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Overweight/obesity: Prevalence and association with maternal and fetal variables in pregnant women with pre-eclampsia

Sobrepeso/obesidade: Prevalência e associação com variáveis maternas e fetais em gestantes com pré-eclâmpsia

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ABSTRACT

Objective: To evaluate the overweight and obesity prevalence in pregnant women with preeclampsia, as well as to test for associations between the maternal anthropometric profile, clinical, and laboratory variables, and fetal outcomes. **Methods:** an analytical cross-sectional study, with 178 pregnant women and their newborns attended at a reference public maternity hospital in the North of Minas Gerais. Information was collected in medical records and interviews. Odds ratio analysis was performed between the studied variables with confidence intervals of 95%, and significance level set as p <0.05. **Results:** the overweight/obesity prevalence in the present study was 73.03%. Regarding the maternal conditions, a statistically significant association was observed for the personal history of pre-

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eclampsia, parity, and platelets, and regarding the birth conditions, a statistically significant association for the cephalic perimeter <33cm was observed. **Conclusion:** the studied group evidenced a prevalence of overweight/obesity higher than 70% and maternal and fetal risk factors for pre-eclampsia, such as positive personal history of pre-eclampsia, number of pregnancies higher than 1, platelets count over 150.000 units/ mm^3, and fetus cephalic perimeter lower than 33cm.

Keywords: Pregnancy, obesity, pre-eclampsia, pregnancy complications, newborn.

RESUMO

Objetivo: Avaliar a prevalência de sobrepeso e obesidade em gestantes com pré-eclâmpsia, bem como testar associações entre perfil antropométrico materno, variáveis clínicas e laboratoriais e desfechos fetais. **Métodos:** estudo transversal analítico, com 178 gestantes e seus recém-nascidos atendidos em uma maternidade pública de referência do Norte de Minas Gerais. As informações foram coletadas em prontuários e entrevistas. Foi realizada análise de *odds ratio* entre as variáveis estudadas com intervalos de confiança de 95% e nível de significância estabelecido em p<0,05. **Resultados:** a prevalência de sobrepeso/obesidade no presente estudo foi de 73,03%. Em relação às condições maternas, foi observada associação estatisticamente significativa para histórico pessoal de pré-eclâmpsia, paridade e plaquetas, e em relação às condições de nascimento, foi observada associação estatisticamente significativa para perímetro cefálico <33cm. **Conclusão:** o grupo estudado evidenciou prevalência de sobrepeso/obesidade superior a 70% e fatores de risco maternos e fetais para pré-eclâmpsia, como história pessoal positiva de pré-eclâmpsia, número de gestações superior a 1, contagem de plaquetas superior a 150.000 unidades/mm3 e perímetro cefálico fetal inferior a 33cm.

Palavras-chave: Gravidez, obesidade, pré-eclâmpsia, complicações na gravidez, recém-nascido.

INTRODUCTION

Obesity represents one of the most prevalent public health problems worldwide, with global estimates pointing to more than 890 million people affected[1]. The increase in the prevalence of obesity significantly impacts the health services, favoring other chronic conditions (such as diabetes, cardiovascular diseases, and non-alcoholic fatty liver disease), increasing expenses with health services, and affecting the productivity chain, due to the years of life lost and expenses with social security[2].

Overweight and obesity are characterized by the excessive accumulation of body fat, especially visceral, arising among many factors, by the imbalance between energy gain and expenditure. Obesity etiopathogenesis is multifactorial and complex, involving several genetic and environmental factors, with emphasis to sedentarism and the consumption of hypercaloric diets[3-4].

In the context of maternal health, obesity is a risk factor for maternal-fetal and neonatal adverse outcomes, increasing the risk of gestational diabetes, hypertensive diseases (above all, pre-eclampsia), miscarriage, postpartum hemorrhage, and abnormal fetal growth [5-6]. Pre-eclampsia (PE) is a multifunctional and multisystem disorder, exclusive to human pregnancy and characterized by an abnormal vascular response to placentation, leading to increased peripheral vascular resistance and placental aggregation[7,8]. Clinically, the main observations are increased arterial hypertension and proteinuria, which develop after 20 weeks of pregnancy in women previously normotensive or superimposed on pre-existing hypertension. Currently, PE is also considered when target-organ lesions occur in the absence of proteinuria[9].

