The Effects of Maternal Obesity and Gestational Diabetes on the Pregnancy Outcomes (HAPO) In Saudi Women, At Tabuk City

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Abstract: Objectives: Is there an association of gestational diabetes mellitus (GDM) and obesity with the adverse pregnancy outcomes in Tabuk City? **Methods:** Neonatal adverse pregnancy outcomes included birth weight; newborn morbidity maternal outcome included primary cesarean delivery, preeclampsia and shoulder dystocia. Body mass index (BMI) was determined at booking time. Multiple logistic regressions were used to examine associations of GDM and obesity with their outcomes. **Results:** Mean maternal BMI was, 30.7. It was found that 29.7% were obese (BMI: 33.0 kg/m2), and GDM was diagnosed in 46.2%. Relative to non-GDM and non-obese women, odds ratio for birth weight.90thpercentile for GDM alone was 1.599 (0.706–3.619), for obesity alone 2.014 (0.755–5.372), and for both GDM and obesity 3.519 (1.565–7.912) showing a very high P value clarifying a significant role of GDM and obesity on the birth weigh outcome. Odds for birth weight.90th percentile were progressively greater with both higher OGTT glucose and higher maternal BMI. Results for primary cesarean delivery and preeclampsia were similar. Both maternal GDM and obesity are independently associated with adverse pregnancy outcomes. Their combination has a greater impact than either one alone. Regarding to the body weight among the studied women, it was found that out of 944 women 334 (35.4%) were over weight, 280 (29.7%) were obese while 330 (35%) were normal weights. Total GDM pregnant women were 436 out of 944 (46.2%), 160 women of them were obese (36.7%). Obesity in pregnancy is a recognized risk factor for many maternal and neonatal adverse outcomes including increased rate of cesarean section, macrosomia, preeclampsia and gestational diabetes mellitus [3-5]. Risks for the fetus and newborn include macrosomia, neonatal hypoglycemia, respiratory distress syndrome, jaundice and also long-term consequences such as T2DM, childhood obesity, metabolic syndrome in adults [9], perinatal mortality and congenital malformations [10,11]. GDM alone may have distinct effects on clinical outcomes independent of obesity. The same is true for maternal obesity [12]. As both share common metabolic characteristics such as increased insulin resistance, hyperglycemia and hyperinsulinemia, examination of the combined association of these common metabolic problems with pregnancy outcomes is very important to be investigated.

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Research Design and Methods

The scientific research and ethical committees of both University Of Tabuk and King Salman Armed Forces Hospital approved the protocol. All the files of the pregnant women who had 75 gm OGTT during the study period and subsequently delivered in the hospital were reviewed and the research members collected data.

Maternal BMI

The measures of maternal weight, used to calculate BMI, were obtained at the time of the OGTT, which is measured after removing shoes. BMI was defined as weight/height squared (kg/m^2). Height was measured at booking with the participant's head facing forward in the horizontal plane. The hospital protocol is that, the height measurement to be taken twice to the nearest 0.5 cm with a stadiometer and if the results differed by more than 1.0 cm, the measurement was repeated. Weight to be measured twice to the nearest one decimal point on a scale calibrated each day. A third weight was taken if the results of the first two measurements differed by more than 0.5 kg. If a third measurement was taken, the average of the two nearest measures was used.

Maternal prepregnancy weight was not recorded in the most patient's files. To take into account weight gain during pregnancy, category limits for BMI at the OGTT that could be considered comparable with non pregnant, World Health Organization (WHO), BMI categories were obtained from a regression of OGTT BMI on prepregnancy BMI and gestational age at the OGTT. This yielded a definition of obesity at 28

weeks as a BMI 33.0 kg/m^2, of overweight at 28 weeks as a BMI of 28.5–32.9, and of normal weight or underweight as a BMI 28.4. As outlined previously (5), these cut points from regression are equivalent to the WHO categories of (nonpregnant) class 1 obesity, BMI 30.0 kg/m2, overweight 25.0–29.9, and normal or underweight 25.0 or less, respectively [13].

