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Original Article

Chronic hypertension with gestational diabetes mellitus: What about complications?

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Abstract. The aim of this study was to evaluate the impact of chronic hypertension and gestational diabetes on pregnancy outcomes. We conducted a historical cohort study of 334 women undergoing singleton births in a Portuguese tertiary care center in Lisbon during 2012. Women were categorized into gestational diabetes mellitus with or without chronic hypertension. Pregnancy outcomes were compared using nonparametric tests. Multivariable analysis was used to control for potential confounders. The rate of preeclampsia in women with both chronic hypertension and gestational diabetes was 26.8% versus 3.8% in women with only gestational diabetes ($p<0.05$). Preterm birth was significantly more frequent in women with diabetes and chronic hypertension, 22.9% versus 9.7%, compared with women who only had gestational diabetes ($p<0.05$). The rate of newborns small for gestational age in women with the two conditions was 19.1% versus 7.6% in women with only gestational diabetes ($p<0.05$), but the rate of large for gestational age newborns in women of chronic hypertension and gestational diabetes was 9.6% versus 3.8% in gestational diabetes ($p<0.05$). The impact of having both chronic hypertension and gestational diabetes in pregnancy leads to poor pregnancy and perinatal outcomes, represented by more maternal, obstetrical and neonatal morbidity.

Keywords: Chronic hypertension; perinatal outcomes; gestational diabetes

Introduction

Gestational diabetes is defined as an abnormal glucose tolerance at any moment of pregnancy [1]. It is believed that 6 to 7% of all pregnancies are complicated by diabetes and that gestational diabetes comprises 90% of all these cases. The prevalence has been growing with the sedentary lifestyle, excess of weight and obesity, which are risk factors, when women decide to delay maternity. Gestational hypertension and preeclampsia are frequently associated with diabetes in pregnancy, with poor results in terms of maternal and perinatal morbidity [2]. Hyperglycemia may contribute to fetal macrosomia, increasing the risk of delivery complications, shoulder dystocia and, hence, leads to a higher rate of cesarean sections. Neonatal complications are essentially associated to respiratory distress and to metabolic disorder, but can also be linked to traumatic delivery, essentially when there is macrosomia. The maternal long-term risks are type 2 diabetes, metabolic syndrome and cardiovascular disease. Lifestyle changes and weight loss are important measures for a risk reduction [3]. In a Portuguese population study that took place in 2012, the prevalence of gestational diabetes in National Health Service users was 4.8%, and between 30-39 years old it was 5.9% and 13.5% for women over 40 years old. The International Association of Diabetes and Pregnancy Study Group (IADPSG) recommendations are implemented in Portugal since 2011 [4, 5].

The factors determining the higher prevalence of diabetes in pregnancy are the same as those observed in chronic hypertension, defined by values of arterial pressure ≥140/90 mm Hg measured before or during the first half of the pregnancy [6]. Chronic hypertension and gestational diabetes are independent risk factors for pregnancy complications and when in association, they can contribute to more maternal and perinatal severe outcomes [7]. The prevalence of chronic hypertension in pregnancy is 2 to 8% varying with age, ethnicity and body mass index [8, 9]. The rate of hypertensive disorder in pregnancy and puerperium in Portuguese women is 6%: 1.5% with chronic hypertension, 2.5% with gestational hypertension, 1.4% with preeclampsia, 0.2% with superimposed preeclampsia,

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0.1% with eclampsia and 0.1% with HELLP syndrome. These data are the result of a first study about the prevalence of this pathology in Portugal [10]. We have no comparative studies in Portugal addressing the impact of chronic hypertension on gestational diabetes or *vice versa.*

The objective of this study was to compare maternal and perinatal results in two cohorts of pregnant women with gestational diabetes: one with chronic hypertension and the other without chronic hypertension.

Materials and Methods

This observational study contained two historical cohorts of singleton pregnant women followed in a tertiary care center in Lisbon, during 2012: one cohort of 237 pregnancies with gestational diabetes (GD) and the other with 97 pregnant women with gestational diabetes and chronic hypertension (CH). This study was approved by the Ethical Committee of Central Hospital of Lisbon and all the participants gave their approved consent.