Several mechanisms link obesity and PE, including insulin resistance (a commonly observed condition in the maternal obesity context), which predisposes to reduced cytotrophoblast migration and uterine spiral artery remodeling, which in turn leads to placental hypoxia. In this condition, the placental release of antiangiogenic and pro-inflammatory factors to the maternal circulation is observed, promoting endothelial dysfunction, characterized by a decreased endothelial production of nitric oxide and increased oxidative stress, resulting in the clinical signs and symptoms that characterize PE[10-11]. Moreover, studies indicate the role of adipokines, such as leptin, adiponectin, and resistin; besides the increment in the systemic pro-inflammatory picture triggered by the production and release of cytokines (e.g., tumor necrosis factor-α and interleukin-6) by the adipocytes[12].

The maternal anthropometric profile has been the current focus of several scientific studies, not only because of the growing prevalence of overweight and obesity during pregnancy but, above all, because of their determining role in pregnancy outcomes, especially in the context of pregnancy comorbidities[13]. Studies that investigate the overweight and obesity prevalence in the context of pre-eclampsia are rare in the Brazilian scientific

literature[14]. In this sense, the present study can provide complementary understandings on the subject, especially in the loco-regional context.

Therefore, the present study aims to measure the prevalence of overweight and obesity in pregnant women with pre-eclampsia attended at a public reference maternity hospital in the north of Minas Gerais and to assess associations between the anthropometric profile and the clinical, laboratory, and fetal outcomes variables.

METHODS

Study design and participants

It is a cross-sectional analytical study performed with 178 pregnant women with a diagnosis of pre-eclampsia attended at a Maternity/Obstetrician center in the Hospital Universitário Clemente de Faria (HUCF) from the Universidade Estadual de Montes Claros, Montes Claros, Minas Gerais, Brazil. The HUCF is a teaching hospital, with all its hospital beds supported by the Unique Health System, being a reference in several clinical areas in the north of Minas Gerais, including gynecology/obstetrics, with assistance to low-, intermediate- and high-risk pregnancies, and performing around 200 deliveries monthly.

The participants were selected from convenience non-intentional sampling, according to the hospital demand, from September 2019 to March 2020, considering the difficulty of random selection. Due to the restrictive measures adopted by the institution during the COVID-19 pandemic, the data collection could not be extended to a longer period.

The following inclusion criteria were adopted: pregnant women aged 18 years old or more (at the data collection moment), admitted to the hospital with a diagnosis of pre-eclampsia, according to criteria previously established[9], with an imminent indication for delivery (regardless of the route); gestation of a single live fetus; with a pre-natal card describing information regarding pre-gestational weight (measured until the end of the 13th gestational week), height and total gestational weight gain; not being a carrier of other pre-gestational or gestational chronic and/or infectious diseases, and those who accepted to participate in the research by signing the Free and Informed Consent Form.

Data collection

The data collection involved a team formed by five researchers (two obstetric nurses, one physiotherapist, and two scientific initiation students), two of them formally employed in the hospital service where the study was performed. The data collection was performed after the team calibration. The obstetric nurses were responsible for surveying the admissions of patients under clinical investigation or with the pre-defined diagnosis of pre-eclampsia (both with the prediction for pregnancy termination) and follow the cases so the other team members could proceed with the data collection, which was organized by a previously established schedule.

The data was primarily collected via interviews with the participants, as well as by retrieving information from the patient's prenatal care or medical chart. For the data collection, a semi-structured questionnaire created by the team of researchers based on the study goals and previous research was applied. The following information was collected: sociodemographic, clinical, laboratory, and anthropometric variables, both maternal and fetal.

Dependent variable

The dependent variable "anthropometric profile" was obtained from the pre-gestational Body Mass Index (BMI) assessed with the formula proposed by the Brazilian Association for the Study of Obesity and Metabolic Syndrome: BMI = weight (Kg)/height^2(m), adopting the following cutoffs: ≥ 18.5 and ≤ 24.9 Kg/m^2(normal weight – eutrophy), ≥ 25.0 and ≤ 29.9 Kg/m^2 (overweight), and ≥30 Kg/m^2 (obesity)[16]. For the statistical analysis, the participants were grouped into two categories: a) eutrophy and b) overweight/obesity.

