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Maternal visceral adiposity and fetal biometry in women with obesity and diabetes

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SUMMARY

OBJECTIVE: The aim of this study was to compare the correlation of maternal visceral adiposity with sonographic variables related to fetal biometry in the second trimester of pregnancy in mothers who were previously obese versus nonobese and gestational diabetic versus nondiabetic.

METHODS: This cross-sectional study included 583 pregnant women who received prenatal care between October 2011 and September 2013 at the *Instituto de Medicina Integral Prof. Fernando Figueira*, northeast of Brazil. Maternal visceral adiposity was measured by ultrasound examination at the same time as fetal biometry. Gestational age was 14.9±3.2 weeks. The correlation between maternal visceral adiposity and fetal biometric variables was evaluated using Pearson's correlation coefficient. Among the groups, the correlation coefficients were compared using Fisher's Z-test. This test was also used to evaluate the null hypothesis of correlation coefficients between pairs of variables.

RESULTS: Maternal visceral adiposity positively correlated with fetal abdominal circumference, estimated fetal weight, head circumference, femur length, and biparietal diameter in pregnant women with obesity, nonobesity, gestational diabetes, and nondiabetes, but the correlation coefficients were statistically similar among the groups.

CONCLUSION: Maternal visceral adiposity positively correlated with fetal biometry in the second trimester of pregnancy in the same manner in pregnant women previously obese and nonobese, as well as in pregnant women with gestational diabetes and nondiabetes.

KEYWORDS: Intra-abdominal fat. Body composition. Ultrasonography, prenatal. Diabetes, gestational. Obesity. Fetal weight.

INTRODUCTION

Obesity and diabetes are major public health concerns that can affect pregnant women and cause adverse maternal and fetal outcomes worldwide. Normal pregnancy is characterized by an insulin resistance state in order to supply the increasing metabolic demands of the developing fetus. The consequence of such physiological insulin resistance is an increase in insulin secretion, and failure to do so leads to gestational diabetes mellitus (GDM)[1]. It is important to note that overweight and obese individuals are more insulin-resistant than their lean counterparts and also more susceptible to beta-cell dysfunction in the pancreas[2].

It is known that the nutritional status of the mother and the consequent hyperglycemia and hyperinsulinemia can directly influence fetal growth. Excessive fetal growth is probably the most frequent and important outcome of GDM. Likewise, the association between maternal obesity and birth weight is also well documented[3]. Both maternal obesity and gestational diabetes have been associated with newborn adiposity[3-5]. Pre-pregnancy and during pregnancy, maternal body composition can influence the body fat mass of the offspring from fetal life through adolescence and can predict the risk of obesity in adulthood[6,7].

Studies suggest that central adiposity has a stronger association with complications related to obesity compared to peripheral adiposity. During pregnancy, there is also evidence that central adiposity, compared to the peripheral, is associated with glucose intolerance, gestational diabetes, and increased birth weight[8,9]. In addition, it has been demonstrated that maternal visceral adiposity has a stronger association with birth weight than maternal body mass index (BMI)[9].

Despite the wide evidence of maternal body composition and metabolism's influence on offspring body composition and cardiometabolic risk, little is known about their role in fetal growth and fat accumulation. The effect of maternal visceral adiposity on fetal growth and body composition is not yet well established, and there is no data on the effect of maternal visceral adiposity on fetal growth among obese and diabetic pregnant women. This study aimed to investigate and compare

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the correlation of maternal visceral adiposity with sonographic parameters of fetal biometry in the second trimester of pregnancy in obese, nonobese, gestational diabetic, and nondiabetic pregnant women.

METHODS

This retrospective cross-sectional study included pregnant women who received prenatal care at the *Instituto de Medicina Integral Prof. Fernando Figueira* (IMIP) between October 2011 and September 2013, and who started their prenatal care before the 28th week of gestation. Participants were excluded from the study if they had pre-pregnancy diabetes mellitus, multiple gestations, mental disability, the absence of a legal representative in adolescents, and fetal abnormalities.

The variables studied to characterize the population were age, gestational age, ethnicity, income, and schooling. The independent variable was maternal visceral adiposity. The dependent variables were the fetal measurements [biparietal diameter (BPD), head circumference (HC), abdominal circumference (AC), estimated fetal weight (EFW), femur length (FL), and the ratios BPD/FL, HC/AC, FL/HC, EFW/BPD, and EFW/HC], obesity, and GDM.

