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GESTATIONAL DIABETES;

SENSITIVITY, SPECIFICITY AND DIAGNOSTIC ACCURACY OF GLUCOSE CHALLENGE TEST IN DIAGNOSIS

Dr. Ayesha Snover[1], Dr. Kinza Alam[2], Dr. Tahir Ahmad Munir[3], Dr. Rabia Sajjad[4], Dr. Farhat Naz[5]

1. Assistant Professor
   Rawal Institute of Health Sciences, Islamabad
2. Assistant Professor
   Rawal Institute of Health Sciences, Islamabad
3. Associate professor
   Rawal Institute of Health Sciences, Islamabad
4. Classified Gynaecologist
   CMH Sargodha
5. Associate professor
   Jinnah Hospital Lahore

Correspondence Address:
Dr. Kinza Alam
House No 36A, Rose Lane 2
Lalazar-I, Rawalpindi Cantt
drkinzairfan@gmail.com

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ABSTRACT… Objective: To find sensitivity specificity and diagnostic accuracy of Glucose Challenge test in diagnosing Gestational Diabetes in Pregnant women. Due to poor socio-economical and educational status, dietary habits and ignorance regarding pregnancy related problems probably increase the prevalence and burden of gestational diabetes mellitus (GDM) and its complications in pregnancy. Best and simple strategy to identify women with gestational diabetes is still lacking and unclear. **Study Design:** Cross sectional study. **Setting and Duration:** This study was performed at Jinnah Hospital Lahore, from Nov 2005 to Dec 2006. **Methodology:** A glucose challenge test (GCT) was performed on 500 selected pregnant women by giving 50-g glucose in water orally. A serum glucose level ≥140 mg/dl after an hour was taken as positive test. To confirm GDM, 75 g glucose in 200 ml of water was given and sugar levels after 2 hrs by Glucometer, >200 mg/dl confirmed GDM. **Results:** An increasing trend in age, gestational age and BMI and a significant difference regarding positive family history of diabetes and gravidity was seen in patients with GDM compared to normal pregnant. The maximum percentage of GDM was noted in multigravida, between 25-29 years, BMI >28kg/m^2, and a gestational age of 28 weeks. The sensitivity of GCT was 80%, specificity 97.8%., and diagnostic accuracy was 96.4%. **Conclusions:** Screening is necessary to identify women with GDM. A 50-g glucose challenge test might be acceptable as a screening test for GDM as it has high sensitivity, specificity and diagnostic accuracy.

Key words: Glucose Challenge test, Sensitivity, Specificity, gestational diabetes mellitus

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INTRODUCTION

Gestational diabetes mellitus (GDM) is defined as any degree of glucose intolerance with onset first recognized during pregnancy and commonly recognized after 20 weeks gestational age[1]. This condition is associated with increased risks for the fetus and newborn, including macrosomia, shoulder dystocia, birth injuries, hyperbilirubinemia, and hypoglycemia, respiratory distress syndrome, childhood obesity, and have an increased risk for the development of type 2 diabetes later in life[2,3]. Maternal risks include preeclampsia, cesarean delivery, and an increased risk of developing type-2 diabetes within 5–15 years of delivery. The prevalence varies significantly among different populations and ethnicities, as well as with the diagnostic criteria used[2-5]. Specific risk factors and the degree of their influence on GDM prevalence are difficult to quantify across populations. However, a number of clinical risk factors have been demonstrated to be associated with an increased likelihood of GDM, including age, ethnicity, and obesity, family history of diabetes, past obstetric history and in populations with a high risk of type 2 diabetes mellitus like American Indians, African Americans, Hispanic/Latino Americans, and Asian Americans[4-6].

However, recently it has been demonstrated in a number of high-quality studies that the risk of a number of important complications associated

with GDM, can be reduces by treatment of GDM with diet or insulin thus improving both perinatal as well as maternal outcome from 4% to 1%[7,8].

In our country, the major portion of the population lives in rural areas with meager facilities in terms of health care delivery. Poor socio-economical and educational status, dietary habits, ignorance regarding pregnancy and pregnancy related problems operate unfavorably and probably increase the burden of GDM. However social practices, taboos associated with pregnancy, unauthorized practitioners and overlook of such conditions even by specialists, due to lack of sensitivity towards importance of this situation have a strong influence on the prevalence of GDM and its complications in pregnancy.

