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ORIGINAL ARTICLE

Concurrence of gestational diabetes and pre-gravid obesity (''diabesity'') in twin gestations

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Abstract

Objective: To assess the effect of the concurrence of gestational diabetes mellitus (GDM) and pre-gravid obesity in twin gestations (''diabesity'').
Methods: We compared perinatal outcomes of twin gestation in mothers with GDM and pre-gravid obesity (1.7%), mothers with GDM but with normal BMI (6.2%), and obese mothers without GDM (7.0%).
Results: Twin pregnancies with ''diabesity'' were associated with significantly higher incidence of stillbirth (OR = 6.4; 95%CI = 1.4, 33.4) and existing chronic hypertension (OR = 4.2; 95%CI = 1.2, 14.8) than in GDM pregnancies without obesity, and with births at 33–36 weeks as compared with the other groups. Otherwise, the comparisons showed remarkable similar results in terms of gestational age, birth weight, preeclampsia, cesarean section rate, and fetal-neonatal outcomes.
Conclusion: It appears that diabesity has a relatively minor effect in twins. If this will be confirmed by other studies, it would be important to elucidate how twins ameliorate the adverse outcomes of diabesity.

Keywords

Gestational diabetes, obesity, twins

History

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Introduction

The effect of gestational diabetes mellitus (GDM) on twin gestation was not extensively evaluated until recently [1]. It appeared that the frequency of GDM in twin gestations is not unanimously increased, mainly because of glucose uptake by a higher (nearly double) fetal mass counterbalancing the diabetogenic effects of hyperplacentosis characterizing a multiple pregnancy [1]. However, it was recently found that the new screening protocol increased 3-fold the incidence of diagnosed GDM in twin pregnancies [2], casting some doubt on the true incidence of GDM in twin gestations.

It was also unknown if the growth promoting effect of GDM is also operative in twin gestations, and if so, does it improve outcomes by reducing the potentially ill-effect of low birth weight associated with twins. Whereas Tward et al. [3] found a continuous relationship between the degree of glucose intolerance and fetal growth and a greater likelihood of high birth weight percentile among twin pregnancies with GDM, other studies did not support this finding [4,5].

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As with singletons, GDM is also expected to be more frequent in pre-gravid obese mothers of twins [6,7]. GDM and obesity have independent and combined effects on obstetric outcomes [8]. Hence, the effect of the concurrence of diabetes and obesity, nicknamed ''diabesity'', is expected to be greater than the sum of each complication. Simmons [8] correctly pointed out that the impact of diabesity on the fetus and mother often becomes circular, as the many mothers with GDM are obese and a significant proportion of those who are obese have GDM. Desoye and van Poppel [9] maintained that the maternal environment in diabesity can modify placental growth and development which may enhance glucose flux to the fetus in early pregnancy. This, in turn, might be involved in fetal programing and accelerate pancreatic beta-cell maturation which is implicated with obesity later in the offspring's life. The purpose of this study was to assess the effect of the concurrence of these two powerful factors in twin gestations.

Materials and methods

We evaluated twin pregnancies that were followed and delivered after 24 weeks' gestation at the Maternity Dr Alfredo da Costa, Centro Hospitalar Lisboa Central, Lisbon, Portugal, during the period 1 January 1999 to

