

DIABETES, OBESITY AND EXCESSIVE WEIGHT GAIN AND PREGNANCY OUTCOMES

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REZUMAT

Obiectiv: Determinarea evoluției perinatale la femeile obeze, cu creștere excesivă în greutate pe perioada nașterii, sau diabetice. **Material și metode:** Nașterile a 82 de femei cu obezitate/creștere excesivă în greutate/diabet, au fost comparate cu un grup de control, format din 43 de nașteri la femei normale. **Rezultate:** S-au observat diferențe semnificative între cele două grupuri în ceea ce privește greutatea copilului la naștere, tensiunea arterială medie, hipokinezia uterină, traumatismele la naștere, stress-ul fetal și fiziologia anormală a placentei. S-au remarcat de asemenea și diferențe semnificative între ratele de secțiuni cezariene. **Concluzii:** Diabetul, obezitatea și creșterea excesivă în greutate pe perioada sarcinii sunt asociate cu o evoluție perinatală nefavorabilă.

Cuvinte cheie: obezitate, creștere excesivă în greutate, diabet, sarcină.

ABSTRACT

Objective: Perinatal outcomes in obese, excessive weight gain and diabetic mothers. **Material and methods:** 82 deliveries of mothers with obesity/excessive weight gain (EWG), 7 - diabetes alone, and 16 cases of obesity/EWG and diabetes compared with a control group of 43 mothers. **Results:** Significant differences were observed between groups with Ob and /or EWG vs control for birth weight ($3420 \pm 593g$, $p=0.006$), mean arterial pressure ($88.51 \pm 9.54mmHg$, $p=0.006$), uterine hypokinesia ($\chi^2=66.78$, $p<.0001$), birth trauma ($\chi^2=49.53$, $p<.0001$), and abnormal placental histology ($\chi^2=24.54$, $p<.0001$). Significant differences were observed in diabetes/obesity/EWG for birthweight (3587.5 ± 642 , $p=.026$), mean arterial pressure ($130.3 \pm 11mmHg$, $p<.001$), fetal distress ($\chi^2=5.61$, $p<.018$), and birth trauma ($\chi^2=33.19$, $p<.0001$). Significant higher caesarean rate was observed in group with diabetes alone ($\chi^2=10.82$, $p<.001$), and diabetes+obesity/EWG ($\chi^2=7.33$, $p<.007$). **Conclusion:** diabetes, obesity and EWG are associated with increased adverse pregnancy outcomes.

Key words: obesity, excessive weight gain, diabetes, pregnancy

INTRODUCTION

Various studies recently published emphasized the association between metabolic disorders including diabetes (type 1, type 2 and gestational diabetes mellitus - GDM), obesity, excessive weight gain and short-term pregnancy outcomes such as, macrosomia, birth trauma, neonatal metabolic complications.¹

Diabetes during pregnancy is associated with several maternal and fetal complications, such as ketoacidosis, polihydramnios, spontaneous pregnancy loss, congenital abnormalities, premature birth, and fetal growth disorders – macrosomia, fetal growth restriction, fetal asphyxia, and high incidence of perinatal hypoxia, neonatal hypoglycemia, hypocalcemia, polycitemia, hyperbilirubinemia, and respiratory distress. Moreover, improving glycemic control in the pregnant woman with diabetes may mitigate the additive adverse effects of diabetes and obesity on pregnancy outcome.²⁻⁴

Obesity defined by pre-pregnancy BMI above 30 kg/m² is associated with a wide spectrum of obstetric and perinatal complications, including increased risks of fetal mortality and morbidity, maternal hypertensive disorders, gestational diabetes, excessive fetal growth and cesarean delivery. The odds ratios for these risks are significant and increase in direct correlation with the severity of obesity, even among women who are overweight without meeting criteria for obesity.

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Although obesity is closely associated with diabetes which, in itself, is associated with similar perinatal complications. Diabetes along with obesity are strongly associated with increased birthweight, and with birth trauma due to large babies.

The excessive weight gain (above 18 kg) during pregnancy varies according to pre-pregnancy BMI, fetal abnormalities, the level of amniotic fluid and could be associated with adverse delivery outcomes. Gaining too much weight during pregnancy is a risk factor causing backache, leg pain, varicose veins, fatigue, hypertension and diabetes. Large babies make vaginal deliveries difficult, increasing the risk for uterine hypokinesia, shoulder dystocia, clavicle fracture and cesarean section.

