DOI: 10.1002/pd.4499
PRENATAL DIAGNOSIS

ORIGINAL ARTICLE

Maternal body mass index influences umbilical artery Doppler velocimetry in physiologic pregnancies

Laura Sarno, Giuseppe Maria Maruotti, Gabriele Saccone, Maddalena Morlando, Angelo Sirico and Pasquale Martinelli

Department of Neuroscience, Reproductive and Dentistry Sciences, University Federico II, Naples, Italy
*Correspondence to: P. Martinelli. E-mail: martinel@unina.it

ABSTRACT

Objectives The aim of our study was to assess whether there is a relationship between maternal body mass index (BMI) and umbilical artery Doppler velocimetry in physiologic pregnancies.

Methods Healthy pregnancy women, referred to our center at or before 32 weeks of gestation, were recruited. According to BMI, they were divided into underweight (BMI < 18.5), normal weight (BMI 18.5–24.9), overweight (BMI 25.0–29.9) and obese women (BMI ≥ 30). At 32^{+0} weeks of gestation, maternal BMI and umbilical artery Doppler velocimetry were recorded. A correlation between pulsatility index of umbilical artery and BMI was assessed by one-way ANOVA test, multiple comparison test (Bonferroni correction) and polynomial regression.

Results One hundred eighty-five women were included. Mean pulsatility index of umbilical artery at 32^{+0} was significantly higher in obese women (0.95 ± 0.01 vs 0.87 ± 0.01 vs 0.67 ± 0.01; $p < 0.05$). We found a positive correlation between Pulsatility Index of Umbilical Artery and maternal BMI ($r^2 = 0.7$; $p < 0.05$).

Conclusion There is a positive correlation between BMI and pulsatility index of umbilical artery. These findings suggest that obesity has a negative effect on feto-placetal vessels. If our data will be confirmed, maternal BMI should be considered in evaluation of umbilical Doppler velocimetry. © 2014 John Wiley & Sons, Ltd.

Funding sources: None
Conflicts of interest: None declared

INTRODUCTION

Body mass index (BMI) is a simple index of weight for height that is commonly used to classify overweight and obesity in adults. It is defined as a person's weight in kilograms divided by the square of his height in meters (kg/m^2). According to the Institute of Medicine, people are classified into four groups: underweight (BMI < 18.5), normal weight (BMI 18.5–24.9), overweight (BMI 25.0–29.9) and obese (BMI ≥ 30).[1]

Nowadays, obesity is one of the most important public health problem. According to a WHO report, in 2008, more than 1.4 billion adults, 20 and older, were overweight. Of these, over 200 million men and nearly 300 million women were obese.[2] We expect that obese people will be more than 700 million in 2015.[3] In Italy, the prevalence of overweight (from 33.9% in 2001 to 36.1% in 2009) and obesity (from 8.5 in 2001 to 10.3% in 2009) has been progressively increasing in the last decade. Overweight and obesity are more common in Southern Italy, and our region has the highest prevalence (51.8%).[4]

Several studies have shown that obesity increases the risk of pregnancy complication such as gestational diabetes, preeclampsia, infections, post-term pregnancy and cesarean section delivery.[5–8] However, it remains unclear whether obesity by itself, independent of diabetes and hypertension, is a predictor of adverse pregnancy outcome.

Furthermore, scanning obese pregnant women is very difficult, and visualization rates of fetal anatomy fell by 14.5% if the BMI was >90th centile.[9]

To the best of our know1edge, there are no previous studies discussing the influence of BMI on umbilical artery (UA) Doppler velocimetry.

The aim of our study was to evaluate a possible relationship between BMI and UA pulsatility index (UA-PI) in physiologic pregnancies.

METHODS

This was a prospective cohort study conducted in a single tertiary referral center over a two-year period from 2012 to 2014. Only uncomplicated pregnancies were included in our study. Inclusion criteria were as follows: singleton pregnancy, gestational age ≤ 32 weeks, absence of fetal structural abnormalities, absence of maternal comorbidities and/or complications and no drugs intake. Pregnancies complicated by fetal abnormality, aneuploidy, antepartum stillbirth, or maternal complications were excluded from analysis. Given the association between smoking and UA Doppler measures,[10]

smokers were excluded as well. Written informed consent was obtained from the women recruited in the study. Gestational age was defined according to the crown–rump length at the first ultrasound scan.

