INTRODUCTION

Metabolic syndrome (MS) is defined by the National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III) as the presence of at least three of the following characteristics: abdominal obesity (abdominal circumference ≥88 cm), triglycerides ≥150 mg/dL, cholesterol, high-density lipoprotein cholesterol (HDL-c) <50 mg/dL, blood pressure (BP) ≥130/85 mmHg, and fasting glycemia ≥100 mg/dL. Different criteria, however, are being used to classify the syndrome during pregnancy and in the postpartum period, when the abdominal circumference is significantly changed.2-4
Despite the contradictions regarding classification in these periods, studies showed a prevalence of MS of 12.4% in pregnant women and 29% in puerperal women. The factors often associated with the syndrome were age, parity, dyslipidemia, gestational diabetes mellitus (GDM), hypertension, and obesity.

The high prevalence found by the studies, the metabolic risks from the physiological changes of pregnancy and the postpartum period, the lack of established parameters to classify the syndrome, and the inconsistencies regarding its prevalence and associated factors in women with no previous diseases suggest the need for research on the topic. Thus, the objective of this study was to evaluate the prevalence of MS and the main maternal factors associated with it in women without pre-gestational diseases, at the beginning of pregnancy and in the immediate postpartum period.

METHODS

Study design

This is a cohort study with 200 pregnant women treated in basic health units of the city of Campina Grande, Paraíba, Brasil. The women were evaluated in the 16th week of gestation (n=200) and re-evaluated during the immediate postpartum period (n=187) in the Instituto Paraibano de Pesquisa Professor Joaquim Amorim Neto (IPESQ), between September 2014 and December 2015. The research was approved by the Research Ethics Committee of the Federal University of Paraíba (CAAE: 03649512.9.0000.5182), and all participants signed an informed consent form (ICF).

Sample Size

The sample size was calculated by the OpenEpi, version 2.3 (Atlanta, GA, USA), assuming a rate of waist circumference increase of 22.8% in the immediate postpartum. For a 85% power and a 95% confidence level, 148 pregnant women would have to be included. This number was increased by 30% to compensate for possible losses during follow-up.

Eligibility criteria

We included pregnant women, confirmed by ultrasound, with gestational age less than or equal to 16 weeks. We excluded women with pre-gestational diabetes mellitus (DM), suffering from psychiatric disorders, chronic maternal diseases (hypertension, heart disease, kidney disease, epilepsy, kidney failure), congenital malformations, and multiple pregnancies.

Data collection and procedures performed

In the 16th week of gestation (+1 week), after signing the ICF, the women underwent an ultrasound to confirm their pregnancy and answered a questionnaire with information about biological, sociodemographic, and obstetric characteristics. Next, we evaluated the diagnostic criteria for MS, its prevalence, and the possibly related maternal risk factors.

MS was diagnosed according to the classification by the NCEP/ATP III and the maternal factors investigated were the thicknesses of visceral and subcutaneous fat, anthropometric measurements, blood pressure (BP), and metabolic profile. After these assessments, the pregnant women were scheduled to return at the 28th week and the immediate postpartum period (≤10 days after delivery). In the 28th week, we carried out only the oral glucose tolerance test (OGTT) and, in the postpartum period, were repeated all previous assessments.

The ultrasound was carried out by the same professional, a specialist in fetal medicine, who also measured the thickness of visceral and subcutaneous fat, according to the technique described by Armellini et al. The maternal BP was measured by the recommended palpation and auscultation methods.

The anthropometric assessment included weight, height, body mass index (BMI), weight gain, circumferences of the waist, arm, and thigh, and the triceps and suprailliac skinfolds. Based on their BMI, the women were classified as underweight, average weight, overweight, or obese. The weight gain was obtained from the difference between the women's weight in each of these moments and their pre-gestational weight self-reported during the filling out of the questionnaire. The circumferences of the waist, arm, and thigh, and the skinfolds were evaluated according to Jackson and Pollock.

The biochemical measurements included total cholesterol, HDL-c, low-density lipoprotein cholesterol (LDL-c), triglycerides, insulin, homeostasis model assessment (HOMA-IR), and levels of fasting glucose. Insulin resistance was determined according to the HOMA-IR [fasting insulin (mU/l) x fasting glucose (mmol/l)/22.5].

