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Blood Glucose Levels and Pregnancy Outcome in a High-risk Population

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Abstract

Objectives: UAE pregnant women have a higher prevalence, of metabolic disorders such as insulin resistance, obesity, diabetes and gestational diabetes. This justifies outcome mapping in relation to blood sugar.

Research design and methods: A hundred ninety-eight healthy UAE pregnant women enrolled in primary health care centers in 2010-2011 were followed in the hospital for outcome of pregnancy.

Methods: Retrospective chart review, Surveyed exposure variables: demographic data, obstetric history, BMI, Blood pressure, Hemoglobin, early trimester glucose levels fasting and 1hr after breakfast, second trimester OGTT. Primary outcomes were: gestational age at delivery, mode of delivery, fetal weight, and baby admission to SCABU or death.

Results: A non-significant trend between birth weight and the different glucose levels was found. Surprisingly, small for gestational age babies are seen in mothers with lower 1 hr OGTT. FBS OGTT was associated with the occurrence of pregnancy complications as PET (p<0.012). Only mothers with high BMI and parity appear more likely to have larger babies (p< 0.008, p<0.038). Delivery complications were more common in older women and those with lower parity (p<0.034, p<0.013), GDM was more common in obese women (p<0.033) and 1 hour OGTT with 2 hr OGTT, FBS OGTT and increasing age (p<0.00001, p<0.008, p<0.012).

Conclusion: OGTT was not helpful in predicting outcome in this population. Large Birth weight babies were not more common in women with higher glucose levels but obesity was associated with larger babies significantly.

Introduction

Gestational diabetes has become a worldwide concern due to its rapidly increasing incidence and associated increased risk of maternal and perinatal morbidity and mortality [1-7]. Providing adequate care for this high risk group may challenge health care systems.

The HAPO study [2] and other recent studies [8] showed a strong association between maternal blood glucose and adverse pregnancy outcome. There is even evidence that elevated glucose levels that are below the levels required for a diagnosis of GDM are already associated with adverse perinatal outcome [1-5]. In addition, the management of pregnant women with mild hyperglycemia seems to improve their perinatal outcome [9,10]. These findings raised concerns regarding conventional glucose cutoff levels for the 75 gm GTT for the diagnosis of GDM. To decrease the numbers of missed cases of hyperglycemia the International Association of Diabetes and pregnancy Study Group IADPSG [11] recommended that a diagnosis of GDM should be made if any of the fasting, 1 hour or 2 hours values of the 75 gm OGTT is high.

However, there is a paucity of data on the validity of these associations and thus the application of these cutoff levels in populations with high pre-pregnancy metabolic risks, or a different ethnicity, and genetics background. The population of the United Arab Emirates (UAE) might provide a unique opportunity for such study due to its high prevalence of metabolic disorders such as diabetes, insulin resistance, obesity and dyslipidemia that may aggravate the adverse GDM effects. UAE has a high prevalence of diabetes (23%), obesity (37.3%), and the metabolic syndrome (22.7%) [8]. Furthermore, it is estimated that nearly one quarter of pregnancies are complicated with GDM [12].

In this study we aim to determine pregnancy outcome in relation to maternal blood glucose levels in a high risk population.

Questions similar to those asked by the HAPO study, using three methods of glucose assessment in pregnancy, are being addressed.

Method

This is a retrospective community-based study. Pregnant women who had their antenatal care between 1st October, 2010 to 31st March, 2011 at the main Primary Health clinics, Al Ain District, Emirate of Abu Dhabi, United Arab Emirates were included in this study. Al Ain city is one of the largest cities in the United Arab Emirates with a population of around 500,000. Included were healthy UAE national women who had one or more glucose tests, during their pregnancy and delivered at Tawam hospital, the tertiary hospital in the city. Tests included were the routinely ordered second trimester OGTT (N=151) and first trimester fasting (N=167) and postprandial glucose (N=67). Pregnant women data were extracted from Electronic Medical Record. Collected data included basic demographics, past obstetric history, vital signs, and results of antenatal investigations, gestational age at delivery, mode of delivery, fetal weight, and admission to SCABU.

This study protocol was approved by Al Ain District human research ethics committee. Written informed consent was given to and completed by all participants.

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Data analysis was done by SPSS v 20. Standard univariate statistics as well as multiple regression methods were used for analysis.

