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Increased Incidence in False Positive Diagnosis of Gestational Diabetes Mellitus with 75gm Oral Glucose Tolerance Test: A Clinical Study in Chinese Women

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ABSTRACT

Background: Currently, most of the countries across the globe follow the International Association of the Diabetes and Pregnancy Study Groups criteria in the diagnosis of gestational diabetes mellitus, which is based on the analysis of Hyperglycemia and Adverse Pregnancy Outcome study. The International Association of the Diabetes and Pregnancy Study Groups criterion comes with its benefits and doubts. Although it has been adopted worldwide, diagnosis of gestational diabetes mellitus with single test and only one positive value has always been debated and is often criticized. This study aimed to assess if the participant with lesser degree of glucose intolerance increases the incidence of false positive diagnosis of gestational diabetes mellitus with 75gm Oral Glucose Tolerance Test based on International Association of the Diabetes and Pregnancy Study Groups criteria.

Methods: This prospective, interventional study was conducted in outpatient department of a tertiary hospital of China over a period of 12 months. 48 patients who were diagnosed with gestational diabetes mellitus in 24-31 weeks of pregnancy by 75mg Oral Glucose Tolerance Test were selected via conventional sampling technique based on lesser degree (less severe, not in need of immediate medical attention) of glucose intolerance. These patients underwent second Oral Glucose Tolerance Test within 2-3 weeks of first test. Patients with normal 2nd Oral Glucose Tolerance Test were observed closely throughout their gestational period and compared with the control group.

Results: The mean values of data of control and case group were compared and 37.5% of the patients failed to reproduce the same result with the second test and all of them having normal maternal and fetal outcome without any treatment of gestational diabetes mellitus (t-test, p=0.05).

Conclusions: With International Association of the Diabetes and Pregnancy Study criteria, more patients with lesser degree of glucose intolerance have been falsely diagnosed and treated as gestational diabetes mellitus.

Keywords: Gestational diabetes mellitus; international association of the diabetes and pregnancy study groups; Oral glucose tolerance test .

INTRODUCTION

Gestational diabetes mellitus (GDM) is diagnosed when women without any history of diabetes mellitus have higher value of blood glucose after 24 weeks of gestations. It is defined as carbohydrate intolerance of variable severity with onset or first recognition during pregnancy.[1] Gestational Diabetes Mellitus was first coined in 1957.[2] With the recent diagnosis criteria, it is estimated to affect 17.8% of the pregnancy[3] and complicating 7% of all pregnancy.[4]

In mother, it causes higher incidence of cesarean section and post partum diabetes mellitus. In the offspring, it causes perinatal/neonatal morbidity, macrosomia, birth injury, shoulder dystocia, hypoglycemia, polycythemia and hyperbilirubinemia.[5] In the diagnosis of GDM, over the years, many different tests have been introduced but eventually with all of their own drawbacks and limitation none of these tests have been recognized as a gold standard.

In China previously, WHO, ADA, NDGG were the common

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criteria used in the diagnosis of GDM. As off 2011 China has also adopted International Association of the Diabetes and Pregnancy Study Groups (IADPSG) cut offs criteria.[6] The IADPSG criterion comes with its own benefits and doubts. Although this criterion has been adopted all over the world, diagnosis of GDM with single test and only one positive value has always been debated and is often criticized.

In this study, we are going to observe the patients throughout the pregnancy, who have failed to reproduce the positive result in the second test and conclude if these patients really needed to be put under the diagnosis of GDM with the first test which has been shown otherwise by the second.

METHODS

This is a prospective, interventional study that was conducted in outpatient department of First Affiliated Hospital of Chongqing Medical University, China over a period of 12 months (March 2014 to March 2015). Patients of 24-31 weeks of gestation underwent routine 75mg Oral Glucose Tolerance Test (OGTT), for the diagnosis of GDM. After excluding women with history of (Diabetes Mellitus (DM), hypertension, Polycystic ovarian syndrome (PCOS), other systemic diseases and with the family history of DM, 48 women who had one or more positive OGTT value of 75mg OGTT with lesser degree of glucose intolerance, were included in this study via convenience sampling technique and was given a second test in the after 2~3 weeks of first test but 18 of them failed to reproduce the same result as the first test. They had negative fasting blood glucose in each subsequent monthly antenatal visit (Figure 1).

