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First-trimester prediction of gestational hypertension through the bioelectrical impedance analysis of the body composition

D. MENICHINI[1,2], E. SPELTA[2], E. ROSSI[2], F. MONARI[2], P.L. DI VINCI[1], E. PETRELLA[2], F. FACCHINETTI[2], I. NERI[2]

[1]Department of Biomedical, Metabolic and Neural Sciences, International Doctorate School in Clinical and Experimental Medicine, [2]Obstetrics and Gynecology Unit, Mother-Infant Department, Policlinic Hospital, University of Modena and Reggio Emilia, Modena, Italy

Abstract. – OBJECTIVE: Obesity is a risk factor for the development of gestational hypertension, with important consequences for both the mother and fetus. This prospective observational study aims to propose an early prediction model of hypertensive disorders in pregnancy among obese women, through the bioelectrical impedance analysis (BIA) at the first trimester, thus allowing early recognition of obese women that are at risk to develop gestational hypertension, in order to target preventive interventions.

PATIENTS AND METHODS: Singleton obese women (BMI ≥ 30 kg/m^2) between the 9th and 12th week of pregnancy were included in the study. The exclusion criteria were chronic diseases, like type 2 diabetes mellitus, hypertension, and other medical pre-existing conditions.

Eligible women were followed up at 20, 28, and 36 weeks of gestation by measuring blood pressure, weight, and body composition with the use of the BIA. The diagnosis of gestational hypertension was made after the 20th week of gestation. Pregnancy and perinatal outcomes were then recorded.

RESULTS: Of the 479 women included in the study, 85 (17.7%) developed gestational hypertension; the remaining 394 (82.3%) resulted to be normotensive. A higher rate of nulliparous women was found in the hypertensive group (50.6% *vs.* 37.6%, $p = 0.02$), together with a higher rate of induction of labor (55.3% *vs.* 40.9%, $p = 0.02$) and of small for gestational age (SGA) newborns (12.9% *vs.* 6.9%, $p = 0.03$). Significant differences emerged in the body composition between the two groups already from the first trimester, indeed women developing gestational hypertension showed elevated values of Total body Mass, FM, FFM, TBW ($p < 0.02$), and of leg's FM, FFM ($p < 0.006$). At the multivariate logistics regression, the risk of developing gestational hypertension resulted higher in women with elevated total body water levels in the first trimester (OR 1.10 95% CI 1.04 -1.92).

CONCLUSIONS: The BIA is a rapid, easy, non-invasive, and inexpensive tool to evaluate the body composition of obese pregnant women. It represents a promising predictor of hypertensive disorders in pregnancy, which allows an early identification of the patients at risk of developing gestational hypertension, thus opening a window of opportunity for strictly monitoring and target preventive intervention.

Key Words:
Obesity, Hypertension, Body composition, Fat mass, Total body water.

Introduction

Obesity during pregnancy represents an important risk factor for both the mother and fetus. It is well established that obese women have a higher risk to develop hypertension and diabetes in pregnancy, thus exposing the fetus to an unhealthy intrauterine environment[1]. This risk is further increased if the woman gains excessive weight during pregnancy.

However, the increase of gestational weight gain (GWG) depends on changes of various components, including anatomical feto-maternal structures (fetus, uterus, amniotic fluid, amniotic membranes, placenta), maternal body fat, and breast tissue, as well as total body water (TBW). Therefore, more accurate measurements should be applied to evaluate the changes in body composition during pregnancy.

Bioelectrical impedance analysis (BIA) is a non-invasive, cheap, and reliable method based on the electrical properties of biological tissue. It measures the resistance to the passage, in the human body, of an imperceptible current at very low intensity (800 mA) and very high frequency (50KHz).

Corresponding Author: Daniela Menichini, Ph.D; e-mail: daniela.menichini91@gmail.com

The measurement of the TBW, given by the sum of intracellular and extracellular water, is then used to estimate the Fat-Free Mass (FFM), mainly consisting of muscle mass and TBW and, differently from the body weight (BW), the Fat Mass (FM), which represents the real amount of adipose in the body.

Such a method provides a valid estimation of total body water either in early or late pregnancy[2].

Several studies[3-6] have shown that pathological changes of maternal TBW are related to gestational maladaptation, such as (gestational) hypertension, edema, and pre-eclampsia[4,7,8].

Moreover, another variable can be obtained by the BIA: the Body Fat Percentage (BFP), calculated as FM divided by total body mass multiplied by 100%. This variable correlates with an increased risk of pregnancy complications, such as gestational diabetes mellitus[9,10] and hypertensive disorders of pregnancy[5,11].