OGTT

Data of pregnant women who underwent a 2-h 75-gm OGTT at or above 24 weeks' gestation were collected. Data included smoking and alcohol use, first-degree family history of diabetes and hypertension, and demographics as well.

Glucose Analysis:

All the 2-h OGTT plasma glucose samples were analyzed at same hospital laboratories.

Diagnosis of GDM

Patients were diagnosed to have GDM according to the new IADPSG recommendations [14]. A patient is diagnosed to have GDM if any of the following values from the 75-gm OGTT is equaled or exceeded: fasting plasma glucose is 5.1 mmol/L (92 mg/dL), 1-h plasma glucose 10.0 mmol/L (180 mg/dL), or 2-h plasma glucose 8.5 mmol/L (153 mg/dL).

Prenatal care and delivery:

Prenatal care, timing and mode of delivery were determined by the standard and recognized hospital practice.

Neonatal data

Neonatal anthropometrics were obtained within 24h after delivery. Anthropometrics included weight, length, and head circumference. Birth weight was obtained without a diaper using a calibrated electronic scale. Length was measured using a standardized plastic length board. Head circumference was measured across the occipital fontanel. The mean coefficients of variation for the anthropometric measurements were birth weight 0.04% and length 0.17%. Weight at delivery was used to determine birth weight.

Outcomes

Birth weight >90th percentile.

The 90th percentiles were determined using the standardized fetal growth chart used in the center with adjustment for gestational age, and parity (0,1,2+). Birth weight above 90th percentile was considered to be present if the birth weight was greater than the 90th percentile for the baby's sex, gestational age, ethnicity and maternal parity.

Primary cesarean sections:

Primary cesarean section was defined as the need for the first cesarean delivery. This study included those patients who had Primary cesarean deliveries only. Total cesarean deliveries as an outcome was not considered in our study because of the various policies of repeat cesarean deliveries and trial of labor after a previous cesarean delivery at the various HAPO study sites.

Shoulder dystocia.

A vaginal delivery is complicated by shoulder dystocia when, after delivery of the fetal head, additional obstetric maneuvers beyond gentle traction are needed to enable delivery of the fetal shoulders. Data were collected from patient records then revised to and compared with the obstetrics record present in the delivery station. No recorded data of shoulder dystocia among our studied groups.

Statistical analyses

Descriptive statistics include means and SD for continuous variables and numbers and percentages for categorical variables. To examine the associations of GDM and obesity, singly and in combination, the participants were divided into four groups: 1) no GDM, no obesity; 2) GDM, no obesity;3) no GDM, obesity; and 4) GDM, obesity.

Two logistic regression models were then fit for each outcome, with no GDM and no obesity used as the referent group.

Model I included adjustment for field center or the variables used in estimating the 90th percentiles for birth weight (sex, ethnicity, center, and parity).

Model II included adjustment for multiple potential confounders, including maternal age and height at the OGTT, smoking, alcohol use, family history of diabetes, gestational age at the OGTT, baby's sex, parity (0, 1, 2+) (except primary cesarean delivery), mean arterial pressure and hospitalization before delivery (except preeclampsia), family history of hypertension and maternal urinary tract infection (preeclampsia only). In addition, to provide an example of the associations of BMI and glucose across the full range of BMI and OGTT glucose singly and in combination, we created a composite OGTT measure that used all three glucose values. The categories for BMI were normal or underweight (28.4), overweight (28.5–32.9), and obese (33.0). According to the results of OGTT, 436 women out of 944 (46.2%) were diagnosed to have GDM.

We then examined the associations of BMI and OGTT glucose with birth weight in a logistic regression analysis with Model II adjustment, and with birth weight in a multiple linear regression analysis with Model II adjustment, including adjustment for gestational age at delivery. Odds ratios (ORs) for birth weight.90th percentile relative to normal glucose and normal or underweight BMI were then obtained for all combinations of BMI and glucose categories by multiplying the OR corresponding to the appropriate glucose and BMI categories. Mean differences in birth weight relative to normal glucose and normal or underweight were obtained for all combinations of BMI and glucose

categories by adding the mean differences in birth weight corresponding to the appropriate glucose and BMI categories.