Results

A Total of 198 pregnant women were included in this study. As in Table 1 the majority of pregnant women were in the age group from 20 to 35 (80.4%) and 45.1% met the new criteria for diagnosing GDM. Obesity, based on pre-pregnancy BMI, was identified in 36.3%. 8.8% of the women delivered before 37 weeks of gestation, 24.2% were induced deliveries, 81.6% delivered normally, 14.2% with C-section and 3.7% assisted. 3.2% had pregnancy complicated with pre-eclamsia or hypertension. Regarding fetal outcome; 2.6% had congenital anomalies, 1.6% were still births or died at day one and 5.8 % admitted to NICU. When plotting the birth weight in relation to gestational week at delivery; 1.7% was small and 12.3% large for gestational age. Table 2 shows p-values of significant (all associations formulated as positive associations) associations of variables studied with linear regression. Neither, age, parity, nor FBS were significantly associated with pregnancy complications. Although it shows several significant associations among studied variables it does not show significant associations between birth weight and the different glucose levels. Although there is a trend between the one hour OGTT and birth weight but this does not reach statistical, significance. Small for age babies are associated with lower 1 hour maternal OGTT.

Table 2 further shows, that mothers with high BMI and parity are more likely to have larger babies (p<0.008, p<0.038). The only other glucose readings with significant predictive value was the FBS OGTT, which was associated with the occurrence of pregnancy complications as PET p<0.012.

Other significant associations in Table 2 delivery complications were more common in older women and with lower parity (p<0.034, p<0.013), GDM more in obese women (p<0.033) and 1 hour OGTT with 2hour OGTT, FBS OGTT and increasing age (p<0.00001, p<0.008, p<0.012).

Obesity was found significantly associated with elevated fasting blood glucose early in pregnancy but not any other glucose non-fasting values and significantly with lower FBS later in pregnancy. As well obese women are more likely to have higher blood pressure, with lower previous birth weight, higher parity, more advanced gestational age and less likely of a history of GDM in previous pregnancies Table 3. Another important outcome is prevalence of abortion which was significantly associated with obesity P=0.025.

Discussion

Despite a high prevalence of GDM (45.1%) and our adequately sized sample, our study failed to detect a relationship between the different readings of glucose in pregnant women, first trimester FBD, and OGTT. In this population we thus failed to replicate major findings from HAPO and similar studies. Only the FOGTT had significant association with the pregnancy complications.

Interestingly our findings seem to challenge the value of OGTT, the gold standard test for GDM, as it appears to be lacking any significant relationship to any important outcome, and glucose levels apparently do not influence perinatal outcomes in the same way as in other ethnicities. Most importantly, there appears to be no relationship between hyperglycemia and macrosomia similar to what was found by a recent study carried out in the same population [13]. In the HAPO study obesity was strongly associated with increased frequency of

pregnancy complications, in particular those related to excess fetal growth and adiposity and to pre-eclampsia [6]. Although in one study neonatal outcome of obese women was comparable to that of women with normal pre-pregnancy body mass index [14] in HAPO [1] both maternal GDM and obesity were independently associated with adverse pregnancy outcomes agreeing with older studies [1]. Our study agrees that the BMI is an important predictor of LGA nevertheless birth weight seems independent of maternal glycaemia. Our sample has a very high prevalence of obesity and overweight, 39.4% and 35.4% respectively. Explanation can be difference in the risk factor mix as the mean BMI was in our study was 29.5 (SD 6.2), higher than in the HAPO study 27.7 (SD 5.1).