At the 28th week of gestation, the women returned to the PESQ to undergo the OGTT, as previously scheduled. The diagnosis of gestational diabetes mellitus (GDM) was based on the confirmed fasting glycemia ≥92 mg/dl at the 16th week of gestation, in addition to an OGTT with any of the following abnormal values:
fasting glycemia ≥92 mg/dl; one-hour levels ≥180 mg/dl, and two-hour levels ≥153 mg/dl.

Data Analysis

Medcalc, version 15.6.1. (Medical Software bvba, Ostend, Belgium), and Epi Info, version 7.1.5 (Atlanta, GA, USA) were used for the statistical analysis. The Student t-test was used to compare the prevalence of metabolic syndrome and its components in these periods. A bivariate analysis was then performed to test the association between the variables studied and MS (ANOVA and Kruskal-Wallis Test). Stepwise logistic regression was performed to identify the main maternal factors associated with the syndrome, including the variables that remained associated with a significance level of 20% in the bivariate analysis. The final model included only the variables that remained associated with the outcomes at a significance level of 5%.

RESULTS

The prevalence of MS at the 16th week was 3.0% (n=6) in comparison to 9.7% (n=18) during the immediate postpartum period (p=0.01). Regarding the criteria for MS classification at the 16th week, the frequency of abdominal obesity (abdominal circumference ≥88 cm), HDL-c <50mg, triglycerides ≥150mg/L, fasting glycemia ≥100mg/dl, and BP ≥130/85mmHg was 100% and 34% (p<0.001), 83.3% and 40.7% (p=0.02), 83.3% and 11.8% (p<0.001), 0% and 0.5% (p=0.84), and 0% and 1% (p=0.93) in the groups with and without the syndrome, respectively (Table 1). During the immediate post-partum period, the frequencies were 77.8% and 40.8% (p<0.001); 88.9% and 39% (p<0.001); 83.3% and 11.2% (p<0.001); 0% and 1.2% (p=0.84); 16.6% and 2.9% (p=0.01), in both groups (Table 1).

The mean age in the groups with and without MS were 31.5±8.4 and 25.4±5.7 years at the 16th week of gestation (p=0.01). In the postpartum period, these averages were 27.0±7.8 and 25.6±5.6 years in both groups, respectively (p=0.38). With respect to formal education, in both periods, the averages were 6.0±3.0 and 9.7±3.8 years at the 16th week, and 8.8±3.2 and 9.8±3.9 years in the postpartum period for the groups with and without the syndrome (p=0.05; p = 0.32) (Table 2).

Regarding the reproductive history of the women, those with MS at the 16th week of pregnancy had an average of 3.8±2.3 pregnancies, 0±0.5 abortions, and 2.5±2.3 deliveries compared with 2.0±1.2 pregnancies, 0.2±0.5 abortions, and 0.8±1.1 deliveries by the women without the syndrome (p=0.01; p=0.46; p=0.001, respectively). In the postpartum period, the averages were of 2.7±1.6 pregnancies, 0.3±0.6 abortions, and 1.4±1.6 deliveries in the group with MS, while in the group without the syndrome the averages were 2.0±1.1 pregnancies, 0.2±0.5 abortions, and 0.7±0.9 deliveries (p=0.02; p=0.82; and p=0.04, respectively). The average interval between pregnancies, at the 16th week, was 4.2±2.3 and 3.5±3.3 years in both groups (p=0.64), at the same time, compared to 3.5±2.4 and 3.4±3.4 years (p=0.80) in the postpartum period (Table 2).

As to the nutritional status of the women, 13.0% (n=26) were classified with low weight at the 16th week of gestation, compared to 1.3% (n=2) in the postpartum period (p<0.001); 48.7% (n=91) and 57.3% (n=107) were classified as eutrophic in both periods (p=0.20), and the women considered overweight or obese were 38.1% (n=76) and 41.3% (n=77) (p=0.62), respectively.