Obese women were considered those with a pre-pregnancy BMI ≥30 kg/m^2. Pre-pregnancy BMI was determined using the informed pre-pregnancy weight and height measured at prenatal care. In the first prenatal care visit, fasting glucose was obtained. It was considered clinical diabetes during pregnancy if the fasting blood glucose was ≥126 mg/dl, if the glycated hemoglobin (HbA1c) was ≥6.5%, or if a random plasma glucose of ≥200 mg/dl was detected. Between the 24th and 28th gestational weeks, those with values <92 mg/dl underwent the oral glucose tolerance test with 75 g intake (OGTT-75g). For this test, fasting values ≥92 mg/dl or ≥180 mg/dl within the first hour, or ≥153 mg/dl in the second hour, were considered GDM[10].

During routine ultrasound examination, maternal visceral adiposity was assessed by ultrasonography, performed by a single qualified sonographer (A.S.R.S.), once for each patient. The thickness of visceral fat was measured in centimeters (cm) from the inner edge of the rectus abdominis muscle, at the linea alba level, in mesogastric region, to the anterior wall of the abdominal aorta (Figure 1)[11]. The measurement was made using Philips 22Ui equipment with a 5- to 9-MHz transducer (Koninklijke Philips, Amsterdam, the Netherlands). Fetal biometry measurements were performed on the same occasion, by the same operator. This technique has been validated[12,13].

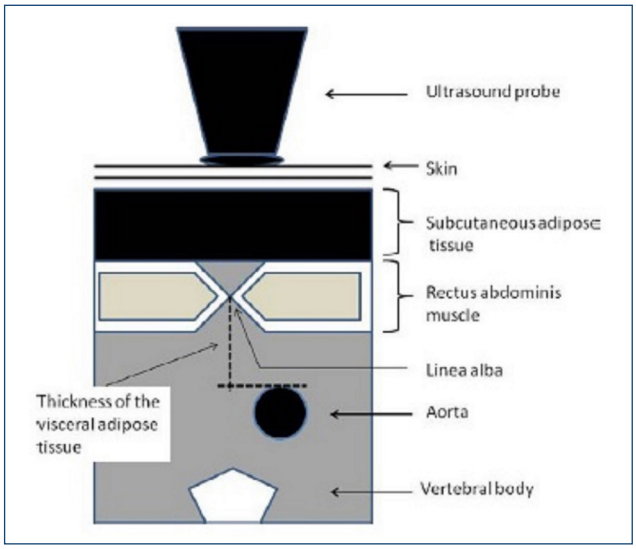

Figure 1. Visceral fat measurement.

Sample size was based on a previous study by these same authors, who evaluated the correlation between maternal visceral adiposity and fetal biometry[14]. The correlations between maternal visceral adiposity and fetal biometric variables were evaluated using Pearson's correlation coefficient. Among the groups, the correlation coefficients were compared using Fisher's Z-test. This test was also used to test the null hypothesis of correlation coefficients between pairs of variables. To test the null hypothesis of adjusted correlation coefficients (partial correlation coefficients), the Student's t-test was used. Statistical analysis was performed with STATA 12.1 SE (StataCorp, Texas, USA). A p-value of less than 0.05 was considered statistically significant.

Participants gave written informed consent, and the research protocol was approved by the IMIP Ethics Committee before the study began, CAAE number 48051515.5.0000.5201, October 15, 2015.

RESULTS

A total of 583 participants were included in the study. The age of pregnant women ranged from 16 to 41 years (mean 26±3 years), and the median number of years of schooling was 12 years. Most of them described themselves as mulattos, and 90% had a mensal income of up to two minimum wages (U$400.00). Of the 583 participants, obesity and gestational diabetes were observed in 163 (35.7%) and 71 (12.2%), respectively. Gestational diabetes was more frequent in pregnant women with obesity as compared to pregnant women without obesity [30/163 (18.4%) versus 31/420 (7.3%), p<0.001]. The ultrasound measurement of maternal visceral

adiposity and fetal biometry was performed at a mean gestational age of 14.9 (±3.2) weeks of amenorrhea, median age of 15.2 weeks, and interquartile range from 13 to 17.2 weeks. The mean visceral adiposity was 7.6 (±1.84) cm. Notably, 14.4% of women were obese (BMI ≥30 kg/m^2), 26.6% were overweight (BMI ≥25 and <30 kg/m^2), and 10.4% developed gestational diabetes.

Maternal visceral adiposity positively correlated with fetal AC, EFW, HC, FL, and BPD in obese, nonobese, gestational diabetic, and nondiabetic pregnant women (Table 1). There was a negative correlation between the ratios of BPD/FL and HC/AC (Table 1). The correlation coefficients were statistically similar among the groups (Table 1). The analysis of the correlation of maternal visceral adiposity and fetal biometric parameters remained statistically significant after controlling for age, gestational age, ethnicity, income, and schooling (Table 2).

