

Lowest threshold values for the 75g oral glucose tolerance test in pregnancy

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Abstract

Introduction: A previous study has suggested that with increasing oGTT thresholds there was a statistically increasing risk of maternal and fetal morbidity in the form of hypertensive disorders complicating pregnancy. The present study aims to identify whether this gradient risk is extant with lower blood glucose values.

Methodology: A total of 1289 75-gm oGTTs were performed during pregnancy. These were divided according to their fasting and 2-hour values into categories: A. Fasting values ≤ 4.5 mmol/l ($n=316$), 4.6-5.5 mmol/l ($n=681$), and ≥ 5.6 mmol/l ($n=292$); and B. 2-hour values ≤ 6.5 mmol/l ($n=453$), 6.6-8.5 mmol/l ($n=433$), 8.6-9.5 mmol/l ($n=176$), and ≥ 9.6 mmol/l ($n=208$). The incidence of hypertensive disease during pregnancy, the macrosomia rate, and the mean birth weight were assessed in each group.

Results: The data confirms that a significant rise in the incidence of hypertensive disease occurs at a fasting blood glucose value of ≥ 5.6 mmol/l, while the macrosomia rate rises after ≥ 4.6 mmol/l. The mean birth weight increased progressively with increasing fasting blood glucose thresholds. There is furthermore a progressive rise in the incidence of hypertension noted with significance being reached at a 2-hour blood glucose value greater than 9.6 mmol/l. However no such relationship appears to be present for the incidence of macrosomia; and there was no significant differences in mean birth weights with increasing 2-hour post-load glucose levels.

Conclusions: The study suggests that fasting blood glucose values may be a better indicator of maternal and foetal adverse risk outcomes with increased adverse foetal outcomes being indicated at levels ≥ 4.6 mmol/l. The 2-hour post-75g oGTT values appear to be useful as adverse risk indicators only at levels ≥ 9.6 mmol/l.

Keywords

Diabetes mellitus, pregnancy, diagnosis, complications

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Introduction

The World Health Organization criteria for the diagnosis of abnormal carbohydrate metabolism during pregnancy have been set to levels similar to the non-pregnant state.¹ These diagnostic criteria therefore ignore the physiological changes of pregnancy and thus include a significant proportion of pregnant women whose carbohydrate metabolism is normal for their pregnant state. This observation has led various bodies, including the Diabetic Pregnancy Study Group of ESAD and the American Diabetes Association, to propose alternative diagnostic criteria based on statistical parameters.^{2,3} We have previously shown that the short-term indicator outcomes, such as hypertensive disease and macrosomia, in women with WHO elevated but ADA normal 2-hour blood glucose post 75g oGTT were mildly but not statistically significantly elevated when compared to presumed normal glucose tolerance individuals. Women with ADA-elevated levels had statistically significant higher risks. The risk level appeared to follow a relationship with increasing 2-hour post-load blood glucose levels.^{4,5} The present study attempts to investigate the risk element of increasing blood glucose levels during 75g oGTT to the development of hypertensive disease in the mother and macrosomia in the child.

Material and methods

The study reviewed the medical data records of 1289 Maltese women who had undergone a 75-g oral glucose tolerance test

during the third trimester of pregnancy. These were subdivided according to their fasting and 2-hour post-load blood glucose values. The fasting values were subdivided into three groups: A. ≤ 4.5 mmol/l ($n=237$), B. 4.6-5.5 mmol/l ($n=760$), and C. ≥ 5.6 mmol/l ($n=292$); and the 2-hour values into four groups: A. ≤ 6.5 mmol/l ($n=453$), B. 6.6-8.5 mmol/l ($n=433$), C. 8.6-9.5 mmol/l ($n=176$) and D. ≥ 9.6 mmol/l ($n=208$). The incidence of hypertensive disease during pregnancy (gestational hypertension/pre-eclampsia), the macrosomia rate (birthweight ≥ 4.0 kg) and the mean birth weight were assessed in each group. Since oral glucose tolerance testing is not routinely carried out on all maternities at the hospital, but only in those women who are considered at particular risk of GDM; there is the possibility that those women with low blood glucose values had risk factors other than glucose intolerance that predisposed them to hypertensive disease and macrosomic infants.

Statistical significance comparing the outcome indicators risks of the various subgroups against the lower glucose bracket was tested using the Chi Square test and the students t test as appropriate using the MedCalc statistical package. A probability value of <0.05 was taken to represent a significant correlation.

Results

There appears to be a progressively increasing rise in the incidence of hypertensive disease with increasing fasting blood glucose levels (Table 1). Statistical significance was however only noted with values greater than or equal to 5.6 mmol/l. Thus the hypertension rate increased from 7.0% in women with a

fasting value ≤ 4.5 mmol/l to 10.6% in women with a fasting blood glucose value of 4.6-5.5 mmol/l ($p=0.09$), and to 21.2% in women with fasting blood glucose ≥ 5.6 mmol/l ($p<0.0001$). The macrosomia rate showed a similar progressive increase. The rate of macrosomia increased significantly from 8.5% to 13.4% ($p=0.04$) at a fasting blood glucose value of ≥ 4.6 mmol/l. The rate increased further to 16.1% ($p=0.007$) with higher values. The mean birth rate also showed a statistically significant increase from 3398 ± 473 g to 3523 ± 507 g in women with a fasting blood glucose ≥ 5.6 mmol/l.