31 December 2015. This is a tertiary perinatal center that cares for the Lisbon area, and serves as a referral center for the south of Portugal. During this period, information about the pregnancy and delivery was registered prospectively on a preset form and subsequently entered into a computerized system. We excluded twin gestations that were delivered only (i.e. were not followed at our service). For this study, we identified twin pregnancies with the diagnosis of GDM, established according to the Carpenter and Coustan criteria [10], and from 2011, using the criteria established by the International Association of Diabetes and Pregnancy Study Groups Consensus Panel. [10] Women with GDM were followed by an endocrinologist and received nutritional consultation. Glycemic control was followed and regularly checked. In this study, we did not differentiate between those who required or did not require medical glycemic control. BMI category was defined by the IOM criteria [11], namely, BMI $\geq$30 kg/m^2 for obesity, and BMI 18.5–24.9 kg/m^2 for normal weight. We compared mothers with GDM with pre-gravid obesity to mothers with GDM but with normal BMI. Both groups were compared with obese mothers without GDM. Gestational age was derived from the last menstrual period that was confirmed by first trimester ultrasound scans and from the day of oocyte retrieval in pregnancies after assisted reproduction. Chorionicity was established by standard ultrasonographic criteria performed by level III ultrasonographers, confirmed by careful examination of the delivered placenta by experienced obstetricians, and double-checked by pathologic examination of the placentas. No elective preterm deliveries are done; however, indicated preterm deliveries were carried out on the basis of maternal and/or fetal conditions. In otherwise normally progressing gestations, we offered, after detailed counseling, elective deliveries at 36–38 completed weeks of gestation. We excluded cases with major malformations.

The following variables were considered in our analysis: maternal age and parity, mode of conception (spontaneous vs. infertility treatment), maternal hypertensive disorders (preeclampsia, gestational hypertension, and chronic hypertension), mode of delivery, gestational age at birth (including subgroups of those born at $\leq$32, 33–36, and >36 weeks), birth weight, frequency of low (<2500 g) and very low birth weight (<1500 g), frequency of Apgar scores <7 at 5 minutes, incidence of stillbirth, early (<7 days of life) neonatal death, and Neonatal Intensive Care Unit (NICU) admission. The analysis of several outcome measures was done on live born twins only. We compared continuous data by using Student's *t*-test for which *p* values <0.05 were considered significant and categorical data by chi-square test or Fisher's exact test for which we derived Odds Ratios and 95% Confidence Intervals. We used SPSS version 23 (Chicago, IL) for statistical analyses. The study was approved by the local institutional review board.

Results

Our dataset included 1794 twin pregnancies followed and born in our hospital during the study period, roughly representing 2.5% of all deliveries. Table 1 shows the comparison of ''diabesity'' mothers ($n = 31$, 1.7%) to mothers with GDM but with appropriate BMI ($n = 112$, 6.2%) and to obese mothers without GDM ($n = 126$, 7.0%).

Twin pregnancies with ''diabesity'' were associated with significantly higher incidence of existing chronic hypertension than in GDM pregnancies without obesity, and with births at 33–36 weeks as compared with GDM pregnancies without obesity and with obesity without GDM. The stillbirth rate among GDM mothers was significantly greater in obese mothers. The comparisons showed otherwise remarkable similar results in terms of gestational age, birth weight, preeclampsia, cesarean section rate, and fetal-neonatal outcomes.

Discussion

Given the pregnancy complications incurred by either GDM or obesity in singleton and twin gestations, one could expect

Table 1. Gestational diabetes mellitus (GDM) with and without pre-gravid BMI vs. non-GDM obese mothers of twins.

