Impact Of Positive GCT With Negative Oral GTT On Perinatal Morbidity: Prospective Cohort Study

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Abstract

Background: Abnormalities in glucose metabolism during pregnancy can lead to significant adverse perinatal outcomes, while the effect of minor glucose metabolism abnormalities is poorly understood.

Objectives: This study was designed to investigate the impact of a +ve glucose challenge test on perinatal morbidity.

Patients and methods: This is a prospective cohort study at Ain Shams University Maternity Hospital that included 200 pregnant women with singleton pregnancies at 24-28 weeks of gestation. These patients were at high risk of developing GDM. A glucose challenge test (GCT) was done on all patients. It was divided according to results into two groups of 100 patients each, a group with positive (GCT) and negative 100 gm glucose tolerance test, and a group 2 patients with negative (GCT) All patients were followed till delivery, documenting adverse maternal or perinatal outcomes. The primary outcome was fetal macrosomia, while secondary outcomes were shoulder dystocia, preterm labor, pregnancy-induced hypertension, NICU admission, and neonatal death.

Results: Among 200 patients included in the study, BMI was 30.17±4.48 in the study group vs 28.31±4.5 in the control group with a P value of 0.004, macrosomia was in 22 (22%) in the study group vs 7 (7%) in the control group. And 19 (19%) cases in the study group need NICU admission vs. 10 (10%) cases in the control group with a P value of 0.032. No significant differences were observed between study groups as regards age, GA, parity, APGAR score at 5 min, shoulder dystocia, PTL, PIH, and neonatal death.

Conclusion: A positive oral glucose challenge test only without gestational diabetes is a risk factor for perinatal morbidity like LGA and NICU admission, so early screening for GDM is advisable.

Key words: glucose challenge test, glucose tolerance test, pregnancy, gestational diabetes, macrosomia, perinatal morbidity.

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BACKGROUND

Carbohydrate metabolism undergoes significant changes during pregnancy especially in the second half leading to a state of glucose intolerance and physiological insulin resistance (1). Gestational diabetes is defined as carbohydrate intolerance first diagnosed during pregnancy (2). It is commonly affecting about 2% -5% of pregnant ladies.

Due to well-known adverse pregnancy outcomes caused by diabetes and affecting both mother and newborn as fetal growth abnormalities mainly macrosomia ,birth traumas and neonatal chemical imbalances such as hypoglycaemia which in turn increases incidence of NICU admission (3),screening for gestational diabetes is recommended by ACOG to be done between 24-28 wks gestation.

They recommend two-step screening and diagnostic procedure, 1st step screening using 50-g glucose challenge test (GCT) then if positive test result(blood sugar ;130-140mg/dl), diagnostic 100 gm, 3-hour glucose tolerance test (OGTT)should be done.

All previously mentioned adverse outcomes are directly related to blood sugar control ,blood sugar adjustment should be the goal during antenatal care.

Adverse effect of minor abnormalities in glucose tolerance such as women with single high reading on OGTT or with +ve screening by GCT and -ve confirmatory test is not well understood but supposed to be increased (4).

So our study aimed to investigate the impact of positive glucose challenge test and negative OGTT on perinatal morbidity.

PATIENTS AND METHODS

This is a prospective cohort study . It was conducted at Ain Shams University Maternity Hospital from January 2022 to September 2022. Study included 200 Pregnant women at 24-28 weeks of gestation, having singleton pregnancy ,Who has high risk of developing GDM such as maternal age>35, Previous polycystic ovarian syndrome, Long-term corticosteroid use, BMI > 30 kg/m2, Previous gestational diabetes, while patients known to be diabetic, women having GCT result >200 mg/dL ,women who had abnormal OGTT during follow up , with Fetal malformations or hydrops were excluded from the study . The study was conducted after approval of Research Ethical Committee, faculty of medicine of Ain Shams University.