Independent variables

The studied independent variables were 1) sociodemographic and clinical maternal: age defined by the obstetric risk, being stratified as ≥18 and ≤ 35, and above 35 years old. The educational level was stratified as ≤ 10 years and ≥ 11 years, the latter corresponding to the years of study required for high school graduation. The per capita income was divided as ≥ R$ 998,00 and < R$ 998,00, value referent to the minimum salary at the data collection time. The prenatal consults stratification followed the minimum recommended by the Ministry of Health, as ≤ 5 consults and ≥ 6 consults. The PE diagnosis was stratified as early-onset (<34

weeks) and late-onset (≥34 weeks). Personal history of PE was categorized as yes or no and referred to episodes of this condition in previous pregnancies. For the family history of PE, we considered the self-reported existence of PE cases in first-degree relatives (mother and sisters). Parity corresponded to the number of babies born alive or dead (≤1 and ≥2). The gestational age at delivery was classified as pre-term (≤ 36 weeks) and term (≥ 37 weeks). The route of delivery was classified as cesarean or vaginal. The PE clinical presentation was classified as mild or severe[10]. The PE prophylaxis was categorized as yes (use of elemental calcium from 1 to 2g/day and/or acetylsalicylic acid from 60 to 150mg/day at night from the 12th week starting until the 20th week of gestation for patients with knownrisk of PE) or no. The laboratory variables were stratified according to the recommendations of the International Society for the Study of Hypertension in Pregnancy (ISSHP) and the Federação Brasileira das Associações de Ginecologia e Obstetrícia, being included proteinuria (≤ 299 mg/24h and >299 mg/24h), the number of platelets (> 150.000/mm^3, 101.000 to 150.000/mm^{3,} and ≤ 100.000/mm^3), aspartate aminotransferase (AST) (<70 U/L and ≥ 70 U/L), LDH (≤599 U/L and ≥ 600 U/L), creatinine (≤1.0 and ≥1.1 mg/dL).The fetal outcomes variables were: birth weight (≤ 2,500 g, from 2,501 to 3,999 g and ≥ 4,000 g), gender (male and female), cephalic perimeter (≥ 33 and< 33 cm), Apgar 1st minute and 5th minute (8-10 – no asphyxia and<8 with asphyxia) and fetal centralization according to obstetric ultrasound (yes or no).

Statistical Analysis

Data were analyzed using the statistical software SPSS® IBM version 24.0. Initially, the data were tested for normality via the Kolmogorov-Smirnov statistical test. Following, the *odds ratio* (OR) values were obtained, along with their respective confidence intervals (CI) 95%, for the evaluation of the odds ratio between one exposition and the analyzed outcomes. The significance was set as $p<0.05$.

Ethical aspects

All the participants were oriented regarding the research and presented their consent, by signing the Free and Informed Consent Form. The research project was approved by the Ethics Committee in Research from Unimontes, number CAAE: 18646619.0.0000.5146, via protocol nº 3.553.143/2019.

RESULTS

In the included sample of pre-eclamptic pregnant women, the prevalence of overweight/obesity was 73.03% (n=130). Table 1 describes the sociodemographic, clinical, and laboratory variables from the participants, stratified by body weight (pregestational eutrophic and overweight/obese). Statistically significant associations were observed for the following variables: personal history of PE and parity. The personal history of PE was superior in the group of women with overweight/obesity (OR 2.21; IC95% 0.98–4.98; p=0.050), as well as parity (> 1 birth) (OR 1.92; IC95% 0.98–3.78; p=0.050). For the other variables under study, statistically significant associations were not observed.

Table 1 – Sociodemographic, clinical and anthropometric characteristics of pre-eclamptic pregnant women stratified by their anthropometric profile, Montes Claros, Minas Gerais, Brazil.

Variables	**Anthropometric profile (BMI)**						
	18.5 to 24.9		≥ 25.0				
	n	%	n	%	OR	CI95%	p-value
Age (years)							0.40
≤ 35	37	28.7	92	71.3	1		
> 35	11	22.4	38	77.6	1.389	0.642-3.006	
Educational level (years)							
≥ 11	31	24.4	96	75.6	1		0.23
≤ 10	17	33.3	34	66.7	1.548	0.762-3.147	
Per capita income (in reais)							
≥ R$ 998.00	11	21.6	40	78.4	1		0.29
< R$ 998.00	37	29.4	89	70.6	0.661	0.306-1.428	
Prenatal consults							
≥ 6 consults	37	26.1	105	73.9	1		0.59
≤ 5 consults	11	30.6	25	69.4	1.249	0.560-2.785	
PE diagnosis							
Late-onset (≥ 34 weeks)	18	26.1	51	73.9	1		
Early-onset (< 34 weeks)	27	26.5	75	73.5	0.980	0.490-1.963	0.95
Personal history of PE							
No	39	31.2	86	68.8	1		
Yes	9	17	44	83	2.217	0.986-4.987	**0.05**
Family history of PE							
No	20	25.3	59	74.4	1		
Yes	24	27.6	63	73.4	1.124	0.563-2.244	0.74
Number of pregnancies							
≤ 1 pregnancy	23	35.4	42	64,6	1		
> 1 pregnancies	25	22.1	88	77.9	1.928	0.981-3.786	**0.05**