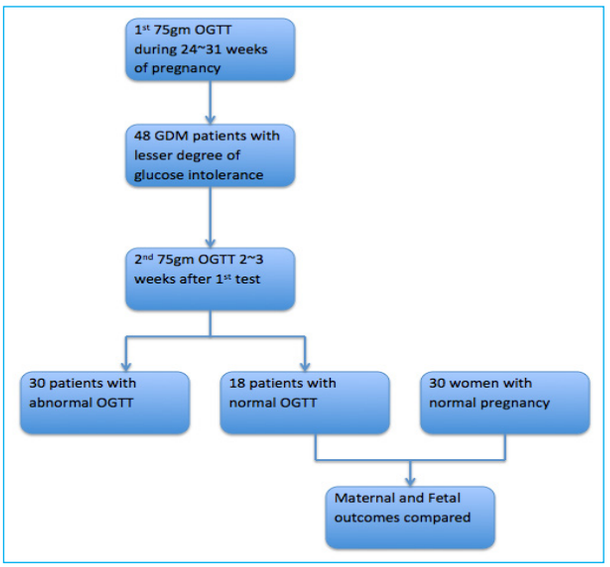

Figure 1. Flow chart showing method of the study.

For the control group we included 30 women with normal pregnancy, without the history of any other systemic disease. These women were also observed throughout their pregnancy.

The pregnancy duration of the 18 women included in our test was very closely monitored and all the ante partum data were collected. The postpartum data of the mother were collected after the delivery and so was the postnatal data of neonate. These data were compared with the similar data collected from 30 normal pregnant women, which was our control group, and seen if any actual difference was present or if there was any abnormality in the pregnancy and outcome of the 18 women who tested positive for GDM in 1st 75mg OGT test with IASDPG criteria.

This study was approved by the Ethics Committee of the First Affiliated Hospital of Chongqing Medical University, China. All patients who participated in this study have agreed to the written informed consent.

RESULTS

The mean values of all the data of control group and case group were compared. T-test of mean values between case and control group at p=0.05 doesn't give significant difference and any actual difference is likely to be due to chance (Table 1).

Table 1. Comparison of means of different categories between case and control group.

Categories	Case (n=18)	Control (n=30)	df= 46
Maternal AGE			
Mean	29.39		27.60
Standard Deviation	3.05		3.90
Standard error	0.7190		0.7120
P value			0.9332
T-test probability			8.43%
B.M.I. (Body Mass Index)			
Mean	21.01		20.43
Standard Deviation	2.20		2.22
Standard error	0.5185		0.4053
P value			0.7008
T-test in percentage			38.66%
G.A. (Gestational Age)			
Mean	277.56		279.00
Standard Deviation	6.14		4.49
Standard error	1.4472		0.819
P value			0.6966

T-test in percentage		39.24%
Baby Birth weight		
Mean	3328.61	3273
Standard Deviation	303.09	329.79
Standard error	71.4389	60.2111
P value		0.5814
T-test in percentage		55.52%
TBL (Total Blood Loss)		
Mean	188.33	182.00
Standard Deviation	65.46	77.48
Standard error	15.4290	14.1458
P value		0.4511
T-test in percentage		76.00%

On the 18 women (case) studied the mean age was 29±3.05 years and on the 30 women (control) studied mean age was 27±3.90 years, there was no significant difference in the two groups (29±3.05 years versus 27±3.90 years, P=0.93). BMI before pregnancy was also similar in both the groups (21.01±2.20 versus 20.43±2.22, P=0.70) so was the gestation age of the women in both groups. Gestational age was converted in days from weeks and was statically measured between two groups (277.56±6.14 days versus 279.00±4.49 days, P=0.69) showing the mean days between the two groups was statically similar.

The categories compared between two groups after the delivery also had similar results. Baby birth weight in the two group was similar (3328.61±303.09 grams versus 3273±329.79 grams, P=0.58) showing no significant difference between the means of two groups and so was in the case of total blood loss of the mother after delivery (188.33±65.46 ml. versus 182.00±77.48 ml., P=0.45) there was no significant difference.

All the categories compared for both case and control had similar results (Figure 2). Results of all the compared categories were within the normal range. None of the patients had any abnormality during pregnancy or after the delivery.

The 18 case studied, which otherwise would have been diagnosed with GDM, none of them had preterm delivery; no one developed preeclampsia or any other complication during the pregnancy. The babies born to all these 18 women, none of the them was presented with shoulder dystocia or large for gestation, none of the babies had abnormal APGAR score and no one needed admission in NICU, all of them were of average weight with normal APGAR scores in 1, 5 and 10 minutes.