The intrauterine environment is assessed crudely by infant's birthweight, which is not the sole indicator of intrauterine nutritional status.⁵

MATERIAL AND METHODS

The purpose of this study was to assess delivery outcomes in healthy singleton pregnancies with a normal pre-gravid body mass index and normal weight gain vs mothers with pre-gravid obesity (BMI > 29.9 kg/m²), excessive weight gain (> 18 kg), diabetes alone, and with the association of all this risk factors.

A retrospective study was carried out in the Department of Obstetrics and Gynecology of Dr I Cantacuzino Clinical Hospital, Bucharest, between 01-12/2007.

This retrospective research study was not applicable for IRB approval, it was based only on the medical records, without including the patients identification details.

The presence of the obesity, excessive weight gain and diabetes was investigated in 148 pregnant women allocated as follows: 43 healthy pregnant women as a control group, and investigational group comprising 82 women with pre-pregnancy obesity and/or excessive weight gain during pregnancy, 7 cases with diabetes alone, and 16 cases with the association of obesity/excessive weight gain and diabetes.

Inclusion criteria were the following:

1. Singleton pregnancy gestational age 35 weeks or greater and less than 42 weeks;
2. Age of mother at the time of delivery between the ages of 18 and 40 years,
3. Mothers with diabetes (ie, type 1, type 2, or gestational diabetes) , obesity and excessive weight gain during pregnancy.

Exclusion criteria for the study were the following:

1. Inflammatory diseases (systemic eritematous

lupus, rheumatoid arthritis);

2. Any tobacco use during pregnancy;
3. Excess alcohol consumption during pregnancy, defined as more than 1 drink a week;
4. Infants with presumed or known chromosomal or severe congenital abnormalities.

Maternal age, body weight before pregnancy, weight gain during pregnancy, maximum weight reached during pregnancy, were obtained by abstraction from medical records. The mother's pre-gravid BMI was calculated using the participants self-reported body weight prior to pregnancy and their height measured at the visit.

Mean (effective) arterial pressure (mAP) replaces systolic (sAP) and diastolic (dAP) arterial pressure values with a unique value calculated using the specific formula: $mAP = dAP + [(sAP - dAP) / 3]$.

The pregnancy outcomes included neonate birth weight, Apgar score, maternal and fetal complications (fetal distress, uterine hypokinesia, and cranial trauma), placental histological findings, cesarean section and the period of hospitalization.

Fetal distress was considered in the presence of fetal bradycardia and or other abnormal fetal heart rate recorded during labor.

Uterine hypokinesia was considered in prolonged active phase of the first stage and/or in the second stage of labor when inefficient uterine contractions require oxytocin perfusion supplementation and/or cesarean delivery in cases of fetal - pelvic dystocia.

Abnormal placental histopathological findings confirmed on optic microscopy, included the presence of calcifications, thrombotic lesions, fibrinoid or hyaline deposits and endothelial vascular placental lesions.

Fetal cranial trauma at delivery was noted in presence of caput succedaneum and/or cephalohematoma. There was no case with subdural or subarachnoid, or intraventricular hemorrhage.

Statistic analysis. Student t-test analysis for ordinal variables and Chi-square test for categorical variables was used when assessed investigational group versus control.

RESULTS

Patients' information (age), selected relevant obstetric and medical data (parity, mean arterial pressure) and main pregnancy outcome (birthweight, presence of fetal distress, uterine hipokinesia, fetal cranial trauma) and abnormal histological findings are presented separately for the 3 maternal categories in Table 1.

Table 1. Maternal demographics and pregnancy outcomes of the normal (<25 kg/m²) vs obese/EWG (≥25 kg/m²), diabetes alone, and obese/EWG associated with diabetes groups.

	Normal	Obese/EWG		Diabetes alone		Diabetes and obese/EWG	
	(n = 43)	(n = 82)	p	(n = 7)	p	(n = 16)	p
Maternal age (yrs)	26.9 ± 4,8	27.9 ± 4.4	0.24	25.1 ± 5	.36	31.4 ± 4.6	0.003
Parity	1.98 ± 0.78	2.02 ± 1.01	0.79	1.38 ± 0.744	.04	3 ± 1.414	0.07
Mean AP (mmHg)	84.12 ± 5.51	88.51 ± 9.54	0.006	87.43 ± 6.68	.159	93.69 ± 7.59	0.000
Gestational age(wks)	39.1 ± 1.2	39.18 ± 1.7	0.94	37.8 ± 2.1	.024	37.8 ± 2	0.026
Birthweight (g)	3173.2 ± 391	3420 ± 593	0.006	3492.8 ± 439	.054	3587.5 ± 642	0.026
Hospitalization (days)	4.47 ± 3.4	6.18 ± 4.2	0.024	6.57 ± 2.63	.127	7.94 ± 4.3	0.002
Fetal distress	12%	13%		14%		31%	
Uterine hipokinezia	2%	14.6%		0		31.3%	
Cesarean section	14%	19.5%		57.1%		37.5%	
Fetal cranial trauma	7%	26.8%		0		43.8%	
Abnormal placental histological findings	37.2%	63.4%		14.3%		50%	