Gestational age at delivery							
Term delivery	18	25.4	53	76.6	1		
Pre-term delivery	30	28	77	72	1.147	0.581-2.267	0.69
Route of delivery							
Vaginal	14	28.6	35	71.4	1		
Cesarean	34	26.4	95	73.6	0.895	0.430-1.863	0.77
PE clinical presentation							
Mild	14	21.5	51	78.9	1		
Severe	34	30.1	79	69.9	1.568	0.767-3.205	0.22
Drug prophylaxis for PE							
No	42	28	108	72	1		
Yes	6	21.4	22	28	1.426	0.540-3.763	0.47
Maternal proteinuria (mg/24 h)							
≤ 299	14	28.6	40	71.4	1		
> 299	4	33.3	8	66.7	0.800	0.211-3.034	0.74
Platelets (units/ mm^3)							
> 150.000	27	22	96	78	1		**0.03**
100.000 to 150.00	14	41.2	20	58.8	0.402	0.180-0.899	
< 100.000	15	45.5	6	54.5	0.338	0.096-1.191	
AST (U/L)							
≤ 70	41	26.1	116	73.9	1		
> 70	5	50	5	50	0.353	0.097-3.320	0.11
LDH (U/L)							
≤ 599	37	26.2	104	73.8	1		
≥ 600	8	32	17	68	1.323	0.527-3.320	0.55
Creatinine (mg/dL)							
≤ 1.0	41	28.9	101	71.1	1		
≥ 1.1	3	37.5	5	62.5	0.677	0.155-2.962	0.60

Abbreviations: PE, pre-eclampsia; AST, aspartate aminotransferase; LDH, lactate dehydrogenase.

Table 2 depicts the evaluation of fetal outcomes according to the participant's stratification as eutrophic versus overweight/obese. Statistically significant differences were found only for the variable cephalic perimeter, where pregnant women with overweight/obesity had three times more chance of having babies with the cephalic perimeter < 33 cm (OR 3.04; IC95% 1.44-6.41; p=0.003).

Table 2 – Fetal outcomes of newborns of pre-eclamptic pregnant stratified according to their anthropometric profile, Montes Claros, Minas Gerais, Brazil.

Variables	**Anthropometric profile (BMI)**						
	18.5 a 24.9		≥ 25.0				
	n	%	n	%	OR	IC95%	p-value
Birth weight (grams)							
≥ 2,501 and ≤ 3,999	10	32.3	21	67.7	1		

≤ 2,500	18	30.5	41	69.5	1.549	0.715-3.356	
≥ 4,000	1	14.3	6	85.7	2.63	0.295-3.498	0.51
Gender							
Male	22	24.7	67	75.3	1		
Female	26	29.2	63	70.8	0.796	0.410-1.545	0.50
Cephalic perimeter (cm)							
≥ 33	27	37.5	45	62.5	1		
< 33	14	16.5	71	83.5	3.043	1.443-6.414	**0.003**
APGAR 1st minute							
No asphyxia	20	76.9	106	72.6	1		
With asphyxia	6	23.1	40	27.4	0.795	0.298-2.123	0.65
APGAR 5th minute							
No asphyxia	0	0	8	100	1		
With asphyxia	46	28	118	72	6.400	0.000	0.08
Fetal centralization							
No	24	25.3	71	74.7	1		
Yes	**8**	**32**	**17**	**68**	**0.718**	**0.275-1.875**	**0.50**

DISCUSSION

The maternal anthropometric condition, evaluated in this study via the pre-gestational body mass index, has been the target of several studies, not only because of the increasing prevalence of maternal overweight/obesity, but even due to its influence on gestational comorbidities, such as pre-eclampsia, and outcomes regarding maternal and fetal health[16-19]. In Brazil, studies regarding the prevalence of overweight/obesity among women with pre-eclampsia, especially in the loco-regional context where the present study was performed, were not identified. Therefore, despite the methodological limitations of the present study, important findings that contribute to a more comprehensive view of the phenomenon studied are given, opening perspectives of interventions regarding maternal and fetal health.