Data were collected from the service database and from the clinical process. Both cohorts had the same surveillance guidelines. Socio demographic variables and pregnancy results were compared in both groups: gestational age at delivery, type of delivery, hypertensive complications or preeclampsia, prematurity, weight and percentile for gestational age of newborns.

Chronic hypertension was defined according to the International Society for the Study of Hypertension in Pregnancy (ISSHP) as an arterial systolic and diastolic pressure (equal or greater than 140/90 mm Hg) before pregnancy or in the first 20 weeks; when elevation of arterial pressure occurred after the 20th week, it was classified as gestational [6].

Preeclampsia was defined according to ISSHP criteria, by the presence of hypertension and proteinuria after the 20th week of pregnancy and superimposed preeclampsia when the criteria of preeclampsia were applied to chronic hypertension [6, 9]. Proteinuria was quantified by a dipstick reading of 1+ or ≥30 mg/dl, confirmed by values of 300mg per 24-hour urine collection. If preeclampsia occurred before the 34th week, it was classified as of early-onset [11]. Indicators of clinical deterioration were: the need for anti-hypertensive drugs during pregnancy in chronic hypertension; the need to terminate pregnancy if there was a clinical worsening of maternal or fetal status, or a diagnosis of preeclampsia.

The definition of gestational diabetes was the presence of a glucose intolerance at any moment of the pregnancy and criteria are defined by International Association of Diabetes and Pregnancy Study Group (IADPSG) since 2011 [3]. It is classified as gestational diabetes, a fast glucose value equal or greater than 92 mg/dl in the first trimester or after an OGTT with 75 g oral glucose between the 24th-28th, by the presence of one or more values equal or greater than (0h ≥ 92mg/dl, 1h ≥ 180mg/dl, 2h ≥ 153mg/dl) [5].

The gestational results were considered in terms gestational age at the time of delivery, preeclampsia, early-onset and severe preeclampsia, fetal growth restriction, birth weight, small for gestational age (birth weight <10th percentile for gestational age) on a Hadlock growth curve and stillbirth.

TABLE 1
SOCIODEMOGRAPHIC AND ANTHROPOMETRIC VARIABLES

Variable	Gestational diabetes (n = 237)	Chronic hypertension + Gestational diabetes (n = 97)	P
Median age (range)	33 (17-44)	36 (23-49)	0.001
Age ≥ 35 yrs (%)	98 (41.4)	63 (55.8)	
Pre-conception BMI			
Median (range)	26 (17-50)	31(20-55)	0.001
≥ 30 yrs: No. (%)	57 (25.6)	56 (58.9)	0.007
≥ 35 yrs: No. (%)	24 (10.5)	21 (21.9)	
Median weight gain (kg)	9	3	0.001
Ethnicity: No. (%)			
Caucasian	166 (70.0)	74 (76.2)	0.026
African	42 (17.8)	22 (22.8)	
Asian	29 (12.2)	1 (1.0)	
Parity: No. (%)			
Nulliparous	114 (48.1)	27 (31.0)	0.001

BMI: Body mass index.

TABLE 2
PREGNANCY AND DELIVERY DATA

Variable	Gestational diabetes (n = 237)	Chronic hypertension + Gestational diabetes (n = 97)	P
MAP >85	0	41 (41.2)	0.001
Therapy			
Diet n (%)	145 (61.2)	61 (62.9)	0.383
Insulin	57 (24.1)	32 (33.3)	0.177
OAD	22 (9.3)	3 (3.1)	
OAD + insulin	13 (5.5)	1 (1.0)	
Hypertensive complications; no. (%)	28 (11.8)	44 (45.4)	0.001
Preeclampsia; no. (%)	9 (3.8)	26 (26.8)	0.001
Median delivery GA	38.2	37.5	0.352
<37 Weeks; no. (%)	23(9.7)	22 (22.9)	0.001
Newborn weight			
>2500g	217 (91.6)	75 (78.9)	
<2500g	20 (8.4)	20 (21.1)	0.001
SGA: no. (%)	18 (7.6)	18 (19.1)	0.001
AGA	210 (88.6)	79 (68.1)	
GGA	9 (3.8)	9 (9.6)	0.03
Mean NB weight	3270g	3180g	0.352
Delivery			
Term; no. (%)	214 (90.3)	74 (77.1)	
Preterm	23 (9.7)	22 (22.9)	0.001
Cesarean section	88 (37.1)	59 (60.8)	0.001