Given the adverse perinatal outcomes associated with hypertension in pregnancy, with this prospective observational study we aimed to propose an early prediction model of hypertensive disorders in pregnancy among obese women, applying the BIA in the first trimester. This model would allow the early recognition of the obese women who are at risk of developing gestational hypertension and who will benefit from preventive intervention early in pregnancy.

Thus, the objective of our study was to evaluate the predictive role of BIA in early identifying obese pregnant women (pre-pregnancy BMI ≥ 30 kg/m^2), who will develop gestational hypertension.

Patients and Methods

The study was approved by the AVEN Ethics Comitee (Area Vasta Emilia Nord) reference number 136/15. Obese women (BMI ≥ 30 kg/m^2) with singleton pregnancies between the 9th and 12th week of gestational age, who referred to the University Hospital of Modena, in Northern Italy (tertiary Hospital) between January 2019 and January 2020, were approached by the research team.

The exclusion criteria were: type 2 diabetes mellitus (DM), chronic hypertension, twin pregnancy and the assumption of dietary supplements/herbal products that can alter the body weight and composition.

Eligible women were included after signing a written consent and then their weight and body composition were collected by using the BIA measurement.

Included women were followed up at 20, 28, and 36 weeks of gestation by measuring blood pressure, weight, and body composition with the use of the BIA at each visit. The diagnosis of gestational hypertension was made after the 20 weeks of gestation, according to the National Institute for Health and Care Excellence (NICE guidelines)[12].

Labor and delivery outcomes were collected using electronic medical records to assess maternal and neonatal health.

Statistical Analysis

Quantitative variables were described as the mean ± standard deviation (SD), whereas qualitative variables were described as the absolute and percentage frequencies. The multivariable prediction model was developed by carrying out the following steps. Firstly, univariate logistic regression models were used to assess the relationship between each body composition independent parameter and the risk of developing gestational hypertension. The variables that were associated with a gestational hypertension risk with a p-value < 0.10 in the univariate analyses were considered for inclusion in a multivariable logistic model. The final prediction model was determined by a stepwise backward selection procedure in which only independent variables, associated with gestational hypertension risk with p-value < 0.05, were retained. Results of logistic models were reported as the Odds Ratio (OR), with 95% of confidence interval and Wald p-value. Statistical analyses were performed by using Stata (16.1, StataCorp LLC, College Station, TX, USA).

Results

A total of 479 women agreed to participate and were included in the study. Among them, 85 (17.7%) developed gestational hypertension and the remaining 394 (82.3%) resulted to be normotensive. No significant differences were observed among groups regarding the mother's sociodemographic characteristics and the BMI classes. The exception is represented by parity, indeed 50.6% of the women developing hypertension were nulliparous, against 37.6% of normotensive women (Table I).

Although the two groups were similar for the sociodemographic characteristics, the body composition resulted already different at the baseline (9-12 weeks of pregnancy) between normotensive women and those who developed hypertension in pregnancy (Table II). Indeed, statistically sig-

Table I. Maternal baseline characteristics.

	Normotensive (N=394)	Hypertensive (N=85)	*p*
Mean Maternal age (mean)	31.9 ± 5.1	33.03 ± 4.78	0.28
Education level			
Low (≤ 8 years)	144 (36.5%)	26 (30.6%)	0.14
High (> 9 years)	250 (63.5%)	59 (69.4%)	
Ethnicity			
Caucasian	304 (%)	73 (%)	0.07
Northern Africa	52 (%)	3 (%)	
Sub-Saharan Africa	21 (%)	6 (%)	
Other	17 (%)	2 (%)	
Smoking habits	27 (%)	6 (%)	0.47
Obesity classes:			
Obese I	200 (50.7%)	36 (42.3%)	0.34
Obese II	124 (31.5%)	30 (35.3%)	
Obese III	70 (17.8%)	19 (22.4%)	
Nulliparity	148 (37.6%)	43 (50.6%)	**0.02**
Family history of Hypertension	180 (45.9%)	48 (57.1%)	0.06
Family history of Diabetes	132 (33.7%)	20 (23.5%)	0.06
Aspirin Prophylaxis	19 (4.8%)	5 (5.8%)	0.65

nificant differences were found in mean values of Total body Mass, FM, FFM, TBW ($p < 0.02$). Focusing on the leg's composition, the FM, FFM, and lean mass were different ($p < 0.006$), while in the arms only the FM resulted different ($p = 0.03$).

For what concerns the pregnancy outcomes, the two groups resulted substantially comparable for the GDM onset that occurred in 167 cases among normotensive women (42.3%) and in 38 cases in the hypertensive group (44.7%, $p = 0.66$). There was one case of eclampsia in each group ($p = 0.11$) and the rate of women with an excessive GWG was similar among normotensive (13.2%) *vs.* hypertensive women (8.2%) ($p = 0.10$). Stillbirth occurred in 3 women in the normotensive group (0.8%) and 1 in the group of women developing hypertension ($p = 0.35$) (Table III), according to the regional ratio[13].