Identifying women with GDM in order to provide treatment has therefore become of eminent importance, but is difficult as clinical signs and symptoms are often absent. Because of the lack of clinical signs and symptoms of GDM, screening tests are essential to identify women with GDM. One of the tests that is used in the diagnostic pathway is the 50-g glucose challenge test[9]. Although currently the 50-g glucose challenge test (GCT) is not recommended in the majority of national guidelines, it could be a useful test in the diagnostic work-up of GDM[10]. Since the two hour oral glucose tolerance test (GTT) is a very time consuming method, but can be used as alternative in patients with high risk factors.

Recently in line with the Expert Committee's recommendation, the World Health Organization and the American Diabetes Association subsequently adopted a hemoglobin A1C level of 6.5 percent or higher as a new diagnostic criterion for diabetes. For people who do not have diabetes, a normal hemoglobin A1C level is around 5%[11].

The aim of this study was to analyze the accuracy of the 50-g glucose challenge test for detection of glucose intolerance in pregnancy in order to evaluate its applicability as first-step screening test for GDM; with its sensitivity, specificity to current oral glucose tolerance test (OGTT).

MATERIAL AND METHODS

This cross sectional study was carried out at department of obstetrics and Gynecology (unit II) Jinnah Hospital Lahore during 2005 to 2006. The sampling technique used was convenient non probability technique. The pregnant women of all parity, with a gestational age of 24-28 weeks, and got registered at Gynae and Obs unit II, Jinnah Hospital Lahore, were included in the study. The pregnant women with known diabetes mellitus, other morbid diseases like heart disease or malignancy, or taking drugs that alert blood glucose level like steroids were excluded from the study. A total of 500 pregnant women were included in the study using convenient non probability sampling technique.

At 1st visit we evaluate the patients for age, duration of pregnancy, gravidity, any obstetric history of all major events, relevant personal history especially dietary habits, nutritional status, past history of any other major illness, history of diabetes in 1st degree relatives and complication related to present pregnancy. General examination included measurement of height, weight and B.P., obstetric examination, and base-line investigations were done if necessary.

Method of performing GCT

Screening test for GDM was performed by giving 50 gm. glucose orally to the patient at any time of the day without dietary preparations. Patient was asked not to take any oral in between. The serum glucose was measured one hour later. If the blood glucose one-hour value was =140 mg/dl the screened test was taken as positive; and with <140 mg/dl was taken as negative.

Method of performing OGTT

This test was performed on all patients who underwent GCT according to WHO recommendations. 75 gm of glucose was dissolved in 200 ml of water and the patient was asked to drink it within 5 minutes. The time was noted and the patient was asked to come back after an hour for the test. A capillary blood specimen was obtained and tested for blood sugar levels by Medisense Optimum Glucometer that works by electrical current

produced by chemical reaction between glucose and glucose dehydrogenase, NAD, and phenanthelin quinine present on the glucose strip.If the blood sugar levels were greater than 140mg%, the test was considered positive and these patients were subjected to OGTT to confirm the diagnosis of gestational diabetes.

The sensitivity, Specificity, diagnostic accuracy and Predictive values of Glucose Challenge test was find out by the following formulas[10].

Sensitivity Test for GCT

Sensitivity Rate = 100 x True Test / (True Positive + False Negative)

Specificity Test for GCTs

Specificity Rate = 100 x True Negative / (True Negative + False Positive)

Diagnostic Accuracy

Diagnostic Accuracy = 100 x (True Positive + True Negative) / (False Positive + False Negative)

Predictive Value for Positive Test

Positive Predictive Value = 100 x True Positive / (True Positive + False Positive)

Predictive Value for Negative Test

Negative Predictive Value = 100 x True Negative / (True Negative + False Negative)

STATISTICAL ANALYSIS

Statistical analysis was done using SPSS 17, Chicago, Illinois. Chi-square test was performed to assess the statistical significance by p values of =0.05 were considered significant. The results are given as mean standard deviation (SD) for normally distributed data and as frequencies (n)and percentages (%) for nominal data.

RESULTS

Table-I shows the demographic data of the patients. The mean age of the study group was less than 25 years. Out of 500 pregnant women who underwent GCT and OGTT, only (n=40) 8 percent of pregnant women were found positive for gestational diabetes. Out of 40 GDM patients only 3.4% (n=17) have positive family history of diabetes mellitus. Concerning the BMI, the GDM patients have slightly higher but non-significant body mass index compared to non-diabetics. The mean gestational age was slightly higher in patients of GDM compared to non-GDM women. The main bulk of the study population and GDM were formed by multiparous women.