There appears to be only a mild increase in hypertensive disease with increasing 2-hour post-load blood glucose levels after 8.6 mmol/l level ($p=0.4$) but reaching statistical significance only with a blood glucose level greater than 9.6 mmol/l ($p=0.003$). There was no apparent significant relationship between 2-hour blood glucose and the macrosomia rate and the mean birth weight (Table 2).

Discussion

The diagnostic criteria for gestational diabetes and IGT have remained a contentious issue. In 1980, the World Health Organization suggested that the criteria used to diagnose diabetes and IGT in the general population could be applied to pregnant women. This view was re-endorsed in 1985 and 1994.¹ Thus, the 1994 WHO criteria for gestational impaired glucose tolerance still required a plasma glucose ≥ 7.0 mmol/l (fasting) or ≥ 7.8 mmol/l (2 hours). These criteria however do not take into account the natural "diabetogenic" effects of pregnancy, and it has been argued that these criteria will

Table 1: Fasting blood glucose thresholds

Fasting blood glucose	≤ 4.5 mmol/l		4.6-5.5 mmol/l		≥ 5.6 mmol/l	
	No.	%	No.	%	No.	%
	N=316		N=681		N=292	
Maternal PIH/PET	22	7.0	72	10.6	62	21.2
				$p=0.09$		$p<0.0001^*$
Macrosomia (>4.0 kg)	27	8.5	91	13.4	47	16.1
				$p=0.04^*$		$p=0.007^*$
Birth weight (gm) Mean + s.d.	3398 ± 473		3451 ± 485		3523 ± 507	
				$p=0.1$		$p=0.002^*$

Table 2: 2-hour post load blood glucose thresholds

2-hour post load blood glucose	≤ 6.5 mmol/l		6.6-8.5 mmol/l		8.6-9.5 mmol/l		≥ 9.6 mmol/l	
	No.	%	No.	%	No.	%	No.	%
	N=453		N=433		N=176		N=208	
Maternal PIH/PET	48	10.6	44	10.2	23	13.1	39	18.8
				$p=0.9$		$p=0.4$		$p=0.003^*$
Macrosomia (>4.0 kg)	47	11.3	57	13.2	23	13.1	29	13.9
				$p=0.3$		$p=0.4$		$p=0.8$
Mean + s.d.	3462 ± 460		3432 ± 524		3436 ± 472		3489 ± 481	
Birth weight (gm)				$p=0.4$		$p=0.5$		$p=0.5$

include a significant proportion of normal pregnant women. Various threshold levels have been proposed, generally based on statistical models. The criteria currently proposed by the American Diabetes Association require two plasma glucose values of ≥ 5.3 mmol/l (fasting) ≥ 10.0 mmol/l (1 hour) and ≥ 8.6 mmol/l (2 hours).³ The latter threshold recommendations appear to be slowly being universally accepted having been adopted by the European Association of Perinatal Medicine.⁶ Our previous studies appeared to confirm the observation that cases defined as mild GIGT by the WHO criteria and normal by the ADA criteria, i.e. 2-hour blood glucose value of 7.9-8.5 mmol/l, were not associated with any apparent statistically significant increase in maternal and infant short-term morbidity, though a non-statistically significant continuum of risk was observed.^{4,5} These observations have been re-confirmed in the present study. These observations contrast with a previously published study that had shown that there was a continuum of risk related to the 2-hour maternal post-75-gram load blood glucose level for the probability of having an assisted delivery and the likelihood of the baby being admitted to a Special Care Unit, even when the 2-hour value was below 8.0 mmol/l.⁷ The significance of the values obtained after a 75-gram glucose load has still to be determined by the large-scale Hyperglycaemia and Adverse Pregnancy Outcome (HAPO) Study.⁸ The present study has confirmed that significant risk to both mother and child in the form of hypertensive disease exhibits itself with post-75 load 2-hour values greater than 9.6 mmol/l, though there appeared to be a non-statistically significant increase exhibited at a 2-hour value of 8.6 mmol/l. The risk has been previously shown to become even more significant with increasing values.^{4,5} Since oral glucose tolerance testing is not routinely carried out on all maternities at the hospital, but only in those women who are considered at particular risk of GDM, it is possible that women defined as normal glucose tolerance had other risk factors, such as obesity and advanced age, that predisposed them to both hypertensive disease and macrosomia. This would influence statistical significance by increasing the rate of these outcomes in women with a normal glucose tolerance test. The inter-relationship between hypertension and macrosomia rates to BMI has been previously demonstrated in the same population.⁹ The present study further suggests that fasting blood glucose values appear to be better indicators of risk and that cut-off risk-significant values may need to be further reduced to 4.6 mmol/l rather than the currently established value of 5.3 mmol/l.

Women with defined mild gestational carbohydrate intolerance with 2-hour post-load values of 8.6-9.5 mmol/l showed no statistically increased risk for short-term morbidity. These women have however been shown to have long-term morbidities related to subsequent onset of carbohydrate

intolerance. Maltese women with a borderline or mild carbohydrate intolerance during pregnancy have been shown to be 3.6 times more likely to develop an abnormal glucose tolerance eight years postpartum when compared to women with a normal glucose tolerance test as defined by the WHO criteria.¹⁰ In spite of the apparent absence of short-term effects of mild GIGT, it may remain prudent to continue advising women with a borderline glucose tolerance test to reduce their refined sugar intake, thus reducing the day-to-day blood glucose loads presented to the developing fetus. The long-term risks to the woman need also be discussed during the antenatal and postpartum visits in order that lifestyle modifications may be made to reduce or delay the advent of adult-onset diabetes.

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