Regarding the perinatal outcomes, we found a difference in the incidence of labour induction in the hypertensive (55.3%) *vs.* normotensive women (40.9%), ($p = 0.02$) and in the rate of SGA newborns (12.9% in the hypertensive *vs.* 6.9% in the normotensive, $p = 0.03$) (Table IV).

Table II. Body composition at first trimester evaluated through the BIA.

(kg)	Normotensive (N=394)	Hypertensive (N=85)	*p*
Total Body Mass	1681.8 ±171.7	1747.0 ± 197.7	**0.002**
Body fat %	44.6 ± 4.0	44.5 ± 3.8	0.91
Total Fat Mass	43.2 ± 9.7	45.9 ± 10.9	**0.02**
Total Free Fat Mass	53.4 ± 5.3	55.3 ± 5.7	**0.003**
Total body water	39.0 ± 3.8	40.5 ± 4.2	**0.002**
Legs Fat Mass	16.0 ± 3.5	17.3 ± 4.2	**0.006**
Legs Free Fat mass	18.7 ± 2.1	19.7 ± 3.1	**0.000**
Legs Lean Mass	17.6 ± 2.0	20.7 ± 19.3	**0.002**
Arms Fat Mass	5.8 ± 1.9	6.3 ± 2.2	**0.03**
Arms Free Fat Mass	5.8 ± 1.8	5.9 ± 1.4	0.55
Arms Lean Mass	5.4 ± 1.8	5.6 ± 1.3	0.56
Body Fat Mass	21.3 ± 4.9	22.4 ± 5.2	0.06
Body Free Fat Mass	28.8 ± 3.12	29.8 ± 2.8	**0.01**
Body Lean Mass	27.6 ± 2.56	28.5 ± 2.7	**0.008**

Mean values ± SD are reported.
Body fat % = FM/(FM+FFM)*100

Table III. Pregnancy outcomes.

	Normotensive (N=394)	Hypertensive (N=85)	*p*
GDM	167 (42.4%)	38 (44.7%)	0.66
Pre-eclampsia	1 (0.2%)	1 (1.1%)	0.11
GWG > IOM recommendations	52 (13.2%)	7 (8.2%)	0.10
Stillbirth	3 (0.8%)	1 (1.2%)	0.35

A multivariate logistics regression analysis evaluating the BIA variables that impact the likelihood of developing gestational hypertension showed that elevated total body water levels in the first trimester led to a higher risk of developing hypertension during the pregnancy (OR 1.10 95% CI 1.04 - 1.92), whereas elevated levels of FM seemed to exert a protective role against the hypertensive disorders in pregnancy (OR 0.02 95% CI 0.02 - 0.81) (Table V).

Discussion

This prospective observational study was conducted on obese women enrolled in the first trimester of pregnancy to evaluate the possibility to predict the onset of hypertensive disorders in pregnancy through the body composition analysis, using the BIA.

Comparing the population of women who developed hypertensive disorders with the normotensive control group, a significant difference in terms of total body water was found. This could be explained by a maladaptation to pregnancy with consequent development of edema as a result of abnormal fluid retention, as already observed in other previous studies[7,14], even if the study population was different (normal weight and non-obese women).

Higher total and district fat mass were also found among women developing gestational hypertension. This could be explained by the higher rate of class II and III obesity found in the hypertensive group, although the difference is not statistically significant. As the literature confirms[15], the risk of developing hypertension during pregnancy increases with increasing BMI. The condition of obesity correlates to increased blood pressure (both systolic and diastolic) already from the first trimester. The risk of developing preeclampsia also increases 2-3-fold with a BMI > 30 kg/m^2 and 4-fold with a BMI > 35 kg/m^2[2,16].

With the multivariable model, we highlighted that elevated total body water levels in the first trimester led to a higher risk of developing gestational hypertension, whereas elevated levels of FM seemed to exert a protective role. This is in accordance with previous studies showing higher TBW values in women who developed gestational hypertension.

Berlit et al[14] demonstrated an increase in body water in patients with preeclampsia. 22 pre-eclamptic pregnant women were compared with 22 healthy pregnant women (uncomplicated course pregnancy). Patients diagnosed with preeclampsia showed significantly higher water content than healthy ones. Similarly, da Silva et al[7] analyzed 65 patients with preeclampsia and compared them with 51 healthy patients in the third trimester, de-

Table IV. Perinatal outcomes.