After detailed discussion with patients, all were accurately informed about the steps of the study and a written informed consent was taken from each patient after full explanation of the study procedure . All patient participated in this study were undergone the following procedures: full history taking include detailed obstetric history ,family history especially for DM ,general examination ,BMI calculation ,abdominal examination and symphysiofundal height measurement ,obstetric ultrasound to assess fetal biometry and exclude anomalies.

300 pregnant women were recruited for the study after matching inclusion criteria for all of them GCT was done using 50 gm glucose (without fasting) , positive test if blood sugar more than or equal 140mg/dl (5), then patients were divided according to results into +ve screening group(study group) and -ve screening group(control group) .

Patients were advised to a full carbohydrate diet for three days before the test. They were instructed to come on the fourth day with at least fasting for 8 hours; the first sample was taken as a fasting sample; they were given a standard 100 gm juice and instructed to drink it slowly. After they finished by 1 hour the second sample was withdrawn then 2 hour and 3rd hour samples. (Carpenter & Coustan criteria Table 1).

Negative patients were taken if zero or one abnormal values oly was present . Patients

with positive test were excluded from the study (n=50) remaining patients from both groups (n=250) were followed regularly every month till delivery if patient developed of PIH (defined as new-onset hypertension with systolic blood pressure >140 mm Hg or diastolic > 90 mm Hg on two occasions at least 6 hours apart,with or without proteinuria based on 2002 ACOG diagnostic criteria, status of the liquor ,any preterm labour before 37 wks gestation was recorded and perinatal outcomes was followed up in terms of macrosomia (birth weight>4000 gm), hypoglycemia, hyperbilirubinemia, shoulder dystocia, birth weight, Apgar score at 5 minutes of life of < 7, admission to the neonatal intensive care unit (NICU), stillbirth or neonatal death, , and respiratory distress syndrome. 50 patients were also dropped out during follow up so 200 pregnant women were only finally analysed.

Induction protocol

Patients underwent controlled ovarian stimulation using the long GnRH agonist protocol for pituitary down-regulation. Ovarian stimulation was done by human menopausal gonadotropin (HMG)(Merional IBSA,Switzerland). The initial dose of HMG was individualized for each patient according to age, FSH level, antral follicle count (AFC) and BMI. Dose adjustments was performed according to ovarian response, which was monitored according to TVS and E2 levels. Serum progesterone was performed on the day of hCG administration (Chorioumon ,IBSA,Switzerland)which was given if 3 or more follicles reached 18 mm.

Blood sample	National Diabetes Data Group Criteria	Carpenter and Coustan Criteria
Fasting	105 mg/dL (5.8 mmol/L)	95 mg/dL (5.3 mmol/L)
1-hour	190 mg/dL (10.5 mmol/L)	180 mg/dL (10.0 mmol/L)
2-hour	165 mg/dL (9.2 mmol/L)	155 mg/dL (8.6 mmol/L)
3-hour	145 mg/dL (8.0 mmol/L)	140 mg/dL (7.8 mmol/L)

Table (1): Criteria for Abnormal Result of 100 g,Three-Hour Oral Glucose Tolerance Tests in Pregnant Women

Sample size calculation: was done using the rate of fetal macrosomia in pregnant women with high risk for diabetes. As reported in previous publication(6) ,the proportion of fetal macrosomia in pregnant women with positive glucose challenge test was approximately 20%, while in pregnant women with negative glucose challenge test it was approximately 5%, both groups had normal 3h oral glucose tolerance test Accordingly, we calculated that the minimum proper sample size was 100 participants in each group to be able to reject the null hypothesis with 80% power at $\alpha = 0.025$ level using Chi-square test for independent samples. Sample size calculation was done using MedCalc® Statistical Software version 19.5.3 (MedCalc Software Ltd, Ostend, Belgium; https://www.medcalc.org; 2020).