	GDM		Non-GDM	Statistics		
BMI	A: Obese	B: Appropriate	C: Obese	A vs. B	A vs. C	B vs. C
N	31	112	126			
Age (mean, SD)	32.6 ± 5.5	32.5 ± 5.1	31.1 ± 5.5	NS	NS	$p = 0.04$
Spontaneous pregnancies	25 (80.6)	70 (62.5)	110 (87.3)	NS	NS	0.2 (0.1,0.5)
Chronic hypertension	6 (19.4)	6 (5.4)	11 (8.7)	4.2 (1.2,14.8)	NS	NS
Preeclampsia	8 (25.8)	15 (13.4)	24 (19.4)	NS	NS	NS
Gestational age (wks)	34.9 ± 2.4	35.4 ± 2.1	35 ± 3.3	NS	NS	NS
<33	4 (12.9)	12 (10.7)	23 (18.3)	NS	NS	NS
33–36	19 (61.3)	61 (54.5)	46 (45.2)	NS	2.1 (1.2,6.3)	2.1 (1.2,3.5)
>36	8 (25.8)	39 (34.8)	57 (45.2)	NS	NS	NS
Birth weight*	2357 ± 597	2201 ± 481	2246 ± 610	NS	NS	NS
<2500 g*	36/57 (63.2)	159/221 (72.0)	158/246 (64.2)	NS	NS	NS
Cesareans births	22 (71)	76 (67.9)	89 (70.6)	NS	NS	NS
Elective CS	17 (54.8)	55 (49.2)	72 (57.1)	NS	NS	NS
Stillbirths	5/62 (8.1)	3/224 (1.3)	6/252 (2.4)	6.4 (1.4,33.4)	NS	NS
5-min Apgar <5*	1/57 (1.8)	3/221 (1.4)	7/246 (2.8)	NS	NS	NS
NICU admission*	13/57 (22.8)	46/221 (20.8)	51/246 (20.7)	NS	NS	NS
Neonatal death*	1/57 (1.8)	3/221 (1.4)	9/246 (3.7)	NS	NS	NS

Data are shown as *N* (%) or mean ± SD. NS = not significant.

*Date exclude stillbirths

that a mutual effect would significantly increase the incidence of adverse outcomes in twin gestations as well. Several observations were made in this study. First, although it appears that twins born to 'diabesity' mothers are heavier than those with GDM alone and those with obesity alone, the differences were not significant, similar to previous observations when GDM cases were compared with non-GDM pregnancies [4–5]. Hence, ''diabesity'' does not confer any advantage in terms of birth weight in twin gestations. Second, ''diabesity'' does not increase the adverse outcomes as compared to GDM alone or to obesity alone, except of more cases of chronic hypertension which probably co-exist with the obesity state. This similarity might be due to the possibility that despite meticulous search for GDM, some of those with obesity only have some degree of glucose intolerance. This possibility is supported by the finding of Tward et al. [3], who described a continuous relationship between the degree of glucose intolerance and twin growth.

It should be remembered that the diagnostic criterion for GDM was changed over time. This should not change the basic assumption that our patients with either diagnostic test had GDM and were treated by the same standards. Moreover, the approach to GDM was not changed with respect to achieving glycemic control. However, our study was not aimed to explore differences in glycemic control among GDM mothers with and without obesity.

It is also possible that using the 2-step approach for the diagnosis of GDM is less suitable for twin gestations and may miss cases with GDM [1]. This observation is indirectly supported by the study of Dinham et al. [2], who observed an abrupt 3-fold increase in the incidence of GDM in twin pregnancies after using the 1-step approach of the 75 g (similar to the case in singletons), 2-h oral glucose tolerance test that was recommended by the International Association of Diabetes and Pregnancy Study Group [10]. Finally, our study showed that the risk of stillbirths increased 6-fold among the ''diabesity'' group as compared to GDM mothers with an appropriate pre-gravid BMI. As we could not find any similar observation, it could be inferred that obesity increases the risk of stillbirth in twins in mothers with GDM (or vice versa), but that this effect is not seen in obesity alone. Despite the statistical significance, we suggest considering this finding with caution because of the rather small numbers involved in this rare outcome.

Our study is unable to comment on any long-term outcomes related to GDM, obesity, or ''diabesity''. In the context of our study, we are also unable to comment on the differences or similarities between ''diabesity'' in singleton and twin gestations. For example, the sample size might be insufficient to exclude a difference in birth weight. Based on the literature in singletons [8,9], diabesity seems to hves a relatively minor effect in twins. If this is true, it would be important to elucidate how twins ameliorate the adverse outcomes of diabesity.

With these unanswered questions in mind, there is an obvious need for further studies on the effect of diabesity on perinatal outcomes.

Declaration of interest

The authors report no conflict of interest.

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