The eutocia or cesarean section done was by the choice of the mother, none of the cesarean done was out of complication. The ratio of eutocia versus cesarean section, in both groups, is shown in (Figure 3).

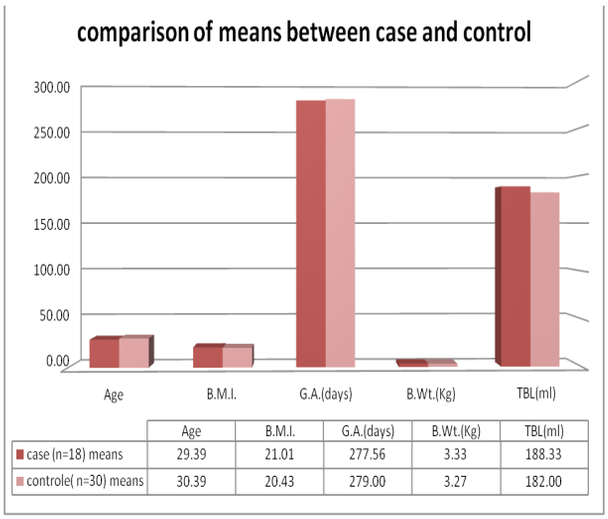

Figure 2. Bar diagram showing the means of different categories between case and control group.

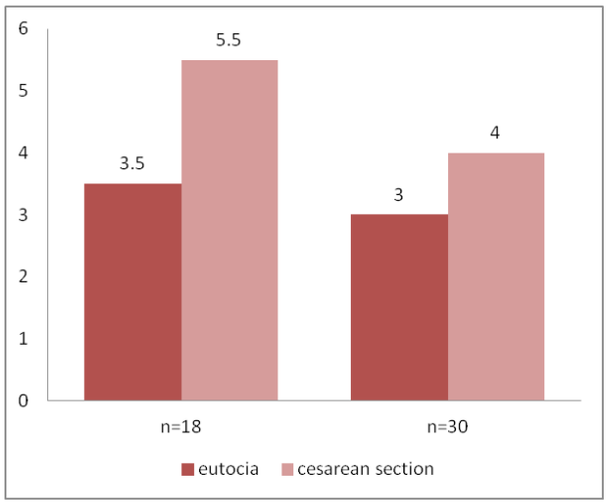

Figure 3. Bar diagram showing Eutocia to C/S ratio.

DISCUSSION

OGT test is of great importance in the diagnosis of GDM. Several different organizations have their own cut off values of this test for the diagnosis of GDM (Table 2). IADPSG criteria have been recognized by different country as more convincing than others. IADPSG has decreased the incident of perinatal complication. Even in china, a study shows that IADPSG has been proven to be reasonable to use.[7] However, in our study, some of the women diagnosed as GDM with lesser degree of glucose intolerance in IADPSG criteria failed to produce

the same in second test. These women, who would be diagnosed as GDM on the basis of IADPSG, had no negative fetal outcome even without the treatment. No statically significant difference was noted between normal pregnancy outcome and these women.

It is a known fact that IADPSG test criteria cut-offs is based on Hyperglycemia and Adverse Pregnancy Outcome (HAPO) data of 23,316 pregnant women, in which 4,150 cases of gestational diabetes would be diagnosed with the new criteria based on an OR risk for adverse outcomes of 1.75 and equivalent to category 5 cut-offs, resulting in prevention of 221 cases of LGA (large for gestational age), 48 cases of shoulder dystocia and 34 cases of birth injury.[8,9] It is the only test covering all the patients, while the tests with selective criteria leaves 50% of the patients undiagnosed[10] but to treat all these extra 50% women just to avoid some cases of perinatal complication is debatable. Even current IADPSG criteria of OR risk for adverse outcomes 1.75 which includes extra 1702 cases of gestational diabetes, compared to the OR risk for adverse outcomes of 2.00, expects to avoid just 140 cases of LGA, 21 cases of shoulder dystocia and 16 cases of birth injury.[11]

There are studies suggesting that untreated GDM has higher rate of prenatal complication like LGA, shoulder dystocia and associate birth injuries.[8,12-14] Yet there is a study suggesting that 78% of cases of LGA will be born to women not diagnosed according to these criteria, as maternal obesity is a stronger predictor of LGA than maternal glycaemia.[11] Therefore, it is hard to say if treating these many extra patients with gestational diabetes is worth this benefit or not.

