 was 16.5 (95%CI, 6.1-44.3, p=0.001). Adjusted Odds ratios for other groups did not reach statistical significance p values for group 1,2,4 were 0.997, 0.997, 0.125 respectively. Adjusted Odds ratio for route of delivery in group 3 was 16.3 (95%CI, 7.3-36.5, p=0.001). Adjusted Odds ratio for route of delivery in group 4 was 8.4(95%CI, 2.8-24.9, p=0.001). In groups 1,2 adjusted odds ratio for route of delivery did not reach statistical significance (p=0.997, p=0.997). GCT levels higher than 140 mg/dl was not found to significantly associated with high birth weight (birth weight > 4000 gr) (p=0.302). Low birth weight rates were compared among patients with GCT level lower and higher than 140 mg/dl. Rates were higher in patients with GCT level higher than 140 mg/dl (%25)(p=0.015). After ad-

justment for maternal age, weight, gravida difference did not reach statistical significance (p=0.331).

Conclusion

The results of the present study demonstrate that glucose intolerance to some extent is independently and significantly associated with an increased incidence of cesarean section and markedly increased proportion of LBW. In this study GCT result between 120-140 mg/dl was found to be significant confounder for LBW. Values lower and higher than this level were not associated with poor pregnancy outcome interms of LBW but this value and higher values up to 160 mg/dl were significantly associated with high C/S rates. High GCT result was not found to be a predictor of high birth weight contrary to previ-

ous studies. Our comment for this result was, patients with GCT result higher than 140 mg/dl ordered 100 gr OGTT and patients with severe glucose intolerance were excluded from the study. Threshold value of 140 mg/dl was not found to be significantly associated with either high birth weight or LBW. This result has shown that normal 100 gr OGTT result is valuable to exclude patients with severe glucose intolerance results in poor pregnancy outcome. In some studies maternal glucose level was significantly associated with birthweight, even when maternal weight and weight gain were considered.^{14,15,16} In 1952, Jorgen Pedersen¹⁷ postulated that maternal hyperglycemia led to fetal hyperglycemia, which evoked an exaggerated fetal response to insulin. Since then, the Pedersen hypothesis has formed the basis for understanding the pathophysiological consequences of diabetes during pregnancy. The objective of the HAPO study was to clarify risks of adverse outcomes associated with degrees of maternal glucose intolerance less severe than overt diabetes mellitus. Questions have been raised regarding the benefits of treating "mild" gestational diabetes mellitus.^{18,19,20} However, one recently published randomized clinical trial, the Australian Carbohydrate Intolerance Study in Pregnant Women (ACHOIS), found reduced perinatal morbidity and mortality when standard contemporary treatment of gestational diabetes mellitus was compared with no intervention. Taken together, the current results and results of the ACHOIS trial²¹ indicate that maternal hyperglycemia less severe than that used to define overt diabetes is related to clinically important perinatal disorders or problems and that their effects can be reduced by means of treatment, although a threshold for the need for treatment is not established. The individual measures from the oral glucose tolerance tests were not highly correlated, and no single measure was clearly superior in predicting the primary outcomes. When adjusted for potential confounders, relative increases in each glucose measure were similarly predictive of birth weight above the 90th percentile. When the glucose measures were analyzed as continuous variables, each was a significant predictor of primary cesarean delivery, with 1-SD increases in glucose level being associated with an increase of 8 to 11% in the odds of delivery by cesarean section.²²

Although treatment of mild gestational diabetes mellitus did not significantly reduce the frequency of a composite outcome that included stillbirth or perinatal death and several neonatal complications, it did reduce the risks of fetal overgrowth, shoulder dystocia, cesarean delivery, and hypertensive disorders.²³

In this study GCT results between 120-140 mg/dl were found to be risk factor for LBW after adjustment of other confounders (including obesity, advanced maternal age, or associated medical complications) and this value and higher values up to 160 mg/dl was positive confounder for C/S rates.

Glukoz Yükleme Testi ve Gebelik Sonucu ile İlişkisi

AMAÇ: Bu çalışma glukoz intoleransı ve gebelik sonucu ilişkisini düşük doğum ağırlığı ve sezaryen oranlarına göre kıyaslama amacı ile dizayn edildi.

GEREÇ VE YÖNTEM: Çalışmaya 258 gebe dahil edildi. Doğum sonrası doğum ağırlığı ve doğum şekli kaydedildi. Elli gram oral glukoz yükleme testi sonuçları kayıtlardan görüldü.

BULGULAR: Ortalama yaş, gravida parite, glukoz yükleme testi sonuçları, doğum ve anne kiloları sırası ile 25,6±5,3, 1,9±1,5, 0,6±0,9, 105,9±26,9 mg/dl, 3235±469 gr, 75,04±12 idi. Korelasyon analizi glukoz yükleme testi sonuçları ile maternal yaş, kilo ve gravida arasında anlamlı ilişki gösterdi (95% CI, r=0,334, p:0,001, r=0,201, p:0,003, r=0,300, p:0,001). Doğum ağırlığı ile anlamlı negatif korelasyon saptandı((r=-0,167,p=0,007). Glukoz yükleme testi sonucu 120-140 mg/dl düşük doğum ağırlığı ile ilişkili saptandı ve 120-160 mg/dl arasındaki değerler artmış sezaryen hızı için etkendi.