Results

The data obtained from a total of 994 women were available for those who completed the OGTT and had undergone glucose testing and delivery inside the context of this study and had no missing key data or improbable results.

Table 1: the characteristics and frequency of outcomes relative to the specific aims of this study.

Items	No & (%) 944(100%)	Mean ± SD
1-Maternal Criteria:		
Age		29.9±5.8
Weight		72.5±16.9
Height		1.5±0.08
BMI (kg/m^2):		30.7±6.4
Normal weight (28.4) **Over weight (**28.5–32.9) **Obese (**33.0)	330 (35) 334 (35.4) 280 (29.7)	
Gestational age at booking (ws):		18.0±8.0
Systolic blood pressure **Diastolic blood pressure**		110.4±11.9 64.4±10.0
Gestational age at 75 OGTT		28.5±3.5
Results of 75 OGTT		
Fasting blood sugar (mmol/L) **1-hr post prandial glucose (mmol/L)** **2-hr post prandial glucose (mmol/L)**		5.03±2.06 8.07±2.1 6.9±1.9
GDM in the current pregnancies:		
+ve	436 (46.2)	
GDMControlled by:		
Diet Diet and insulin	404 (92.7) 32 (7.3)	
Obesity among GDM	160 (16.9)	
Mode of delivery:		
CS Vaginal Assisted vaginal	230 (24.4) 684 (72.5) 30 (3.2)	
Types of CS:		
Primary Secondary	136 (59.2) 94 (40.8)	
II-Fetal Outcomes:		
Baby weight (kg.) **Baby weight >90 percentile**	 94(10.0)	3.01±0.53

Table (1) showed that among the participant, the mean maternal BMI at the time of the OGTT was 30.7 kg/m^2. Obesity was present in 29.7% and 46.2% of them met the new IADPSG criteria for GDM. It was also found that 16.9% of those diagnosed with GDM were obese.

Table 2: the association between maternal GDM, obesity and maternal outcomes.

Variable	B	SE	Wald	P value	Odd Ratio (OR)	95.0% C I interval	
						Lower bound	Upper bound
Maternal Outcomes: CS (primary)							
No GDM, no obesity	- 0.391	0.224	3.043	0.081	0.676	0.436	1.049
GDM, no obesity	0.198	0.270	0.539	0.463	1.219	0.718	2.069
No GDM, obesity	0.197	0.354	0.309	0.578	0.217	0.608	2.436
GDM, obesity	0.875	0.292	8.976	**0.003**	**2.400**	1.354	4.255

Table (2) showed that there was a significantly greater odd of CS as a maternal outcome for the group who has GDM and obesity compared to the other groups (P= 0.003 and OR= 2.400) followed by the group who has GDM and no obesity (OR=1.219).

This means that GDM has a common risk factor in both groups.

Table 3: the association between maternal GDM, obesity, and fetal outcomes.

Variable	B	SE	Wald	P value	Odd Ratio (OR)	95.0% C I interval	
						Lower bound	Upper bound
Fetal outcome Birth weight >90 percentile							
No GDM, no obesity	**-0.772**	**0.349**	**4.901**	**0.27**	**0.462**	**0.233**	**0.915**
GDM, no obesity	**0.469**	**0.417**	**1.269**	**0.260**	**1.599**	**0.706**	**3.619**
No GDM, obesity	**0.700**	**0.501**	**1.957**	**0.162**	**2.014**	**0.755**	**5.372**
GDM, obesity	**1.258**	**0.413**	**9.267**	**0.002**	**3.519**	**1.565**	**7.912**

Table 3 showed that there was significantly greater odd of birth weight >90 percentile as a fetal outcome for the group who has GDM and obesity compared to the other groups, (P= 0.002 and OR= 3.519).

Discussion and Conclusion:

This study adds to the previous HAPO study reports by examining the impact of GDM and obesity alone as well as their combined impact on adverse pregnancy outcomes in Tabuk population. The combination of these factors showed a greater risk of adverse pregnancy outcomes than either GDM or obesity alone.