All the women recruited underwent a feto-maternal assessment at 32^{+0} weeks of gestation. Maternal weight and height were measured, and BMI was calculated and recorded on a dedicated database. Women were divided into four groups, according to Institute of Medicine recommendations.[1] Demographic, clinical and anamnestic data were regularly recorded. At the same appointment, a fetal ultrasound examination was performed. The UA was examined using color Doppler, and the PI was measured according to a standard protocol[11] and recorded. In brief, UA-PI values were obtained in free loops of the umbilical cord, and the UA-PI was calculated by the automatic trace. Ultrasound examinations were performed with a Voluson E8 (GE Medical Systems, Zipf, Austria) ultrasound machine equipped with a 3.5-MHz convex probe, during fetal quiescence, in the absence of fetal tachycardia, and keeping the insonation angle with the examined vessels as small as possible. After delivery, maternal and neonatal outcome was collected.

Statistical analysis was performed using Statistical Package for Social Sciences (SPSS) v. 19.0 (IBM Inc., Armonk, NY, USA). Data were shown as means ± error standards (ES) or number (percentage). Differences in UA-PI among groups were assessed by one-way ANOVA test and Bonferroni correction. A polynomial regression was performed to analyze the relationship between UA-PI and maternal BMI. *p*-value <0.05 was considered statistically significant.

RESULTS

One hundred eighty-five singleton physiologic pregnancies were included in our study. At 32^{+0} weeks of gestation, 3 (1.6%) women were underweight, 99 (53.5%) normal weight, 43 (23.2%) overweight and 40 (21.6%) obese. Considering that the number of underweight pregnant women was extremely low in our cohort, we decided to exclude them from our analysis. Maternal age (28.2 ± 4.9 vs 28.6 ± 5.3 vs 28.5 ± 6.2; $p = 0.89$) and rate of nulliparity (50 (48.5) vs 16 (37.2) vs 17 (42.5); $p = 0.43$) were similar in normal weight, overweight and obese women. All the recruited women were Caucasian.

Mean UA-PI at 32^{+0} weeks of gestation was significantly higher in obese women (0.95 ± 0.01 vs 0.87 ± 0.01 vs 0.67 ± 0.01; $p < 0.05$, one-way ANOVA test) even after multiple comparison by Bonferroni correction ($p < 0.05$). We found a positive correlation between UA-PI and maternal BMI ($r^2 = 0.7$; $p < 0.05$; Figure 1). Neonatal outcome was not significantly different among groups as shown in Table 1. No neonatal complications were reported.

DISCUSSION

Nowadays, obesity is becoming a very important healthy issue. The percentage of obese adults is constantly rising.[2]

The main finding from our cohort was the presence of a positive correlation between maternal BMI and UA-PI. According to these results, in uncomplicated pregnancies, the bigger is the maternal BMI, the higher the resistance in UA.

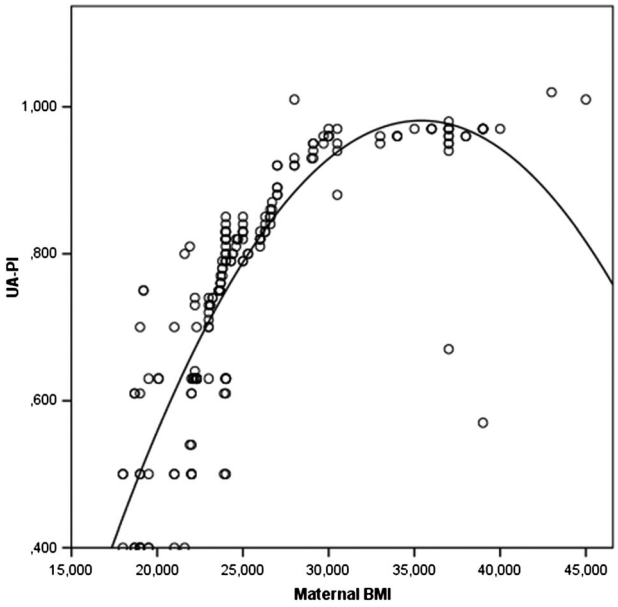

Figure 1 Correlation between UA-PI and maternal BMI ($r^2 = 0.7$; $p < 0.05$)

Table 1 Neonatal outcome stratifying by maternal BMI

Variables	Normal weight, *N* = 99	Overweight, *N* = 43	Obese, *N* = 40
Gestational age at delivery	38.6 ± 0.2	38.5 ± 0.2	38.1 ± 0.2
Birth weight	3341 ± 37.1	3449 ± 67.9	3427 ± 55.4
5 min Apgar	9.2 ± 0.1	9.2 ± 0.1	9.3 ± 0.1
5 min Apgar ≤ 7	—	—	°

An additional finding in our cohort was the absence of significant differences in the fetal birth weight and other fetal outcome measures among the three BMI groups.