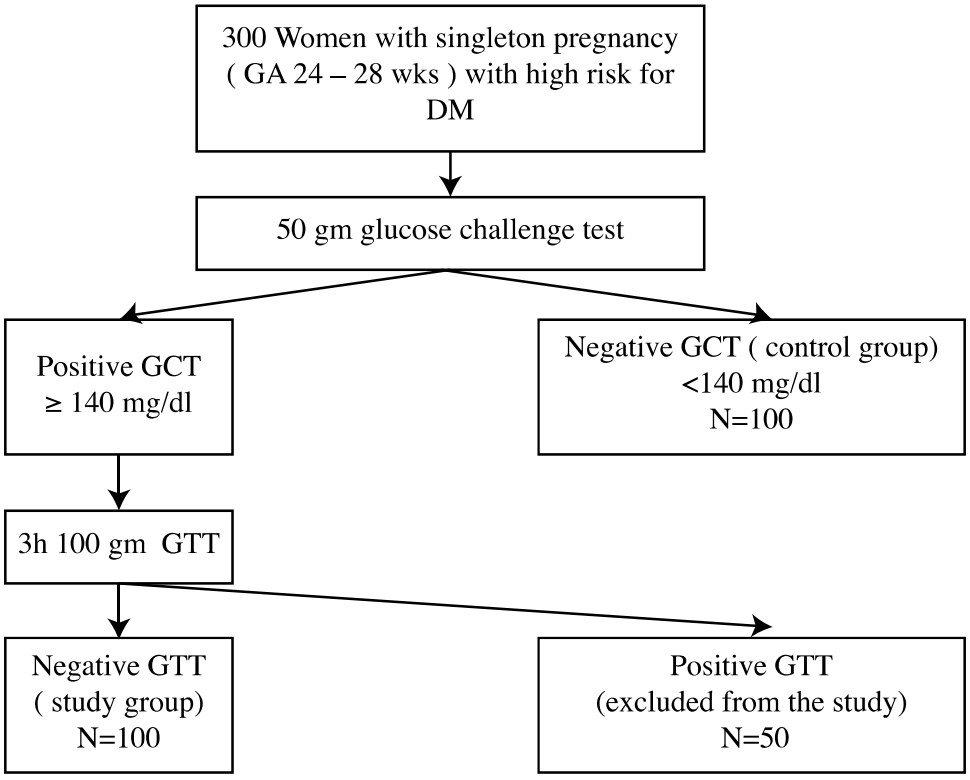
Statistical analysis:

The Social Package of Statistical Analysis ver. 24 was used for data collection, tabulation, and analysis (IBMCorp., Armonk, New York). Kolmogorov–Smirnov test test was used to check the normal distribution. We used the mean and SD to express the normal distributed numerical data, and we used median and interquartile range for the numerical skewed data. The numbers and percentages were used for expressing the qualitative data. We used the unpaired t-test to

compare the normally distributed numerical data. Mann-Whitney test was used for comparing the skewed numerical data. If appropriate, the chi-squared test or Fisher's exact test was used for qualitative categorical data. P less than 0.05 was considered significant.

RESULTS

Figure 1:Flow chart for study participants



NB: 50 patients also were dropped out from the study during follow up from both groups.

Demographic characteristics of study participants :

Table (2) showed that there was no statistically significant difference between study groups as regard age, GA and parity while there was statistically significant difference between study groups as regard BMI which being higher in positive GCT (study group) than negative GCT (control group).

Table (2): Demographic characteristics of study participants

variable	Control group	Study group	P Value
Age[1]	28.82±6.16	29.47±5.98	0.449* NS
BMI[2]	28.31±4.5	30.17±4.48	0.004* HS
GA[3]	38.20±1.10	37.94±1.2	0.111* NS
Parity[4] • **PG** • **P1-3** • **P≥4**	 25 (25%) 58 (58%) 17 (17%)	 21 (21%) 63 (63%) 16 (16%)	0.746# NS

[1,2,3]Values (continuous quantitative data) are given as mean±SD, while 4Values (numerical data) are given as numbers (percentage)Kolmogorov–Smirnov test was used to examine the normal data distributional characteristics of age, BMI, GA of all study cases.

*t-test test for normally distributed data.