The average maternal weight in the groups with and without the syndrome was 72.4±15.4 kg and 62.4±11.2 kg (p=0.03) at the 16th week of gestation, while in the postpartum period, it was 68.7 ± 15.1 kg and 65.0±10.3 kg (p<0.20) (Table 3). The mean BMI was 28.3±5.1 and 24.5±4.0 (p<0.001) at the 16th week of gestation when compared to 28.3±3.0 and 25.7±4.1 (p=0.01) in the postpartum period (Table 2). There was

TABLE 1. DIAGNOSTIC CRITERIA FOR MS, ACCORDING TO THE NCEP/ATP III CLASSIFICATION, IN WOMEN WITH AND WITHOUT THE SYNDROME. CAMPINA GRANDE, PARAÍBA, BRASIL, 2015.

|                        | MS at the 16th week (n=200) | MS in the immediate postpartum period (n=187) | p#  |
|------------------------|-----------------------------|---------------------------------------------|-----|
| Abdominal circumference ≥88cm | 100 (6) | 34 (66) | <0.001 | 77.8 (14) | 40.8 (69) | <0.001 | 0.02 |
| HDL-c (mg/dl) <50mg/dL  | 83.3 (5) | 40.7 (79) | 0.02 | 88.9 (16) | 39 (66) | <0.001 | 0.49 |
| Triglycerides (mg/dl) ≥150mg/dL | 83.3 (5) | 11.8 (23) | <0.001 | 83.3 (15) | 11.2 (19) | <0.001 | 0.05 |
| Fasting blood glucose (mg/dl) ≥100mg/dL | 0 (0) | 0.5 (1) | 0.84 | 0 (0) | 1.2 (2) | 0.84 | 0.92 |
| BP ≥130/85mmHg         | 0 (0) | 1 (2) | 0.93 | 16.6 (3) | 2.9 (5) | 0.01 | 0.15 |

MS: Metabolic syndrome; HDL-c: high-density lipoprotein cholesterol; BP: Blood pressure; *ANOVA. # Student’s t-test.
an association between maternal weight gain and the presence of MS (p<0.001).

The average thickness of visceral fat was 5.9±1.2cm and 5.2±1.3cm (p=0.20) at the 16th week, while in the immediate post-partum period, it was 5.5 ± 1.9cm and 5.6±1.5cm (p=0.83) in the groups of women with and without MS (Table 2). No association was found between the thickness of visceral fat and the syndrome (p=0.88). The mean subcutaneous fat thickness was 2.9±0.8 and 2.3±0.8 (p=0.07) at the 16th week when compared to 3.0±1.0 and 2.4±0.8 (p=0.01) in the post-partum period, in both groups, respectively (Table 2). An association was found between the subcutaneous fat and the presence of MS (p<0.001).

### TABLE 2. BIOLOGICAL, ANTHROPOMETRIC, AND SOCIODEMOGRAPHIC CHARACTERISTICS, VISCERAL AND SUBCUTANEOUS FAT, AND METABOLIC PROFILE OF WOMEN WITH AND WITHOUT MS. CAMPINA GRANDE, PARAÍBA, BRASIL, 2015.