We used a sample composed of physiologic pregnant women who delivered at term to avoid the influences of potentially confounding factors, such as preeclampsia or diabetes.[12]

The findings from the present study suggest that the mechanism underlying the higher prevalence of pregnancy complications among obese women is mediated by placental insufficiency.

Obesity seems to have a negative influence on feto-placental vessels; therefore, a woman with a higher BMI needs higher resistances in fetal UA to deliver a wellbeing fetus, compared with the ones with a normal or lower BMI. Indeed, it has been previously reported that obesity is related with adverse feto-maternal outcome.[13]

Association between obesity and adverse pregnancy outcome is well established from previous studies,[14,15] and increase in the risk of pregnancy complication such as gestational diabetes, preeclampsia, infections, post-term pregnancy and caesarean section delivery has been previously demonstrated.[5–8] Obesity has also been investigated as an independent risk factor for adverse fetal outcome. The association between obesity and adverse fetal outcome has been reported in large cohort studies, and obesity has been

proven to increase the risk of late fetal death in nulliparous women, even in the absence of any hypertensive disease.[15]

However, Chalouhi *et al.* demonstrated that obese women who are glucose-tolerant and non-hypertensive may not be at increased risk of perinatal mortality, but they analyzed only the neonatal UA blood gas parameters, without considering UA Doppler velocimetry.[16]

Moreover, it has been previously reported that apparently healthy obese women have a lower microvascular reactivity.[17] Inappropriate secretion of several adipokines by the excessive amount of white adipose tissue seems to participate in the pathogenesis of obesity-related pathologic processes including endothelial dysfunction and inflammation.[18] This process could also influence uterine and placental perfusion.

A proinflammatory maternal and fetal environment has been proposed to be involved in mediating adverse maternal and fetal outcomes in obese pregnant women.[19] Adiponectin plays a vasoprotective role in the systemic circulation by preventing vascular smooth muscle proliferation, thus maintaining vessel caliber. Leptin is implicated in atherosis, in the genesis of vascular calcification and vascular smooth muscle proliferation, thus limiting caliber and distensibility of vessels. An imbalance among those mechanisms may effect placental circulation in maternal obesity. A higher prevalence of vascular lesions in the placenta of obese women has also been recently demonstrated.[20] Maternal obesity has been shown to be associated with a higher risk of vascular lesions of maternal and fetal origins and villous lesions of maternal and fetal origins. Interestingly, the increase in the risk of vascular lesions was consistent in obese women in a subsample of women with no hypertensive diseases and diabetes,[20] confirming the value of obesity as an independent risk factor for placental vascular damage.

Our findings support this speculation. Indeed, a higher UA-PI in the group of women with higher BMI might reflect the presence among this group of a higher prevalence of placental insufficiency.

Obese women are expected to give birth to bigger neonates.[21,22] The absence of a significant difference in the birth weight among the three groups, namely the absence of higher birth weights in the neonates of obese mothers, may suggest a higher prevalence of occult growth restriction in that group. Hence, fetuses of obese mothers may have achieved a weight within the population standards (thus appearing normal in weight), despite failing to reach their potential of growth (thus appearing smaller than they should), as an effect of placental hypoxemia. Recent studies suggest that a fetus does not have to be small to be growth restricted and that fetal Doppler indices may be a better marker than the fetal size for placental insufficiency, fetal hypoxemia and failing to reach the potential of growth.[23] Our finding of increasing resistance in the UA in well-grown fetuses of obese mothers may furthermore suggest that a higher proportion of these fetuses are suffering placental insufficiency.

To the best of our knowledge, this is the first published study about this issue.

The main limitation of our study is the limited sample size, even if the strong correlation found is quite cheering.

Further studies with enlarged samples should be performed to confirm our data. Moreover, it should be important to confirm the reported relationship at every gestational age and to extend this analysis to the other feto-placental vessels and to pathologic fetuses. If our data will be confirmed, maternal BMI should be considered in evaluation of UA Doppler velocimetry.

WHAT'S ALREADY KNOWN ABOUT THIS TOPIC?

- Obesity increases the risk of pregnancy complications and maternal and neonatal outcome.
- Obesity can influence vascular reactivity and endothelial functions.

WHAT DOES THIS STUDY ADD?

- This is the first study assessing the relationship between maternal BMI and umbilical artery Doppler velocimetry.
- We found a positive correlation between maternal BMI and pulsatility index of umbilical artery. According to these results, in uncomplicated pregnancies, the bigger is the maternal BMI, the higher the resistance in umbilical artery.

