Low pregestational Fat Mass and subsequent maternal cardiovascular maladaptation in early pregnancy. The missing link for preeclampsia

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ABSTRACT

Objective: Aim of the study is to identify patients at high risk of hypertensive complication during pregnancy throughout the assessment of pre-pregnancy maternal fat mass and TVR.
Methods: 38 healthy, normotensive women were subjected to Bioimpedance during the antenatal visit and to haemodynamic measurement throughout the USCOM method during the antenatal visit and in the first trimester.
Results: Patients were divided into two groups during the first trimester: Group A (n = 22) with TVR<1200 dynes.sec.cm-5, Group B (n = 16) with TVR>1200 dynes.sec.cm-5. There were no significant differences between the two groups in terms of maternal age, parity, gestational age and BMI. Cardiac output, stroke volume and TVR were statistically different between the two groups during the preconceptional visit and during the first trimester. Fat Mass (FM) was significantly greater in the low TVR group (p <0.05) while no statistically significant difference was found in the other bioimpendance parameters.
Discussion: Our data showed the poor accuracy of BMI in expressing the maternal body composition compared with bioimpendance. Moreover, in the group with low TVR is possible to identify a subgroup with high fat mass that could be at higher risk of late preeclampsia difficultly recognizable throughout TVR and BMI. On the other side a too low fat mass might negatively influence maternal adaptation to pregnancy.
Conclusion: Fat mass could be a better marker of body composition and a target to monitor the effectiveness of dietary changes improving maternal and neonatal outcome.

Keywords: Total vascular resistance; bioimpedance; early and late preeclampsia; fat mass; pregestational BMI

SOMMARIO

Obiettivo: Scopo dello studio è identificare pazienti ad alto rischio di complicanze ipertensive in gravidanza attraverso la valutazione della massa grassa pregestazionale e delle TVR.
Metodi: 38 donne sane, normotese sono state sottoposte a bioimpedenziometria durante la visita preconcezionale e a valutazione emodinamica attraverso il metodo USCOM durante la visita prenatale e nel primo trimestre.
Risultati: Le pazienti sono state divise in due gruppi durante il primo trimestre: gruppo A con TVR <1.200 dynes.sec. cm-5, mentre il gruppo B con TVR> 1200 dynes.sec.cm- 5. Non ci sono state differenze significative tra i due gruppi in termini di età materna, parità, età gestazionale e BMI. Valori significativamente differenti in termini di gittata cardiaca, gittata sistolica e TVR sono stati riscontrati tra i due gruppi durante la visita preconcezionale e durante il primo trimestre. La fat mass (FM) è risultata significativamente maggiore nel gruppo A, mentre nessuna differenza statisticamente significativa è stata riscontrata negli altri parametri bioimpedenziometrici.
Discussione: Dai dati emerge la scarsa precisione del BMI nell'esprimere la composizione corporea materna rispetto alla bioimpedenziometria. Inoltre, nel gruppo con TVR basse si identifica un sottogruppo con FM alta a maggior rischio di preeclampsia tardiva. Dall'altro lato una FM troppo bassa potrebbe influenzare negativamente l'adattamento materno alla gravidanza.
Conclusione: La valutazione della FM e dei suoi cambiamenti indotti dalla dieta potrebbero rappresentare un utile strumento per migliorare l'outcome materno-fetale

INTRODUCTION

Several studies have demonstrated the correlation between maternal overweight and obesity and pregnancy complications such as pregnancy-induced hypertension[(1)]. Moreover, maternal weight changes between consecutive pregnancies correlates linearly with risks of these obesity related pregnancy complications, suggesting a causal relationship[(2)].

Perlow and Morgan[(3)] observed hypertension in pregnancy to be very significantly frequent in obese women. Many other findings have also confirmed the link between hypertension and excessive weight gain[(4)].

In the non-pregnant obese population, a 10% reduction in body weight is recommended by the National Institutes of Health as an initial weight loss target to confer health benefits[(5)].

Currently, maternal body composition evaluation in pregnancy is based on BMI measurement. These index, although provides distinction into normal, overweight and obese

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patients is little accurate in describing body composition in terms of fat mass, fat free mass and water distribution. Bioimpendance, through definition of free fat mass and fat mass percentage provides the more accurate identification of those patients who need a diet restriction, despite of a normal BMI. With the improvement of prenatal and peripartum care, pre-pregnancy BMI and weight change in women during pregnancy are gradually gaining attention.

In particular, many authors suggest that obese women are at major risk to develop a late form of preeclampsia[6]. The concept of early and late PE is more modern, and it is widely accepted that these two entities have different etiologies and should be regarded as different forms of the disease. Early-onset PE (before 34 weeks) is commonly associated with abnormal uterine artery Doppler, foetal growth restriction (FGR), and adverse maternal and neonatal outcomes. In contrast, late-onset PE (after 34 weeks) is mostly associated with normal or slight increased uterine resistance index, a low rate of fetal involvement, and more favorable perinatal outcomes[7, 8].