Table-II shows demographic analysis of patients with Gestational Diabetes mellitus.

The maximum number of patients with positive GDM has age duration between 25-29 years, while the patients above 30 years showed least evidence of GDM. The multigravida showed a significant to develop GDM compared to pimigravida, while a less percentage (42.5%) of GDM have a positive family history of diabetes mellitus. The GDM was significantly more in patients having a BMI more than 28 kg/m^2 compared to those with BMI <27 kg/m^2. The GDM also showed a relation with duration of gestation, the patients having more gestational age have more percentage of GDM.

Demographic Variables	Gestational Diabetes (n=40)	Normal Glucose tolerance (n=460)	Total (n = 500)	p value
Age (years)	25.03 ±2.9	24.63 ± 4.3	24.7 ± 4.10	>0.05
Gestational Age (weeks)	26.17 ± 3.37	25.96 ± 3.27	26.1 ± 3.30	>0.05
BMI (kg/m^2)	26.6 ± 3.99	25.24 ± 4.02	26.40 ± 4.1	>0.05
Family H/O diabetes mellitus	17 (3.4%)	483 (96.6%)	500 (100%)	<0.001
Gravidity	40 (8%)	460 (92%)	500 (100%)	<0.001

Table-I. Demographic data of the experimental group

Values are expressed as Mean ± SD and Percentage. BMI = Body mass index Kg/m = Kilogram per meters H/O = History of

Variables	Number (n=40)	%age	Chi square	p value
Age (years)				
<20	4	10		
20-24	15	37.5	24.2	0.000
25-29	20	50		
≥ 30	1	2.5		
Gravidity				
Primigravida	14	35	3.60	0.05
Multigravida	26	65		
Family History of DM				
Positive	17	42.5	0.90	0.34
Negative	23	57.5		
BMI				
≤ 27 kg/m^2	15	37.5	2.51	<0.001
≥ 28 kg/m^2	25	62.5		
Gestational week				
24	3	7.5		
25	4	10		
26	8	20	7.7	>0.05
27	10	25		
28	15	37.5		

Table-II. Distribution of Gestational Diabetes Mellitus women by different variables

DM = Diabetes Mellitus BMI = Body mass index

Test	Value	Sensitivity rate = 100(32/32 +8) = 80%
True Positive	32	Specificity rate= 100 (450 / 450 +10) = 97.8%
True Negative	450	Diagnostic Accuracy = 100 (32 + 450/32 + 450+10 + 8) = 96.4%
False Positive	10	Positive Predictive value = 100 (32/ 32 + 10) = 76.1%
False Negative	8	Negative Predictive Value = 100 (450 / 450 +8) = 98.2%

Table-III. Sensitivity, Specificity, Diagnostic Accuracy, and Positive and Negative Predictive Value for Glucose Challenge Test

A total of 500 patients were screened for gestational diabetes by glucose challenge test. Only (n=40), 8% patients showed a positive GCT. The oral glucose tolerance test was performed on patients who showed positive GCT; a true positive OGTT was detected in 32 patients, while false positive in 10 patients. Out of 500 patients, 458 showed negative GCT, out of which 450 were true negative and 8 were found to be false negative by OGTT. On the whole, out of 500 patients, 40 were diagnosed as GDM by OGTT.

The sensitivity of GCT was 80%, and specificity 97.8%., while the diagnostic accuracy was 96.4%. The positive predictive value of GCT was 96.2%, while negative predictive value was 85.4%.

DISCUSSION

Our result showed 8% of the patients diagnosed as GDM, which is in consistence with a number of studies[12,13] who reported prevalence for GDM ranges from 1%-14% of all the pregnancies, depending upon population studied and diagnostic criteria used. However, the results were found to be contradictory with Ramirez et al[14] who reported the GDM prevalence of 17.2%, the

difference may be due to ethnic group and duration of study.

It is universally accepted that the incidence of GDM is high in Asian, Mexicans, Native Americans and African-American women[15].

Out of the 40 gestational diabetic patients, the maximum of 20 patients (50%) belonged to the age group of 25-29 years and 15 patients (37.5%) were between 20 to 24 years i.e.8 7.5% of all the gestational diabetic patients were between the ages of 21 to 30 years. Coustan et al reported a similar finding of 56% of GDM cases under 30 years of age[16]. Similar conclusion has been reported by Hughes et al with maternal age ranging from 17 years to 41 years among the positive cases, mean age being 29.4 years[17]. However Green et al opined that there was an increased incidence of GDM with increasing age[18]. But Granat et al reported that only 18.7% of their patients were of older age group[19].