Chi-Square Testsused to determine P value

P value <0.05 significant so P value of study groups is not significant.

NS: non-significant, HS: highly signific

Maternal and neonatal outcomes are tabulated in **table (3)** showed that there was no statistically significant difference between study groups as regard birth weight, APGAR score at 5 min, shoulder dystocia, PTL, PIH and neonatal death while there was statistically significant difference between study groups as regard macrosomia as 22% of positive GCT cases had macrosomia compared to 7% of negative cases. Similarly, NICU admission was higher among positive cases compared to negative cases (19% vs. 10%). While table (4) showed that using logistic regression and after adjustment to all relevant factors, it was found that Positive GCT (study group) have higher risk for NICU admission compared to negative GCT (control group) (AOR=2.30, CI: 1.01-5.2).

Table (3):Comparison between study groups as regard pregnancy outcome

Variable	Control group	Study group	95% CI	P value
Birth weight	3189.5±408.02	3315.5±621	---	0.092* NS
APGAR score 5 min	8.56±0.84	8.37±1.09	---	0.17* NS
Macrosomia **No** **Yes**	 93 (93%) 7 (7.0%)	 78 (78%) 22 (22%)	3.74(1.5-9.2)	0.003# HS
Shoulder dystocia **No** **Yes**	 98 (98%) 2 (2.0%)	 96 (96%) 4 (4.0%)	2.04 (0.36-11.4)	0.683** NS
PIH **No** **Yes**	 86 (86%) 14 (14%)	 82 (82%) 18 (18%)	1.34(0.63-2.88)	0.440# NS
PTL **No** **Yes**	 93 (93%) 7 (7.0%)	 90 (90%) 10 (10%)	1.46(0.53-4.04)	0.447# NS
NICU **No** **Yes**	 90 (90%) 10 (10%)	 81 (81%) 19 (19%)	2.32 (1.06-5.3)	0.032# HS
Neonatal Death **No** **Yes**	 100 (100%) 0 (0.0%)	 100 (100%) 0 (0.0%)	-----	-----

*t-test test for normally distributed data.

Chi-Square Tests used to determine P value

**fisher exact test used to determine P value

P value <0.05 is significant so P value of study groups is not significant.

NS: non-significant, HS: highly significant

Table (4):Logistic Regression model to study independent factors affecting NICU admission.

	AOR*	P value	Sig.	95% Confidence interval for AOR	
				Lower	Upper
Age	.976	.588	NS	.895	1.065
GA	.728	.214	NS	.441	1.202
Parity	1.279	.193	NS	.883	1.851
Birth weight	1.000	.732	NS	.999	1.001
PIH	.663	.490	NS	.206	2.132
PTL	.697	.670	NS	.132	3.666
Positive GCT	**2.308**	**.045**	**S**	**1.018**	**5.234**

*Adjusted odds ratio

**Reference group Gravidity (one)

DISCUSSION

Main finding

In our study, there were no statistically significant differences between negative GCT and positive GCT regarding the sociodemographic data regarding age, GA, and parity. Still, BMI was higher in the positive group. Also, the present study showed no statistically significant difference between study groups regarding birth weight, APGAR score at 5 min, shoulder dystocia, PTL, PIH, and neonatal death. At the same time, there was a statistically significant difference between study groups regarding macrosomia, as 22% of positive GCT cases had macrosomia babies compared to 7% of negative points. Similarly, NICU admission was higher among positive patients than negative cases (19% vs. 10%).