A novel method to evaluate an adequate placentation is the assessment of Total Vascular Resistance (TVR) which represents the steady component of the afterload and includes the uteroplacental circulation with a contribution of 20% to 26% to the total reduction of systemic vascular resistance in the second trimester[9]. These changes take place during early phases of pregnancy: since the 5th week and most of TVR fall (85 %) is seen at 16 weeks of gestation[10].

OBJECTIVE

Aim of the study is to assess the pre-pregnancy maternal fat mass in women with high and low TVR values assessed antenatally and during the first trimester of pregnancy in order to identify a group of patient at higher risk of poor maternal-neonatal outcome and that will beneficiate of preconception counselling about the importance of a change of diet.

METHODS

A prospective observational study to test our hypothesis was proposed to be conducted at the San Giovanni Calibita Fatebenefratelli Hospital, Department of Obstetrics and Gynaecology in Rome over a continuous period from June 2013 to May 2014. Approval of the local ethics committee was obtained based on a submitted protocol and informed consent was obtained from all patients prior to enrolment. We included 38 healthy, normotensive women during the first trimester of pregnancy (from 5+0 to 11+6 weeks of gestation) previously attending an antenatal “first visit” .

Inclusion criteria according to the protocol were:

1) Normal BP at enrolment
2) Singleton pregnancy
3) Certain dates of pregnancy
4) Absence of maternal disease

Exclusion criteria according to the protocol were:

1) Undetermined gestational age
2) Tobacco use
3) Multiple pregnancy
4) Maternal heart and other pre-existing chronic disease
5) Chromosomal abnormalities and/or foetal abnormalities suspected on ultrasound
6) Use of medication other than iron supplements
7) Conception by assisted reproductive techniques

During the antenatal visit, patients were subjected to Bioimpedance in order to evaluate body water, fat mass and fat free mass distribution and to haemodynamic measurement throughout the USCOM method. For each patients were calculated pre-pregnancy BMI index. Pre-pregnancy BMI was calculated as the ratio of weight prior to pregnancy (kg) divided by height (m2). During the first visit in pregnancy, patients were subjected again to haemodynamic measurement throughout the USCOM method.

Retrospectively, we divided our study population in two groups according to the TVR evaluated during the first trimester of pregnancy: Group A (n =22) includes patients with TVR<1200 dynes.sec.cm-5, while Group B (n =16) includes patients with values TVR> 1200 dynes.sec.cm-5.

BIA measurement

Electrical bioimpedance (BIA) readily measures TBW, ECW and intracellular water (ICW) without intervention. This method relies on the conductance of an alternating electric current to determine the total conductor volume of the body. Because water and electrolytes are the main factors affecting electrical conductance, TBW is assessed by impedance sensors as changes in BIA and converted to a display module. BIA measurements were performed on each subject after a period of rest to allow impedance equilibration. Body mass index (BMI) was calculated according to the formula weight/height2. BIA was measured by determining resistance (R, Ω-Ohm) and reactance (Xc, Ω-Ohm) using the Tefal scale (Tefal, Rowenta). The device utilises a tetrapolar impedance plethysmograph, with 4 aluminium foil electrodes on the nonconductive surface of the skin. The women, were examined fully clothed but without shoes or socks, supine on a table made of nonconductive materials. The BIA was measured at 50 kHz (BIA50). The TBW was calculated using the prediction formula of Lukaski[11], while ECW was calculated using the prediction formula of Segal[12], and ICW as the difference between the two values (ICW=TBW-ECW).

Haemodynamic measurement

Haemodynamic measurements were acquired with the USCOM 1A. The USCOM has been validated against invasive gold standards and flow probes and has proof of effectiveness in pre-eclampsia[13]. USCOM uses continuous-wave Doppler to determine CO by a non-imaging transducer placed at the suprasternal notch to measure transaortic or transpulmonary blood flow. To calculate CO the transducer is placed in the suprasternal notch or in parasternal interspace, and the Doppler beam directed across the aortic or pulmonary valve to acquire a spectral Doppler flow profile displayed as a time-velocity plot. Once the optimal flow profile is obtained, the trace is frozen on the screen, and the flow profiles automatically traced allowing the stroke volume (SV) to be calculated as the product of the velocity-time integral and the cross-sectional area (CSA) of the chosen valve. The CSA of the aortic valve is determined from the proprietary height-indexed regression equations. The CO is then calculated from the product of the heart rate (HR) and SV. Input of blood pressure provides for calculation of TVR.

STATISTICAL ANALYSIS

Clinical data were compared by means of indipendent samples Student's t-test. Differences were considered as significant with p <0,05.