Variables			
Age Groups	<=20	10	5.3
	21-35	152	80.4
	36-40	24	12.7
	>40	3	1.6
Pregnancy Complications	NO Pregnancy Complications	184	96.8
	Pregnancy Complications	6	3.2
Any Complications	No Complications	160	85.6
	Complications	27	14.4
Delivery Complication	No Complications	118	62.4
	Complications	71	37.6
GDM	No GDM	73	54.9
	GDM	60	45.1
Fetal Abnormality	No	185	97.4
	Yes	5	2.6
Obesity	Normal	44	25.1
	Over weight	62	35.4
	Obese	69	39.4
FBS early 1st Trimester	<=4.2	39	26.4
	4.21-4.9	65	43.9
	>=5	44	29.7
1 hour PP early 1st Trimester	<=7.3	62	98.4
	7.31-9.5	1	1.6
FBS OGTT	<=4.2	40	28.0
	4.21-4.9	70	49.0
	>=5	33	23.1
First hour OGTT	<=7.3	70	50.4
	7.31-9.5	34	24.5
Second Hour OGTT	<=5	36	25.0
	5.1-7.9	80	55.6
	>=8	28	19.4
Birth weight	SGA	2	1.7
	LAGA	42	36.8
	HAGA	56	49.1
	LGA	14	12.3
Labor induction	Induction	46	24.2
	Spontaneous	143	75.7
Mode of delivery	SVD	155	81.6
	C-SECTION	27	14.2
	Assisted Delivery	7	3.7
Preterm	<37	15	8.8
Full term	>=37	155	91.1
Admit to ICu	Yes	11	5.8
	No	170	94.2
Died/stillbirth	Yes	3	1.6
	No	187	98.4

Table 1: Characteristics of the patients included.

Obese mothers	0.01
More Parity	0.038
More Delivery Complications	0.008
Younger AGE	0.034
Less Parity	0.013
associations	
Pregnancy Complications	0.001
Higher FBS OGTT	0.012
Higher Two Hour OGTT value	0.000
Higher FBS OGTT value	0.008
Older AGE	0.012
Obese mothers	0.033

Table 2: Significant associations studied with linear regression.

Variable	Beta	P value
2nd Trimester FOGTT	-8.354	0.004
2nd Trimester 1st hour OGTT	2.832	0.066
2nd Trimester 2nd hour OGTT	-2.494	0.088
SBP	-10.289	0.002
DBP	4.840	0.017
Previous Birth weight range	-7.474	0.005
1st Trimester FOGTT	11.003	0.002
Parity	6.497	0.007
Gestational age at delivery in current pregnancy	7.125	0.006
GDM history in previous pregnancies	-6.195	0.008
HB	-2.805	0.068
Abortion History	2.321	0.025

Table 3: Significant associations with obesity studied with linear regression.

Additionally in this study higher BMI is association with higher rates of abortion history which adds to the importance to direct efforts in community based weight management programs in women as this is a risk to fertility and pregnancy and delivery complications.

In addition the difference in the expression of the effect of the high prevalence of GDM and its competition with other risk factors expression is possibly due to other factors or co-morbidities such as anemia and vitamin D deficiency [15]. Both of these co-morbidities are prevalent and have a significant influence on birth weight [16,17]. In our study sample anemia prevalence was 36.2% and in the Emirate of Abu Dhabi Weqaya screening program vitamin D was deficient in 56.9% and insufficient in 40% of the women in the child bearing age. Both deficiencies reflect adverse dietary and lifestyle habits that may as well influence the birth weight of their babies.

A number of research studies [13,18-21] indicate the importance of other factors in addition to glucose levels and GDM status of the mother as ethnicity educational levels health care access and vitamin D level in addition to factors studied in this study such as parity, obesity, and GDM status. It was found that gestational diabetes mellitus appears to be more common in those with low vitamin D status [15] and in the

HAPO [22] study a correlation was found between 25-hydroxy vitamin D and beta-cell function suggesting that vitamin D may influence glucose metabolism through this mechanism.

Ethnicity itself is an independent determinant of macrosomia as it was found in a study of 385 Cree and 5644 non-Native women in Canada. The potential effect of ethnicity (Cree vs. non-Native) was determined after statistically adjusting for age, parity, pregravid weight, height, net rate of weight gain, gestational diabetes mellitus (GDM) and smoking status. The prevalence of macrosomia among the Cree was 34.3% vs. 11.1% among non-Natives highlighting the importance of ethnicity [21]. Further research in the gulf Arab ethnic group with inclusion of all different variables is needed to explore to what extent confounding has diluted the effects of hyperglycemia in this high GDM and glucose intolerance population.

Limitation of this study is including six month cohort and longer period could have increased sample size and power.

Conclusion

OGTT was not helpful in predicting outcome in this population and macrosomia was not significantly associated with higher glucose levels. Influence of glucose blood levels and other determinants of pregnancy outcome in Arab UAE population need to be explored in larger cohort to investigate possible confounders. Of importance obesity is emerging as a stronger association with larger babies which necessitate prioritizing efforts to target these risk factors in this population.

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