Without selectiveness of the individual taking OGTT in IADPSG criteria, the prevalence of the women being diagnosed GDM with lesser degree of glucose intolerance

Table 2. Different diagnostic test for GDM.

Organization	Type of test	Glucose load (g)	Cut-off points	Who should be screened?
WHO 1999	One-step	75	FPG: 126 mg/dl (7.0 mmol/7) OR 2-h: 140 mg/dl (7.8 mmol/l)	Not mentioned
ADA 2003	Fasting or random non-challenge test in general. The OGTT recognized as a Valid test	NA	FPG: 126mg/dl (7.0 mmol/l) Random: 200 mg/dl (11.1 mmol/l)	Selective
Fifth International Workshop Conference on GDM 2007	Two- or one-step	50 (GCT) and 75 *OR* 100 (OGTT)	GCT: 140 mg/dl (7.8 mmol/l) or 130 mg/dl (7.2 mmol/L) OGTT 75 g: FPG 95 mg/dl (5.3 mmol/l) 1-h 180 mg/dl (10.0 mmol/l) 2-h 155 mg/dl (8.6 mmol/l) 3-h 140 mg/dl (7.8 mmol/l) – 3 h only measured for 100 g OGTT	Selective
NICE 2008	One-step	75	FPG 126 mg/dl (7.0 mmol/l) 2-h: 140 mg/dl (7.8 mmol/l)	Selective
ADA 2010	Two- or one-step	50 (GCT) and 100 (OGTT)	GCT: 140 mg/dl (7.8 mmol/l) or 130 mg/dl (7.2 mmol/L) OGTT: FPG 95 mg/dl (5.3 mmol/l) 1-h 180 mg/dl (10.0 mmol/l) 2-h 155 mg/dl (8.6 mmol/l) 3-h 140 mg/dl (7.8 mmol/l)	Selective
IADPSG 2010	One-step	75	FPG 92 mg/dl (5.1 mmol/l) 1-h: 180 mg/dl (10.0 mmol/l) 2-h: 153 mg/dl (8.5 mmol/l)	Universal
ADA 2011	One-step	75	FPG 92 mg/dl (5.1 mmol/l) 1-h: 180 mg/dl (10.0 mmol/l) 2-h: 153 mg/dl (8.5 mmol/l)	Universal

has increased dramatically, to these women the benefits of therapy are modest. As IADPSG has a lowest cut offs than any other criteria and with its single value positive diagnosis, it is possible that more false positive cases with no risk of having prenatal complication are being treated with GDM.

Moreover, with high risk diagnosis like GDM, irrespective of the degree of glucose intolerance, there always exist chances of pregnancy resulting into the interventions like earlier delivery, cesarean section and admission of the neonates in special care nurseries. Therefore, the proposed diagnostic cutoffs have to be considered.

In 1964, O'sullivan and Mahan proposed criteria for diagnosis of GDM to indicate a higher chance of developing type 2 diabetes mellitus for the mother.[15] It didn't mention perinatal or postnatal complication. With the introduction of the IADPSG criteria in 2010, as it is based on HAPO study of negative fetal outcome, more focus has been shifted towards the short term fetal issues than the long term maternal issues. In HAPO study, maternal issues, outcome or follow up however was not addressed.[8]

Studies has been carried out with more focus in perinatal complication with IADPSG, but none of the studies has been carried out to determine how many of these women will fall in the low risk perinatal complication zone and how many will be falsely diagnosed with this test. Neither any other large group studies has been carried out to determine how many women with the current IADPSG is converted into overt diabetes. Even though, almost all the clinical trials suggest the increase incidence of GDM with IADPSG cut offs, no exact false positive rate has been issued with this test.

In our study of 18 women diagnosed as GDM by the 1st test with 2nd normal test, all had normal pregnancy and fetal outcome. So, it would be quite unfair to these women if they would be diagnosed or treated as GDM. But according to IADPSG, all of these women would be diagnosed as GDM and when a diagnosis is made, the treatment follows too. Therefore, the cut offs should be corrected in such a way that it can cover the actual high-risk patient with GDM who negative fetal outcome without treatment will actually have, sparing the patient with very minimal to no chances of having negative fetal outcome.

CONCLUSIONS

Administration of 75gm OGTT with IADPSG criteria, 37.5% of women failed to produce same test twice and there was no significant difference between mean values. Therefore, a bigger and stronger study involving both maternal and perinatal complication must be carried out to establish new cut-off criteria for OGTT which can justify all cases being diagnosed with GDM.

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