RESULTS

In total 38 women were selected in our study. The study population was divided into two groups on the basis of the values of TVR: Group A (n = 22) includes patients with TVR<1200 dynes.sec.cm-5, while Group B (n = 16) includes patients with values TVR>1200 dynes.sec.cm-5. **Table 1** summarizes the main characteristics of the study population. There were no significant differences between the high and low TVR groups in terms of maternal age, parity, or gestational age at the time of assessment and BMI.

Table 1
Maternal characteristics

	Group A TVR<1200 (n=22)	**Group B TVR>1200 (n=16)**	***p***
Age (years)	30.6±4.9	31.5±3.8	ns
Parity	1.02±0.6	1.01±0.8	ns
Gestational Age (weeks)	8.0±1.4	7.69±1.4	ns
Gestational Age (days)	1.9±1.5	1.2±1.8	ns
Pre-pregnancy BMI (Kg/m^2)	22.4±3.1	21.9±2	ns

Pre pregnancy haemodynamic and body impedance variables are showed in **Table 2** and **3** respectively, and displayed as mean ± standard deviations.

There were no statistical differences between SBP, DBP and HR in either high or low TVR group.

Mean Doppler determined haemodynamic parameters of CO, SV and TVR were statistically different between the two groups. Mean BIA parameters demonstrated no statistically significant difference in TBW, ICW, ECW and FFM between the two groups.

Fat Mass (FM) was significantly greater in the low TVR group (p <0.05).

Table 2
Pre-pregnancy haemodynamic values

	GROUP A	**GROUP B**	**p**
SBP	119.9±10.5	123.5±5.7	ns
DBP	70±15.5	72.6±6.5	ns
CO	6.8±1	5.6±0.3	<0.05
TVR	1120±77.2	1350.8±124	<0.05
SV	87.4±10.6	72.8±18.7	<0.05
HR	80.9±9,4	75.5±10.9	ns
TFC	377.5±32.5	352.7±29.1	ns

Table 3
Pre-pregnancy bioimpedence parameters

	GROUP A	GROUP B	p
TBW	32.6±2.2	31.9±2.2	ns
ICW	14.6±2.4	17.1±2.6	ns
ECW	17.9±3.4	14.8±2.7	ns
FM	17.2±2.5	14.9±5	<0.05
FFM	44.4±4.4	4.6±3.1	ns

First trimester haemodynamic parameters are showed in **Table 4**. Values of CO, SV and TVR were statistically different between the two groups.

Table 4
First trimester haemodynamic parameters

	GROUP A	GROUP B	p
SBP	117.9±14.5	121.5±7.7	ns
DBP	75±11.7	75.6±8.1	ns
CO	7.1±0.8	5±1	<0.05
TVR	1020±88.9	1390.5±216.4	<0.05
SV	88.4±10.6	70.8±13.9	<0.05
HR	80.9±9.4	75.5±10.9	ns
TFC	377.5±32.5	352.7±29.1	ns

DISCUSSION

Many authors focused on the association between a high risk of maternal and foetal complication with maternal body mass index (BMI) among overweight and obese women. These data suggest that the use of maternal BMI is an advantage because it is a valid proxy for adiposity and that the correlation between maternal BMI and total body fat is high, especially in early pregnancy[14].

From the analysis of demographic characteristics of our study population we found no differences in antenatal maternal BMI, that are similar between the two groups whereas from the antenatal bioimpendance analysis we found a statistically significant difference in terms of fat mass distribution.

This first result could be explained by the poor accuracy of BMI in expressing the maternal body composition compared to bioimpendace analysis. We divided our patients on the basis of the TVR in order to earlier identify a group of patients at high risk to develop pregnancy complication and we evaluated the body composition for both groups. Unexpectedly, we found a low fat mass in the group of patients at high risk (TVR>1200), confirming the results of our previous study.

This finding is interesting because may suggest that in the group with low TVR is possible to identify a subgroup with high fat mass; this group could be at higher risk of late preeclampsia that

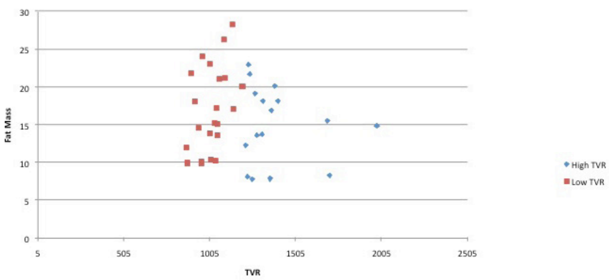

Figure 1. *Correlation Fat Mass/TVR*

could be difficultly recognizable throughout TVR and BMI (Fig 1).

On the other side it is possible that a too low fat mass might negatively influence the maternal adaptation to pregnancy.

Several study focused on the importance of improving antenatal maternal BMI in order to reduce the pregnancy related complications. In our study, we demonstrate that fat mass could be a better marker of body composition and a target to monitor the effectiveness of dietary changes.

In conclusions, an exhaustive prenatal counselling based on the sensitization of patients on dietary and lifestyle change could improve pregnancy outcome.

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