Interpretation

In our study, there were no statistically significant differences between negative GCT and positive GCT regarding the sociodemographic data regarding age, GA, and parity. These results agreed with the study of Temming, et al. (6), who found no statistically significant differences between the normal GCT group and elevated GCT group regarding age and gestational age at delivery. The present study also showed that there was no statistically significant difference between study groups as regards birth weight, APGAR score at 5 min, shoulder dystocia, PTL, PIH, and neonatal death. At the same time, there was a statistically significant difference between study groups regarding macrosomia, as 22% of positive GCT cases had macrosomia babies compared to 7% of negative cases. Similarly, NICU admission was higher among positive and negative cases (19% vs. 10%). The study by Temming et al,2016, proved that women with elevated 1-hour GCT (normal GTT) had s an increased risk of CS, macrosomia, shoulder dystocia, preterm labor and difficult labor t among women. These findings suggest that patients with abnormal glucose testing below the threshold of GDM diagnosis are at risk of adverse obstetric outcomes (6). Similar to our study is that of Shinohara et al. on 2248 pregnant Japanese women at 24-28 GA; the primary outcome was the incidence of LGA. They performed a 1-hour glucose challenge test and OGTT. The incidence of LGA was 9.4% (211/2248), and the women with false +ve GCT results were 11.4% (257/2248). After adjusting the different variables (age, weight before pregnancy, parity, and weight gain during pregnancy, the False +ve Glucose challenge test results were significantly

associated with an increased risk of LGA (OR, 1.51; 95% CI, 1.02 to 2.23). [7-8]

Also, our study analyzed more risk factors for NICU admission with a relatively large sample size in Egyptian women. It showed that using logistic regression and after adjustment to all relevant aspects, it was found that case groups (Positive GCT) have a higher risk for NICU admission compared to (negative GCT) groups (AOR=2.30, CI: 1.01-5.2).

In the retrospective cohort study of Ankumah et al. 2016, 602 women with GDM were members of the study of singleton pregnancies complicated by GDM. They studied different maternal and neonatal outcomes; the maternal outcomes were CS rates, Type 2 DM, PET, and failed TOLAC. The neonatal outcomes were SGA, LGA, difficult labor, and shoulder dystocia. Their results showed that Shoulder dystocia (3.1 vs. 1.0%) and PET(16.4 vs. 10.6%) were increased significantly in the group of women diagnosed with GDM using 1-hour GCT ≥ 200 mg/dL than those with women diagnosed by GDM using a +ve OGTT following a 1-hour GCT of 135-199 mg/dL with adjusted odds ratio and 95% confidence interval were 1.80 (1.10-2.94) and 5.10 (1.25-20.76), respectively (9).

Conversely, Freidman et al performed a retrospective study chart review that included 387 black pregnant patients to assess the incidence of GDM(between 24 and 28 weeks) according to various 1-hour GCT different cut-off values (they used 130 mg/dL or above and 100 gm 3H GTT). They found that the incidence of GDM was 31.2 by using 1-hour GCT(130 mg/dL or higher) and was 10.7 using -hour GCT(130-140) and the incidence reached 72.0% by using 1-hour GCT(180 mg/dL or higher). They recommended using 130 mg/dL as the threshold for a +ve GCT and suggested using a GTT to confirm the diagnosis of gestational diabetes for screening values up to 200 mg/dL.

Korucuoglu et al also found a +ve correlation between increasing glucose challenge tests with adverse neonatal outcomes. 152 Women with glucose challenge test≥180 mg/dL had an increased incidence of macrosomia and Large for Gestational age neonates and higher rates of NICU admission for hypoglycemia and hyperbilirubinemia than women with glucose challenge test <180 mg/dL. (11) .

Strengths and limitations

Strengths of this study include the sample size. This study confirmed the findings of adverse outcomes in those with an elevated 1-hour GCT without GDM, in the Egyptian population. In addition, it is a prospective cohort study that allow evaluation of both maternal and neonatal outcomes. it also allowed analyzing more risk factors for NICU admission than previous studies. Our study has some limitations. First, it was conducted at a single center so extrapolation of our results to the general population might be difficult. Therefore, a large-scale, multicenter, cohort study is needed to confirm these results in the general population. second, the generalizability of our findings may be limited by the homogeneity of this cohort, which contained only Egyptian patients.

CONCLUSION

Our study confirms that +ve oral glucose challenge test only without gestational diabetes is a risk factor for perinatal morbidity like LGA and NICU admission.

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