| Characteristic                        | MS at the 16th week (n=200) | MS in the immediate postpartum period (n=187) | p     |
|---------------------------------------|-----------------------------|----------------------------------------------|-------|
|                                       | Yes % | No % | p  | Yes % | No % | p  |
| Age (years)                           | 31.5±8.4 | 25.4±5.7 | 0.01 | 27.0±7.8 | 25.6±5.6 | 0.38 | 0.80 |
| Formal education                       | 6.6±3.0 | 9.7±3.8 | 0.05 | 8.8±3.2 | 9.8±3.9 | 0.32 | 0.02 |
| Pregnancies                           | 3.8±2.3 | 2.0±1.2 | 0.01* | 2.7±1.6 | 2.0±1.1 | 0.02* | 0.79 |
| Abortions                             | 0.0±0.5 | 0.2±0.5 | 0.46* | 0.3±0.6 | 0.2±0.5 | 0.82* | 0.79 |
| Birth interval                        | 4.2±2.3 | 3.5±3.3 | 0.64 | 3.5±2.4 | 3.4±3.4 | 0.89 | 0.07 |
| Parity                                | 2.5±2.3 | 0.8±1.1 | <0.001* | 1.4±1.6 | 0.7±0.9 | 0.04* | 0.23 |
| Visceral Fat                          | 5.9±1.2 | 5.2±1.3 | 0.20 | 5.5±1.9 | 5.6±1.5 | 0.83 | 0.83 |
| Subcutaneous fat                      | 2.9±0.8 | 2.3±0.8 | 0.07 | 3.0±1.0 | 2.4±0.8 | 0.01 | 0.01 |
| Systolic BP                           | 116.8±4.6 | 112.5±10.4 | 0.35 | 123.4±17.8 | 115.0±11.0 | 0.02 | 0.02 |
| Diastolic BP                          | 66.8±14.1 | 68.2±96.6 | 0.74 | 81.0±12.2 | 74.4±10.4 | 0.04 | 0.04 |
| Pre-gestational BMI                   | 29.0±5.7 | 24.4±4.3 | 0.01 | 28.0±5.7 | 24.1±4.0 | p<0.00 | 0.02 |
| Height                                | 1.5±0.0 | 1.5±0.6 | 0.18 | 1.5±0.6 | 1.8±0.6 | 0.63 | 0.13 |
| Weight                                | 72.4±15.4 | 62.4±11.2 | 0.03 | 68.7±15.1 | 65.2±10.3 | 0.20 | 0.20 |
| BMI                                   | 28.3±5.1 | 24.5±4.0 | <0.001* | 28.3±3.0 | 25.7±1.4 | 0.01 | <0.001 |
| Weight gain                           | 14.4±12.6 | 208.3±83.3 | 0.27 | 11.6±6.9 | 4.8±4.9 | <0.001 | 0.03 |
| Waist circumference                   | 98.9±12.4 | 88.0±9.6 | <0.001 | 98.6±8.5 | 91.9±9.5 | <0.001 | <0.001 |
| Arm circumference                     | 34.1±6.3 | 28.0±3.4 | <0.001 | 29.4±2.3 | 28.5±3.1 | 0.13 | 0.13 |
| Thigh circumference                   | 30.8±7.7 | 29.6±11.0 | 0.72 | 41.7±10.1 | 38.2±9.2 | 0.21 | 0.21 |
| Suprailiac fold                       | 30.3±16.4 | 22.8±8.9 | 0.05 | 26.2±7.8 | 22.6±6.0 | 0.03 | 0.05 |
| Triceps fold                          | 28.1±11.5 | 21.3±5.6 | <0.001 | 26.2±7.8 | 22.6±6.0 | 0.03 | 0.03 |
| Total cholesterol                     | 195.3±10.0 | 168.4±30.9 | 0.03 | 209.4±47.4 | 215.0±42.6 | 0.62 | 0.62 |
| Fasting glucose                       | 67.5±4.4 | 70.2±15.5 | 0.66 | 73.0±11.7 | 69.3±8.6 | 0.12 | 0.61 |
| Insulin                               | 9.3±5.8 | 5.7±4.0 | 0.03 | 7.1±4.9 | 5.5±3.6 | 0.13 | 0.13 |
| HDL-c                                 | 50.5±11.2 | 45.0±2.5 | 0.23 | 49.8±10.5 | 39.0±6.5 | <0.001 | <0.001 |
| LDL-c                                 | 106.6±16.7 | 108.5±24.8 | 0.32 | 121.7±46.5 | 143.0±39.6 | 0.06 | 0.06 |
| Triglycerides                         | 218.1±51.7 | 108.5±53.1 | <0.001 | 245.0±92.3 | 111.5±22.3 | <0.001 | <0.001 |
| HOMA-IR                               | 24.2±19.8 | 14.3±14.4 | 0.08 | 24.2±21.1 | 17.4±12.0 | 0.05 | 0.05 |

MS: Metabolic syndrome; BMI: body mass index; GDM: gestational diabetes mellitus; BP: Blood pressure; HDL-c: high-density lipoprotein cholesterol; LDL-c: low-density lipoprotein cholesterol; HOMA-IR: model for the evaluation of homeostasis; IQR: interquartile interval. Values were expressed as mean± standard deviation. * Student’s t-test. # Kruskal Wallis test.

### TABLE 3. FINAL LOGISTIC REGRESSION MODEL FOR FACTORS ASSOCIATED WITH MS IN THE 16TH WEEK OF GESTATION AND IN THE IMMEDIATE POSTPARTUM PERIOD. CAMPINA GRANDE, PARAÍBA, BRASIL, 2015.

| Characteristic                      | Odds Ratio | 95% CI | Coefficient | P-value |
|-------------------------------------|------------|--------|-------------|---------|
| 16th week (n=200)                   |            |        |             |         |
| Pre-gestational BMI                 | 1.08       | 1.00-1.17 | 0.08 | 0.04 |
| HDL-c                               | 1.02       | 1.00-1.04 | 0.02 | 0.02 |
| Immediate postpartum (n=187)        |            |        |             |         |
| Triglycerides (evaluated in the im- | 1.04       | 1.01-1.07 | 0.04 | <0.001 |
| mediate puerperium)                 |            |        |             |         |