(kg)	Normotensive (N=394)	Hypertensive (N=85)	*p*
Preterm birth	31 (7.8%)	9 (10.6%)	0.58
Labor induction	161 (40.8%)	47 (55.3%)	**0.02**
Cesarean Section	98 (24.9%)	24 (28.2%)	0.53
Birthweight	3275 ± 51.0	3322 ± 56.3	0.14
SGA	27 (6.9%)	11 (12.9%)	**0.03**
LGA	44 (11.2%)	9 (10.6%)	0.43
Need for resuscitation	19 (4.8%)	2 (2.3%)	0.15
NICU admission	16 (4.0%)	5 (5.8%)	0.48
Pathologic BE	28 (7.1%)	3 (3.6%)	0.11
pH < 7.21	39 (9.9%)	10 (11.8%)	0.30
Apgar 5' < 7	8 (2.0%)	3 (3.5%)	0.20

Table V. Multivariable logistic regression for the risk of developing hypertension in pregnancy.

	OR	95% CI	*p*
Total Body Mass	1.00	0.99 - 1.01	0.56
Body fat %	0.99	0.92 – 1.06	0.91
Total Fat Mass	1.07	0.86 - 1.32	0.51
Total Free Fat Mass	0.02	0.02 - 0.81	**0.03**
Total body water	1.10	1.04 – 1.92	**0.04**
Legs Fat Mass	1.26	0.85 - 1.88	0.24
Legs Free Fat mass	1.15	0.89 - 1.47	0.26
Legs Lean Mass	1.34	0.94 - 1.98	0.10
Arms Fat Mass	0.55	0.29 - 1.08	0.07
Arms Free Fat Mass	1.05	0.23 - 4.84	0.94
Arms Lean Mass	1.17	0.23 - 5.72	0.84
Body Fat Mass	0.87	0.70 - 1.08	0.21
Body Free Fat Mass	1.07	0.78 - 1.42	0.64
Body Lean Mass	1.13	0.67 - 1.88	0.63

tecting higher values of resistance, TBW, and extracellular water (ECW) in pre-eclamptic women.

On the other hand, in another study conducted by Valensise et al[4], a progressive decrease in TBW was demonstrated during the three trimesters of pregnancy in women who developed gestational hypertension. However, it was a population of normal-weight women, therefore not comparable to that of our study. Also, the study by Levario-Carrillo et al[5] showed that TBW was significantly increased in women who developed gestational hypertension and even more in those with preeclampsia, compared to the control group.

Instead, we found that higher values of lean mass (FFM) appeared to play a protective role against hypertensive disorders of pregnancy. This finding has been confirmed in the literature by a recent Cochrane review[17] (2017), where a reduction in the incidence of gestational hypertension was observed in women who received dietary advice (aimed at reducing fat mass and increasing lean mass).

In another meta-analysis[18] that evaluated the effect of a lifestyle intervention on the possible modification of metabolic risk factors for the development of preeclampsia, it was observed that overall diet and lifestyle modifications have the potential to reduce the risk of developing preeclampsia. Hence it becomes increasingly important to know as much early as possible which woman is at increased risk to develop gestational hypertensive disorders to apply lifestyle modifications in the first trimester, which could reduce the risk and possibly avoid the onset of hypertension later in pregnancy.

It is well established that the best obesity treatment is the combination of a calorie restriction, which is essential for weight loss, and physical activity, which on the one hand contributes, albeit minimally, to weight loss, and on the other, it brings a whole series of additional benefits, primarily the preservation of lean mass, which would decrease with caloric restriction alone[19-21].

Another finding that emerged from our study is that the condition of nulliparity is statistically more frequent in the hypertensive group. This finding is not surprising, as nulliparity is scientifically recognized as a major risk factor for hypertensive disorders during pregnancy[22].

For what concerned the perinatal and neonatal outcomes, the induction of labor resulted statistically more frequent in the hypertensive group and this data agree with the fact that hypertension, especially if not controlled, represents one of the major causes of induction[23].

Similarly, the higher rate of SGA infants in the hypertensive group could be explained by undiagnosed intrauterine growth retardation, a frequent complication of hypertensive disorders in pregnancy[23].

Conclusions

The BIA is a rapid, easy, non-invasive, and inexpensive tool to evaluate the total water level and, generally, the body composition of obese pregnant women. It appeared to be a useful predictor of hypertensive disorders in pregnancy, allowing early identification of the patients at risk of developing gestational hypertension, thus opening a window of opportunity for strictly monitoring and target preventive lifestyle intervention.

Conflict of Interest

The authors declare that they have no conflicts of interest.

ORCID ID

Daniela Menichini: 0000-0002-8531-7124.

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