The maternal age at delivery was significant higher in the group with diabetes associated with obese/EWG. This is an important issue and is explained by the relative trend of delay of pregnancy planning in diabetic women.

Hypertensive disorders

There was a progressive trend in hypertension and preeclampsia among the obese/EWG ($p < 0.005$) and in association obesity/EWG with diabetes ($p < 0.0001$).

Interestingly among women with diabetes alone and normal group, mean arterial pressure had no significant difference, suggesting that only obese/EWG mothers had an increased risk for elevated values of mean arterial pressure.

Neonatal outcomes

There is observed a slight decrease of mean gestational age at delivery when compared the group with diabetes alone (37.8 ± 2.1 wk, $p = 0.024$) and diabetes associated with obesity/EWG (37.8 wk ± 2 p = 0.026) to control group (39.1 wk ± 1.2).

Other important fetal outcome is represented by birthweight which is an indicator of fetal growth.

When compared with normal weight women, obese/EWG patients had higher risk for having large for gestational age babies with statistical significant differences in obese/EWG alone ($p = 0.006$) or in association with diabetes ($p = 0.026$).

Fetal distress

The overall fetal distress rate was not statistically different in studied groups, except the association of diabetes&obesity/EWG ($\chi^2 = 5.61$, $p < 0.018$).

Chi-square test indicates there was no significant difference in the proportion of fetal distress in the obese alone - $\chi^2 = 0.15$, $p < 0.69$, and in diabetic alone $\chi^2 = 0.035$, $p < 0.85$.

Fetal cranial trauma

There was significant difference in the proportion of fetal cranial injury after vaginal delivery in obese/EWG ($\chi^2 = 49.53$, $p < 0.0001$), and also in association diabetic and obese/EWG women ($\chi^2 = 33.19$, $p < 0.0001$).

In diabetes alone no traumatic complication was seen in studied cases, probably because of the mode of delivery - by elective cesarean section (in 57% of cases), which has a protective role, reducing the risk of fetal trauma.

Labor abnormalities

Uterine hypokinesia requiring oxytocin supplementation is significant higher in obese/EWG ($\chi^2 = 66.78$, $p < 0.0001$) and in association diabetic and obese/EWG women ($\chi^2 = 69.84$, $p < 0.0001$).

Cesarean section rate has a statistical higher rate in group with diabetes alone ($\chi^2 = 10.82$ $p < 0.001$), and in diabetes associated with obesity/EWG ($\chi^2 = 7.33$, $p < 0.007$).

Placental histological findings

Represented mainly by the presence of calcifications, thrombotic lesions, fibrinoid or hyaline deposits in optic microscopy, are observed in significant higher rate only in groups of women with obesity/EWG during pregnancy - 63.4% ($\chi^2 = 24.54$, $p < 0.0001$).

As compared to control, there was no significant difference in the proportion of placental findings in diabetes alone and in the association of diabetes and obesity/EWG.

There was recorded only one case of fetal intrauterine demise, at a patient with preeclampsia and excessive weight gain.

Period of hospitalization

The overall period of hospitalization was statistically significant higher in the obese/EWG ($p < 0.024$) and diabetic & obese/EWG women ($p < 0.002$). The increase in the hospitalization of the women in these groups in most of the cases is due mainly to neonatal anomalies and complications associated.

DISCUSSION

The primary purpose of this study was to better understand the impact of maternal metabolic conditions such as obese/EWG, and diabetes (type 1, type 2, and gestational diabetes) on perinatal outcomes.

The significant higher rate of fetal distress observed in diabetes & obese/EWG women could be one of the most important fetal outcome. In this metabolic complex probably a key role has the association of hypertensive disorders, vascular placental abnormalities, macrosomia, fetal growth restriction, and fetal asphyxia during labor.

Our study showed significant differences in birthweight between groups of mothers with obese/EWG alone, and association of obesity with diabetes.