SONUÇ: Glukoz yükleme testi sonucu 120-140 mg/dl düşük doğum ağırlığı ile ilişkilidir ve 120-160 mg/dl arasındaki değerler artmış sezaryen hızı için etkendir.

Anahtar Kelimeler: Doğum ağırlığı, Glukoz yükleme testi, Gebelik sonucu

References

1. Jarrett RJ. Castro-Soares J. Dornhorst A. et al. Should we screen for gestational diabetes? *BMJ* 1997;315:736-9
2. Jarrett RJ. Gestational diabetes: a nonentity? *BMJ* 1993; 306:37-8
3. Alberti KG. Zimmet PZ. Definition, diagnosis and classification of diabetes mellitus and its complications. I. Diagnosis and classification of diabetes mellitus provisional report of a WHO consultation. *Diabet Med* 1998; 15:539-53
4. Yang X. Hsu-Hage BH. Zhang H. et al. Gestational diabetes mellitus in women of single gravidity in Tianjin City, China. *Diabetes Care* 2002;25:847-51
5. Healthy People 2000: National Health Promotion and Disease Prevention Objectives. Washington DC: US Dept of Health and Human Services. DHHS publication PHS 1991:91-50212.
6. Martin JA. Hamilton BE. Sutton PD. at al. Births: final data for 2002. *Natl Vital Stat Rep* 2003;52:1-113
7. Kieffer EC. Maternal obesity and glucose intolerance during pregnancy among Mexican-Americans. *Paediatr Perinat Epidemiol* 2000;14:14-9.
8. Cervantes A. Keith L. Wyshak G. Adverse birth outcomes among native-born and immigrant women: replicating national evidence regarding Mexicans at the local level. *Matern Child Health J* 1999;3:99-109

9. Jensen DM. Damm P. Sorensen B. et al. Clinical impact of mild carbohydrate intolerance in pregnancy: a study of 2904 nondiabetic Danish women with risk factors for gestational diabetes. *Am J Obstet Gynecol* 2001;185:413-9.
10. Sermer M. Naylor CD. Gare DJ. et al. Impact of increasing carbohydrate intolerance on maternal-fetal outcomes in 3637 women without gestational diabetes. *Am J Obstet Gynecol* 1995;173:146-56
11. Metzger BE. Coustan DR. Summary and recommendations of the Fourth International Workshop-Conference on Gestational Diabetes Mellitus. *Diabetes Care* 1998;21:161-7.
12. Jarrett RJ. Reflections on gestational diabetes mellitus. *Lancet* 1981;2:1220-1.
13. Spellacy WN. Miller S. Winegar A. et al. Macrosomia: maternal characteristics and infant complications. *Obstet Gynecol* 1985;66:158-61.
14. Kieffer EC. Nolan GH. Carman WJ. et al. Glucose tolerance during pregnancy and birthweight in a Hispanic population. *Obstet Gynecol* 1999;94:741-6.
15. Nolan CJ. Riley SF. Sheedy MT. et al. Maternal serum triglyceride, glucose tolerance and neonatal birthweight ratio in pregnancy. *Diabetes Care* 1995;18:1550-6.
16. Scholl TO. Sowers MF. Chen X. et al. Maternal glucose concentration influences fetal growth, gestation and pregnancy complications. *Am J Epidemiol.* 2001;154:514-20
17. Pedersen J. Diabetes and pregnancy: Blood sugar of newborn infants. (Ph.D. thesis. Copenhagen: Danish Science Press 1952:230.
18. Hunter DJS. Keirse MJNC. Gestational diabetes. In: Chalmers I, Enkin M, Kierse M, eds. *Effective care in pregnancy and childbirth.* Oxford, England: Oxford University Press 1989:403-10.
19. Brody SC. Harris RH. Whitener BL. et al. Screening for gestational diabetes: systematic evidence review. Rockville, MD: Agency for Healthcare Research and Quality 2003.
20. Tuffnell DJ. West J. Walkinshaw SA. Treatments for gestational diabetes and impaired glucose tolerance in pregnancy. *Cochrane Database Syst Rev* 2003;3:CD003395.
21. Crowther CA. Hiller JE. Moss JR. et al. Effect of treatment of gestational diabetes on pregnancy outcomes. *N Engl J Med* 2005;352:2477-86.
22. The HAPO Study Cooperative Research Group. Hyperglycemia and Adverse Pregnancy Outcomes *N Engl J Med* 2008;358:1991-2002.
23. Mark B. et al. A Multicenter, Randomized Trial of Treatment for Mild Gestational Diabetes. *N Engl J Med* 2009;361:1339-48