MAP: median arterial pressure; GA: gestational age; OAD: Oral anti- diabetics; SGA: Small for gestational age; AGA: Adequate for gestational age; GGA: Great for gestational age; NB: Newborn.

Statistical analysis

The data were registered in an informatics database. To compare categorical variables between the study groups, Chi-square test or extension to exact Fisher test were used;

TABLE 3
PREGNANCY HYPERTENSIVE COMPLICATIONS

Complication		No. (%)	aOR	95% CI
Hypertensive				
BMI ≥ 30	GD GD+CH	57 (25) 56 (58)	4.2	1.38-12.70
Nulliparity	GD GD+CH	114 (48.1) 27 (31)	1.89	0.94-3.72
Preterm birth	GD GD+CH	23 (9.7) 22 (22.9)	6.08	1.44-25.70
Cesarean section	GD GD+CH	88 (37.1) 59 60.8)	2.36	1.22-4.57
Age ≥35 yrs	GD GD+CH	24 (10.5) 21 (21.9)	1.792	0.90-3.56
Preeclampsia				
Chronic hypertension	GD GD+CH	0 (3.8) 97 (26.8)	9.4	2.4-37.3
Cesarean section	GD GD+CH	59 (37.1) 88 (60.8)	7.2	1.9-27.1

GD: gestational diabetes; CH: chronic hypertension; PE: preeclampsia.

for the analysis of continuous variables the non-parametric test of Mann-Whitney was used. Univariate analysis was used to assess differences in baseline demographic and pregnancy characteristics and in the results between the 2 groups. Unadjusted odds ratios (ORs) with 95% confidence intervals (CIs) were calculated to quantify the risk of hypertensive complications, preeclampsia and preterm birth in women with superimposed preeclampsia and preeclampsia. Multivariate logistic regression was used to calculate adjusted odds ratios (aORs) for preeclampsia and hypertensive complications in the groups. All statistical analysis was performed with Statistical Package for Social Sciences (SPSS) version 20.0. Tests with probability values of $p<.05$ were considered significant.

Results

The analysis of socio demographic and anthropometric variables shows that the mean maternal age was superior in the cohort of chronic hypertension with gestational diabetes (35.5 vs. 32.9; $p<0.001$) with more women being over 35 years old (55.7% vs. 41.4%). The body mass index (BMI) was superior in this cohort (30.9 vs. 27.1; $p<0.001$). In the cohort of chronic hypertensive disease associated to gestational diabetes, Caucasian women were more frequent, but Asian women were more present in the cohort of gestational diabetes without chronic hypertension, corresponding to a growing prevalence of diabetes in this group of immigrants. Gestational diabetes without chronic hypertension had more nulliparous (48.1% vs. 31.0 %; $p=0.001$) (Table 1).

Therapeutic measures had no differences in the two cohorts (Table 2). The cohort of chronic hypertension used insulin therapy more frequently, but without significance; however, weight gain during pregnancy was superior in the cohort of gestational diabetes without chronic hypertension (Table 1). The cohort of chronic hypertension and gestational diabetes had a higher incidence of preterm birth (22.9% vs. 9.7%; $p=0.001$), more hypertensive complications (43.3% vs. 11.8%) ($p<0.001$), more preeclampsia (22.7% vs. 3.8; $p<0.001$), a higher rate of cesarean sections (62.5% vs. 37.1%; $p=0.001$), more small for gestational age infants (SGA) (19.1% vs. 7.6%; $p<0.001$), but also more large for gestational age infants LGA) (9.6% vs. 3.8%) (Table 2).