The previous HAPO studies had shown significant independent associations of higher maternal glucose concentrations [16,17] and maternal obesity [18] with adverse pregnancy outcomes.

In Riyadh, the prevalence of GDM was 12.5% and 3.8% by World Health Organization and American Diabetes Association criteria respectively [19].

In the U.S., 7% or 200,000 pregnant women are currently diagnosed with GDM [20]. Using the IADPSG criteria will increase the number of women diagnosed with GDM [14].

Much of this potential increase in the frequency of GDM in the U.S. and other developed countries can be attributed to the increase in obesity in women of reproductive age [21].

In KSA, approximately 60% of women of reproductive age are overweight or obese [22].

Prevalence of obesity was higher among women (33.5%) [23]. A recent study revealed that 31.5% of Saudi females of childbearing age are overweight and 21.1% are obese [24].

In Saudi Arabia 2005 prevalence of obesity among females is 43.8 % [25].

Obesity is an increasing problem in other areas of the world, where many of the HAPO field centers were located.

We defined obesity in pregnancy corresponding to WHO criteria [13]. WHO consultation concluded that the WHO BMI cutoff points should be retained as international classifications [26].

GDM and maternal obesity are independently or in combination associated with adverse pregnancy outcomes. In addition, Table 3 clearly illustrates the strong association of a combination of obesity and abnormal maternal glucose level with the outcomes.

Finally, GDM and obesity seem to influence a number of the outcomes through similar mechanisms. The HAPO Study supports the Pedersen hypothesis that increased maternal glucose concentration shows a strong continuous relationship with fetal growth [27]

In a recent study that used continuous glucose monitoring in obese, Harmon et al [28] found that obese women with normal glucose tolerance have higher daytime and nocturnal glucose profiles compared with normal weight women. There is also evidence that circulating levels of other nutrients such as lipids and amino acids, which are influenced by insulin and insulin resistance, are increased in both GDM [29] and obesity [30] and may contribute to hyperinsulinemia, fetal growth, and adiposity.

The newly released data on the characterization of fatty acid binding proteins, lipid transporters, and enzymes for fatty acid esterification in the human placenta have now improved our understanding of how maternal lipids may contribute to increased fetal fat accretion [31].

Other associations may have different mechanisms. For example, we found a higher risk of preeclampsia in obese non-GDM women (OR 1.147, Table 2) than in non-obese GDM (OR 0.40). Obese women are more insulin resistant as compared with normal weight women [32]; hence increased insulin resistance may be relevant to the development of preeclampsia in obese women and women developing GDM. However, obesity in addition to GDM was associated with a greater risk of preeclampsia than either factor alone (OR 6.825, Table 2), thereby implicating other potential mechanisms such as inflammation in the development of preeclampsia in this high-risk group.

The utility of the HAPO Study is that it provides objective evidence upon which to base future strategies to improve perinatal health.

The randomized controlled trials of Crowther et al [33] and Landon et al [34] for the treatment of mild GDM, using current management protocols, in which only 8–20%of mild GDMs required insulin therapy, reported improved outcomes including decreased risks of birth weight.90th percentile and preeclampsia. Maternal weight gain was decreased in the treated GDM as compared with the control group in both studies.

Avoidance of excessive gestational weight gain in obese women may improve perinatal outcomes such as birth weight.90th percentile. About 50–60% of overweight and obese women gain more weight during pregnancy than that recommended in the 2009 [35], hence avoidance of excessive gestational weight gain should result in decreased postpartum weight retention for future pregnancies, thereby decreasing the vicious cycle of obesity affecting obese pregnant women and their offspring.

However, further research is needed to determine which lifestyle treatment options best improve perinatal outcomes in obese women.

Summary,

Both maternal GDM and obesity are independently associated with adverse pregnancy outcomes. The combination of the two, however, has a greater impact than either one alone. Although management of GDM requires strict glucose control, it results in lower frequencies of adverse outcomes.

Optimal management of maternal obesity per se has yet to be defined. Until the results of ongoing research studies are available, avoidance of excessive gestational weight gain, moderate exercise, and a prudent diet are reasonable recommendations for obese pregnant women.

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