REFERENCES

1. Weight gain during pregnancy. Committee Opinion n.548 ACOG Obstet Gynecol 2013;121:210–2.
2. Obesity and overweight, WHO (available at: http://www.who.int/mediacentre/factsheets/fs311/en/)
3. Caballero B. The global epidemic of obesity: an overview. Epidemiol Rev 2007;29:1–5.
4. Indagine multiscopo annuale sulle famiglie"Aspetti della vita quotidiana" 2009 (available at: http://www3.istat.it/dati/catalogo/20110121_00/inf_10_05_la_vita_quotidiana_nel_2009.pdf)
5. Metwally M, Ong KJ, Ledger WL, and Li TC. Does high body mass index increase the risk of miscarriage after spontaneous and assisted conception? A meta-analysis of the evidence. Fertil Steril 2008;90(3):714–26.
6. Ehrenberg HM, Dierker L, Milluzzi C, and Mercer B. Prevalence of maternal obesity in an urban center. Am J Obstet Gynecol 2002;187(5):1189–93.
7. Poobalan AS, Aucott LS, Gurung T, *et al.* Obesity as an independent risk factor for elective and emergency caesarean delivery in nulliparous women—systematic review and meta-analysis of cohort studies. Obes Rev 2009;10(1):28–35.
8. Sebire NJ, Jolly M, Harris JP, *et al.* Maternal obesity and pregnancy outcome: a study of 287,213 pregnancies in London. Int J Obes (Lond) 2001;25(8):1175–82.
9. Wolfe HM, Sokol RJ, Martier SM, Zador IE. Maternal obesity: a potential source of error in sonographic prenatal diagnosis. Obstet Gynecol 1990;76:339–42.
10. Machado Jde B, Plínio Filho VM, Petersen GO, Chatkin JM. Quantitative effects of tobacco smoking exposure on the maternal–fetal circulation. BMC Pregnancy Childbirth 2011 Mar 31;11:24. doi: 10.1186/1471-2393-11-24.
11. Bhide A, Acharya G, Bilardo CM, *et al.* ISUOG practice guidelines: use of Doppler ultrasonography in obstetrics. Ultrasound Obstet Gynecol 2013 Feb;41(2):233–9.
12. Maruotti GM, Rizzo G,Sirico A, *et al.* Are there any relationships between umbilical artery pulsatility index and macrosomia in fetuses of type I diabetic mothers? J Matern Fetal Neonatal Med 2014 Feb 3. doi: 10.3109/14767058.2013.879706.
13. Owens LA, O'Sullivan EP, Kirwan B,et al. ATLANTIC DIP: the impact of obesity on pregnancy outcome in glucose-tolerant women. Diabetes Care 2010;33(3):577–9.

14. Cnattingius S, Bergström R, Lipworth L, Kramer MS. Prepregnancy weight and the risk of adverse pregnancy outcomes. N Engl J Med 1998;338(3):147–52.
15. Higgins L, Greenwood SL, Wareing M, *et al.* Obesity and the placenta: a consideration of nutrient exchange mechanisms in relation to aberrant fetal growth. Placenta 2011;32(1):1–7.
16. Chalouhi SE, Salafia C,Mikhail M, Hecht R. Maternal body mass index does not affect neonatal umbilical artery blood gas parameters. J Pregnancy 2013;2013:654817. doi: 10.1155/2013/654817. Epub 2013 Feb 21.
17. Pienaar PR, Micklesfield LK, Levitt NS, *et al.* Insulin resistance is associated with lower acetylcholine-induced microvascular reactivity in nondiabetic women. Metab Syndr Relat Disord 2014;12(3):178–84.
18. Adamczak M, Wiecek A. The adipose tissue as an endocrine organ. Semin Nephrol 2013;33(1):2–13.
19. Denison FC, Roberts KA, Barr SM, Norman JE. Obesity, pregnancy, inflammation, and vascular function. Reproduction 2010;140(3):373–85. doi: 10.1530/REP-10-0074. Epub 2010 Mar 9.
20. Huang L, Liu J, Feng L, *et al.* Maternal prepregnancy obesity is associated with higher risk of placental pathological lesions. Placenta 2014 pii: S0143-4004(14)00198-2. doi: 10.1016/j.placenta.2014.05.006.
21. Sebire NJ, Jolly M, Harris et al. JP, *et al.* Maternal obesity and pregnancy outcome: a study of 287,213 pregnancies in London. Int J Obes Relat Metab Disord 2001;25(8):1175–82.
22. Cedergren MI. Maternal obesity and the risk of adverse pregnancy outcome. Obstet Gynecol 2004;103(2):219–24.
23. Morales-Roselló J, Khalil A, Morlando M, Papageorghiou A, Bhide A, *et al.* Changes in fetal Doppler indices as a marker of failure to reach growth potential at term. Ultrasound Obstet Gynecol 2014;43(3):303–10. doi: 10.1002/uog.13319.