Although the overall mean birthweight in diabetes women alone seems to be not significantly different ($p = 0.054$) in studied group, there is an important statistical difference of gestational age at delivery among diabetic group (37.8 wk), which plays a key role in birthweight. However, the babies born to diabetic mothers are in fact large for gestational age, because they were delivered earlier, either by premature labor, or by cesarean section.

A large number of studies have reported maternal BMI and diabetes having positive linear relationship on neonate birthweight.⁶⁻⁸ This association has been shown in other European samples as well.^{9,10}

Most probably, the fetal origins hypothesis and

maternal environment during pregnancy had profound effect on in utero fetal growth.

There is a strong correlation between maternal height and weight and fetal growth. The taller and heavier a woman prior to conception, the more her infant will weigh at birth.

The interaction of maternal pre-pregnant weight and weight gain on fetal growth are interesting relative to the underline physiology of fetal growth. Other studies show that lean or underweight women will need to have a significant increase in weight gain in pregnancy in order to have a normally grown fetus. By contrast the obese/EWG women will more likely have a larger babies, even with little or no weight gain.¹¹

Maternal parity has also an effect on fetal growth. In our study, obese women are correlated with a slight increase of parity rate.

The placental histological findings could be an indicator of placental dysfunction and decreased placental perfusion. Probably the magnitude of adverse perinatal outcome is underestimated and placental alterations remains one important marker of vascular adaptation to maternal metabolic alterations, and hypertensive disorders such as preeclampsia. In diabetic placentas were observed frequently histological abnormalities which are not specific, but are of increased importance in relation with perinatal outcomes.

Recent studies have shown that in cases of gestational diabetes or impaired glucose tolerance, the fetal exposure at increased levels of nutrients, has determined hyperglycemia and hyperinsulinemia.

These exposures increase the risk for LGA or macrosomia at delivery and also uterine hypokinesia. The current study reveals that hypokinesia or low uterine contractility and inability to "push" is not a risk factor for fetal poor outcome per se in obese women.

The underline mechanism of uterine contractility shows an increasing with cervical dilatation, with maximal force probably at fully dilatation.¹²⁻¹⁴ Fetal expulsion is facilitated by voluntary maternal pushing effort by the concerted contraction of abdominal muscles simultaneously with a forced expiratory effort against a closed glottis. Studies showed that obese women have similar pushing abilities of normal women. Although obese women may require oxytocin augmentation more often to correct intrauterine pressure during active labor, their ability to push is equivalent to women with BMIs in the normal range. Thus, the increased incidence of labor complications reported in obese patients cannot be explained by inadequate intrauterine pressure or maternal expulsive efforts in the second stage.¹⁵

Previous studies link obstetrical emergencies like shoulder dystocia with predisposing factors, such as fetal macrosomia, vacuum extraction, forceps deliveries, and prolonged active and second stages of labor.^{16,17}

The relative small number of cases with shoulder distocia (3 cases) and clavicle fracture (3 cases), occurred only in the group with excessive weight gain during pregnancy. This finding could suggest the key role of this metabolic condition in fetal growth.

Babies born to mothers with excessive weight gain probably have an increased birthweight, with cranial diameter in normal or upper limits but with thoracic and shoulder (biacromial) diameters higher.

It remains unclear in the literature whether the increased frequency of caesarean delivery in obese women is linked to acute maternal or fetal emergencies (preeclampsia, abruption placentae, prolapsed cord, variable decelerations) or more subtle diagnoses, such as cephalopelvic disproportion.¹⁸⁻²¹

Improvement in obstetrical management has reduced the incidence of fetal injury (cranial trauma, shoulder distocia, clavicle fracture), but in the studied groups the risk of fetal cranial injury remains high, therefore patients having prepregnancy obesity/excessive weight gain and /or diabetes should be included in high risk pregnancy.

Although there are an unequal and low number of investigational groups, especially for the group with diabetes alone, there have been noticed similar results with other international studies, revealing the impact of maternal environment during pregnancy which has a profound effect on in utero fetal growth and on labor complications.

CONCLUSIONS

In summary, our study suggest that obese/EWG women associated with diabetes (i.e. type 1, 2 or gestational diabetes) have a highest risk of adverse perinatal outcome than other studied group of women, only with diabetes alone, or obesity/EWG alone.

Further studies should be done for understanding the impact of maternal diet and treatment on neonatal growth, birthweight and perinatal outcomes. The keyrole played by of placenta in adverse perinatal outcomes is underestimated and should be further investigated.

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