Multivariate regression analysis confirmed that hypertensive complications are associated with obesity (58% vs. 25%; aOR 4,2; IC 95%, 1.38-12.70); African ethnicity (22.8% vs. 17.8%; aOR: 28.7; IC 95%, 2.3-34), preterm birth (22.9% vs. 9.7%; aOR 6,1; IC 95%, 1.44-25.70) and higher cesarean section rates (60.8% vs. 37.1%; aOR 2.36; IC95%, 1.22-4.57). In the presence of gestational diabetes and chronic hypertension there is a greater risk to have preeclampsia (26.8% vs. 3.8%; OR: 9.4; IC 95%, 2.4-37.3) and cesarean section (60.8% vs. 37.1%; aOR: 7.2; IC 95%, 1.9-27.1) than when only gestational diabetes is present (Table 3).

Discussion

In this study we intended to address the question: in a pregnancy complicated by gestational diabetes and chronic hypertension what can be expected?

In gestational diabetes, the presence of chronic hypertension contributed to a worst pregnancy result. Chronic hypertension is usually present in older women and in the present study we have confirmed that chronic hypertensive women have larger body mass index and obesity.

In women with chronic hypertension and gestational diabetes it was necessary to prescribe a greater insulin dosage in order to achieve metabolic control, which suggests that there is an insulin resistance in gestational diabetes with chronic hypertension; we think that the number of cases enabled us to find a statistical significance. The reason is not only the larger body mass index, but also probably the chronic hypertension, by unknown reasons.

In this study, we found a lower weight gain in women with chronic hypertension than in women with gestational hypertension, probably due to a more intense role of dietary measures. In women with chronic hypertension and gestational diabetes there were more cases complicated by preterm birth, and of small for gestational age newborns, owing to more preeclampsia complications with maternal or fetal deterioration status; but we had also in this group more newborns large for gestational age, probably due to a more difficult metabolic control. African ethnicity has an increased risk to have chronic hypertension and this is also present in this study [15, 16]. We had no cases of maternal or perinatal mortality.

The relationship with carbohydrate metabolism in gestational diabetes when there is simultaneously chronic hypertension is under investigation [17]. Some authors have concluded that carbohydrate metabolism is different, and there is probably a link between insulin resistance and chronic hypertension [18]. When both pathologies are present the metabolic control is more difficult and greater doses of insulin are needed. This group has more adiposity,

but this is possibly not the only factor, and median arterial pressure (MAP) in the first trimester may be a good predictor of insulin resistance.

In our study we confirmed this predictive role of first trimester median arterial pressure; 41% of women with chronic hypertension had an elevated MAP and in this group we had more therapy for arterial pressure control and also more insulin use.

For the explanation of the worst metabolic control in women with chronic hypertension with gestational diabetes some theoretical hypothesis were tried. Gestational diabetes is the result of an exaggerated insulin resistance characteristic of the pregnancy; if there is the association with obesity and dyslipidemia, endothelial dysfunction, oxidative stress and inflammatory response can be more expressive and can contribute to worsening the chronic hypertension pathological findings [19].

After delivery, it is important to do the diabetes-screening test to diagnose type 2 diabetes, a fast abnormal glucose or a glucose tolerance reduction. Lifestyle changes are also important to prevent metabolic syndrome, type 2 diabetes, vascular dysfunction and atherogenesis, which are characteristics of cardiovascular diseases. The prevention and correction of obesity is a major measure that should begin in childhood.

Conclusion

This is an observational study introducing IADPSG criteria for the diagnosis of gestational diabetes. These results show the negative influence of chronic hypertensive disease and obesity in gestational diabetes and pregnancy. It is the first study of diabetes and chronic hypertension in pregnant Portuguese women with the new diagnosis criteria. Our conclusions are similar to other studies and prove the importance of obesity prevention for cardiovascular risk prevention.

Conflict of Interest

The authors declare no conflicts of interest.

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