In present study it is turned out that GDM has more association with larger BMI. The results are in agreement with Cypryk et al[20] who concluded that women with BMI >30, have greater risk of developing GDM. Nohira et al[21] also reported that women with increased weight gain during pregnancy have greater chance to develop GDM during pregnancy.

There is a general agreement regarding increasing age and parity as one of the most common risk factor for developing GDM. We observed an incidence of 35% GDM individuals in primigravida and 65% in multigravida. Our results are in agreement with a number of studies (John et al Al-Rowaily et al[22,23] who found a higher incidence (59.9%) of GDM in multigravida, while the results from Jawa et al[24] has noticed more occurrence of GDM in primi gravida 42.7%, however, Granat et al did not find any correlation between parity and alterations of carbohydrate metabolism in their study[19].

Various factors help in identifying women who are at higher risk of developing abnormal glucose tolerance during pregnancy. The most important of these being past history of diabetes in first degree relatives, still birth and birth of overweight infant. In our study we observed that 17 out of 40 (42.5%) cases of gestational diabetes had a positive history of diabetes in first-degree relatives. Rhee and Catherine also reported more than 50% cases of GDM with positive history of diabetes in first-degree relatives respectively in their series[25,26]. However Campbell et al observed that only 9% of his GDM cases gave a history of diabetes in first-degree relatives[27].

We in this study use GCT and then who were positive for GCT underwent OGTT. In many potentially relevant studies dealing with the 50-g glucose challenge test in pregnant women, the OGTT was only performed if the 50-g glucose challenge test was considered to be abnormal. This design characteristic, known as partial verification, is encountered in many studies on diagnostic accuracy: to minimize the burden of possibly redundant additional testing in women with a negative screening test result, only abnormal screening test results are verified by the reference test[28].

Depending on the application of the test (screening or alternative diagnostic) and the consequences of false-positive and false-negative test results, certain combinations of accuracy values are preferred. These values depend on whether it is more harmful to classify women as false-positive or false-negative, taking all possible consequences of such results into account. In the case of GDM, regarding the nature and consequences of the disease, one should aim for an adequate detection rate, albeit not at the cost of an unacceptable false-positive rate. If the 50-g glucose challenge test is used as a screening test, a higher sensitivity rate than74% would probably be warranted to accept a false-positive rate of 83%. Moreover, if one considers using the 50-g glucose challenge test as a diagnostic test for GDM, higher detection rates are required. As the prevalence of GDM in the general population is relatively low, a clinically useful test would thus have to have a high positive LR (>10)[29].

A glucose loading test like the 50-g glucose challenge test in theory seems an adequate method to mimic post prandial glucose levels, and therefore to measure the degree of glucose (in) tolerance in pregnancy. A health technology report concerning various screening strategies for GDM stated that the cost-effectiveness of a number of studies find that screening with the 50-g glucose challenge test, and then testing screen-positives with the OGTT, was less costly than going straight to universal OGTT. However, a high-quality cost-effectiveness analysis developed by the UK's National Institute for Health and Clinical Excellence (NICE) guideline development group found that two screening strategies dominated: selection by American Diabetes Association (ADA) criteria, followed by the 75-g OGTT; and selection by high-risk ethnicity, followed by the 75-g OGTT. In view of these findings and as an extension to the results of the cost-effectiveness analysis of the NICE guideline development group, it would be interesting to consider the cost effectiveness of a strategy that consists of selection based on various risk factors, followed by screening with a 50-g glucose challenge test, followed by an OGTT in the case of an abnormal test result of the 50-g glucose challenge test, and to compare this in a randomized controlled trial with other screening strategies[10].

CONCLUSIONS

Screening is necessary to identify women with GDM. High sensitivity is often warranted in screening tests, as a false-negative test result (in which disease remains undiscovered) is considered to be more harmful than a false-positive test result (in which a reference test is unnecessarily performed). A good detection rate of the 50-g glucose challenge test might be acceptable as a screening test for GDM.

Using the OGTT for screening could be a lesser burden and more cost-effective than a two-step method in which a glucose loading test might be performed twice. As the sensitivity of GCT was 80%, specificity 97.8%., diagnostic accuracy 96.4%; positive predictive value 96.2% and negative predictive value was 85.4% so the 50-g glucose challenge test can be used as diagnostic test for GDM.

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