* Stepwise logistic regression. 95% CI: 95% confidence interval; BMI: body mass index; HDL-c: high-density lipoprotein cholesterol.
Compared to the 16th week of gestation, in the postpartum period, there was a greater proportion of women that presented increased levels of fasting glucose (0.5% and 1.3%) (p=0.32), triglycerides (16.3% and 22.6%) (p=0.60), total cholesterol (16.3% and 63.2%) (p=0.21), and LDL-c (44.4% and 84.8%) (p=0.20) in the groups with and without MS. After analyzing both periods, the proportion of women with low levels of HDL-c increased slightly in the postpartum (58.2%) when compared with the 16th week (57.0%) (p=0.03). The Frequency of GDM was 2.8% (n=5).

The mean levels of total cholesterol were 195.3±10.0 mg/dl and 168.6±30.9 mg/dl (p=0.03) in women with and without metabolic syndrome at the 16th week of gestation and 209.4±47.4mg/dl and 215.0±42.6 (p=0.62), simultaneously, in the postpartum period. The average of fasting glucose, after comparing both groups, were 67.5±4.4mg/dl and 70.2±15.5 mg/dl (p=0.66) at the 16th week, while in the post-partum period, they were 73.0±11.7mg/dl and 69.3±8.6 mg/dl (p=0.12) (Table 2).

The average levels of insulin were 9.3±5.8 mU/l/ml and 5.7±4.0 mU/ml (p=0.03) for women with and without MS at the 16th week of gestation, and 7.1±4.9mU/ml and 5.5±3.6 mU/ml (p=0.13), respectively, in the postpartum period. Regarding the triglyceride levels in both groups, the averages were 218.1±51.7mg/dl and 108.5±53.1 (p<0.001) at the 16th week, and 245.0±92.3mg/dl and 111.5±22.3 (p<0.001) post-partum (Table 2). As for resistance to insulin, the mean HOMA-IR was 24.2±19.8 and 14.3±14.4 (p=0.08) at the 16th week of gestation, while during the post-partum period it was 24.2±22.1 and 17.4±12.0 (p=0.05) in the groups with and without MS. (Table 2).

After logistic regression analysis, the pre-gestational BMI (p=0.04) and HDL-c (p=0.02) remained significantly associated with MS in the 16th week. Unlike our results, other studies showed an association between pre-gestational BMI indicative of overweight and obesity and the presence of MS in the postpartum period.9,16,18 In these studies, however, MS was diagnosed in the postpartum period in women with a diagnosis of GDM who, according to the pre-gestational BMI, were overweight/obese and whose levels of fasting glucose were high.9,16,18

In relation to the biochemical analysis, only the levels of HDL-c in the 16th week and the triglyceride levels in the postpartum period remained significantly associated with MS in this study. Corroborating these findings, a study carried out at the beginning of the gestation showed higher average levels of triglycerides (192.5±87.5 mg/dl and 105±61.2 mg/dl) and lower HDL-c (456.79±114.2 mg/dl and 532.92±152.26 mg/dl) in women with MS in comparison to those without it.4

Other studies have reported conflicting results, with findings of a correlation between MS and insulin resistance15 and between MS and hypertension;6,16,19 however, unlike in the present study,
pregnant women with GDM and women with various degrees of glucose intolerance were included in these samples.

A limitation of this study is the risk of an overestimated prevalence of MS due to the difficulty in classifying it in both periods through the pre-established criteria. The strengths of this study are the homogeneity of the sample, the small number of losses, and the inclusion of healthy women.

Studies on metabolic syndrome and its associated risk factors in pregnant women can assist in predicting the disease during pregnancy and in the postpartum period, allowing the use of preventive strategies to reduce maternal and child damage in the short and long term.

CONCLUSION

The frequency of metabolic syndrome was higher during the immediate postpartum period, and a pre-gestational BMI indicative of overweight/obesity and abnormal levels of HDL-c at the 16th week of pregnancy, in addition to abnormal levels of triglycerides in the immediate postpartum period, seem to represent important risk factors for the development of metabolic syndrome in these periods.

No conflicts of interest. The study was approved in the Ethics and Research Committee by the CAAE: 03649512.9.0000.5182, on the 26/03/2014.

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