In the present study, the prevalence of overweight/obesity was 73.03%. This finding is alarming since studies performed in the general population of pregnant women evidence prevalence that varies from 20 to 40%[18]. Obesity increases two to three-fold the general risk of pre-eclampsia increasing progressively with the increase of BMI. It is important to highlight that not only the late and light forms of pre-eclampsia increase but also the early and severe pre-eclampsia, which are associated with a greater perinatal morbimortality.

Little is known about the pre-eclampsia predisposition mechanisms of women with pre-gestational overweight/obesity. Studies have associated the increase in pre-gestational

BMI to a greater risk of pre-eclampsia[13,20], which may be mediated by i) systemic inflammatory alterations arising from the low-grade inflammation commonly present in obesity, which is especially mediated by interleukin-6 and tumor necrosis factor-alpha; ii) increased release and production of oxygen reactive species that act in the placenta favoring the PE physiopathological alterations, including endothelial dysfunction; iii) alterations in the glycemic and lipid homeostasis, especially driven by the insulin resistance state and cardiovascular diseases, such as arterial hypertension[10].

In our study, an association between the anthropometric state and primiparity was observed. Several studies evidence a greater chance of developing PE in the primiparity[21,22]. Noteworthy, a meta-analysis compared 26 studies and evidenced that primiparity was associated with a 2.4-fold increased risk of developing PE[23]. Several physiopathological explanations are given for this association. For example, it was proposed that pre-eclampsia is the consequence of a maternal immune reaction against paternal antigens expressed in the placenta, and this reaction might result in a defective trophoblastic invasion and subsequent placental dysfunction. The lower risk of pre-eclampsia in multiparous women was attributed to the desensitization after exposure to paternal antigens in the placenta during previous pregnancies. A lower risk was also attributed to the softer trophoblastic invasion after modification of the maternal spiral arteries during the first pregnancy.

Consistent with other studies, the present work evidenced that a previous pre-eclampsia diagnosis (personal history of PE) was associated with a greater risk for this condition in the current pregnancy[23]. Corroborating, Boyd et al.[24] evidenced that early- and intermediate-onset PE in previous pregnancies were associated with 25- and 20-fold increased risk, respectively, of developing PE with the same characteristic on a subsequent pregnancy with the same partner as compared to pregnancies without this history[24]. Moreover, a study developed in Jordan reported a 2.3-fold increased risk of developing PE in the first pregnancy than on the subsequent ones[21]. Regarding the PE recurrence in subsequent pregnancies, the evaluation of parameters such as sexual partner (progenitor) and implementation of prenatal drug prophylaxis for PE, might interfere in this variable analysis. In our study, these variables were removed from analysis due to the lack of information.

Regarding fetal outcomes, the present study observed a greater chance of newborns of overweight/obese mothers being born with a cephalic perimeter < 33 cm (OR 3.04; IC 95%

1.44-6.41). The cephalic perimeter value is intimately related to the cerebral volume, and its measure is routinely performed with all newborns, to compose the fetal growth assessment[25]. The scientific literature lacks studies associating PE, maternal obesity, and newborn cephalic perimeter. However, the maternal metabolic profile may exert a direct influence on fetal development[25-30].

As is known, obesity is a risk factor for PE development, and this condition may predispose, among several fetal conditions, to a decreased intrauterine growth and prematurity, important factors that affect the newborn anthropometric parameters[31]. However, a cephalic perimeter below the cutoff applied in the present study does not necessarily predict impairments of the neuropsychomotor development. However, newborns with a cephalic perimeter below the expected for their age must be more closely monitored by their parents and health professionals. Therefore, despite not being observed in the present study statistically significant differences for prematurity and birth weight, for example, it is inferred that overweight/obesity might have an unfavorable influence on this fetal anthropometric parameter.

CONCLUSION

Finally, despite the methodological limitations, the present study is one of the few reports of the national scientific literature that addresses this topic. Clinically, besides contributing to a greater comprehension of pre-eclampsia in the obesity context, our findings may drive changes in pre-gestational practices, especially those concerning the anthropometric profile, and determine the need for greater surveillance of pregnant women with overweight/obesity in the prenatal follow-up.

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