DISCUSSION

The present study showed that there was a statistically significant correlation between maternal visceral adiposity and fetal biometric parameters in the second trimester of pregnancy, even after controlling for gestational age, in groups of obese, nonobese, gestational diabetic, and nondiabetic women. There was no statistical difference when the correlation coefficient of the previously obese and nonobese groups was compared. Neither there was a statistical difference when the correlation coefficient of the gestational diabetic and nondiabetic groups was compared.

Obesity and gestational diabetes are strongly associated with neonatal macrosomia and adiposity[3,4]; therefore, one would expect a greater correlation between fetal biometry and maternal visceral adiposity in these groups, compared to controls. However, the exact roles of fetal growth determinants remain to be elucidated. There is evidence of the association between

Table 1. Pearson's correlation coefficients between maternal visceral adiposity and fetal sonographic parameters in the second trimester of pregnancy in obese, nonobese, diabetic, and nondiabetic women.

Fetal biometric parameters	Obese		Nonobese		p††	Diabetic		Nondiabetic		p††
	r (n)	p†	r (n)	p†		r (n)	p†	r (n)	p†	
Abdominal circumference (AC)	0.60 (82)	<0.001	0.54 (501)	<0.001	0.424	0.67 (38)	<0.001	0.49 (443)	<0.001	0.132
Estimated fetal weight (EFW)	0.57 (80)	<0.001	0.54 (491)	<0.001	0.677	0.70 (38)	<0.001	0.50 (429)	<0.001	0.072
Head circumference (HC)	0.59 (82)	<0.001	0.53 (501)	<0.001	0.475	0.64 (38)	<0.001	0.49 (443)	<0.001	0.182
Femur length (FL)	0.58 (82)	<0.001	0.52 (501)	<0.001	0.477	0.62 (38)	<0.001	0.48 (443)	<0.001	0.248
Biparietal diameter (BPD)	0.58 (82)	<0.001	0.54 (501)	<0.001	0.617	0.65 (38)	<0.001	0.49 (443)	<0.001	0.194
Ratio BPD/FL	-0.27 (82)	0.013	-0.28 (501)	<0.001	0.971	-0.31 (38)	0.062	-0.28 (443)	<0.001	1.110
Ratio HC/AC	-0.43 (79)	<0.001	-0.27 (493)	<0.001	1.868	-0.37 (38)	0.021	-0.24 (432)	<0.001	1.585
Ratio FL/AC	0.01 (82)	0.903	0.14 (501)	0.002	1.688	0.01 (38)	0.950	0.14 (443)	0.003	1.542
Ratio EFW/BPD	0.69 (44)	<0.001	0.54 (264)	<0.001	0.124	0.71 (25)	<0.001	0.51 (246)	<0.001	0.156
Ratio EFW/HC	0.66 (44)	<0.001	0.52 (264)	<0.001	0.206	0.71 (25)	<0.001	0.51 (246)	<0.001	0.149

†Fisher's Z-test to test the hypothesis that Pearson's correlation coefficient was zero. ††Fisher's Z-test to test the hypothesis of equality of Pearson's correlation coefficients.

Table 2. Pearson's partial correlation coefficients between maternal visceral adiposity and fetal sonographic parameters in the second trimester of pregnancy in obese, nonobese, diabetic, and nondiabetic women, after adjusting for age, gestational age, ethnicity, income, and schooling.

Fetal biometric parameters	Obese		Nonobese		p††	Diabetic		Nondiabetic		p††
	r (n)	p†	r (n)	p†		r (n)	p†	r (n)	p†	
Abdominal circumference (AC)	0.59 (58)	<0.001	0.54 (322)	<0.001	0.615	0.73 (32)	<0.001	0.53 (400)	<0.001	0.078
Estimated fetal weight (EFW)	0.60 (58)	<0.001	0.57 (316)	<0.001	0.755	0.74 (32)	<0.001	0.55 (391)	<0.001	0.085

†Student's t-test (Stata 12.1: command pcorr). ††Teste Z.

maternal obesity and fetal body composition in the third trimester of pregnancy[12], while another study found no association between maternal obesity and fetal growth in the third and second trimesters[13,14]. Another interesting study evaluated the association between newborn adiposity and fetal growth[14-17]. They demonstrated an association of newborn adiposity with EFW in the third trimester, but not in the second trimester[18]. In contrast, fetal growth in the third trimester was not associated with adiposity in adulthood. One study evaluated the relationship between birth weight and the growth rate in the third trimester with body composition and metabolism of glucose in adulthood using differences between pairs of twins. Birth weight was inversely associated with both visceral and subcutaneous fat in adulthood; on the contrary, there was no association with insulin resistance. In contrast, fetal growth rate during the third trimester was not associated with visceral or subcutaneous fat in adults. These data suggest that distinct metabolic and anthropometric trajectories, which influence the risk of developing type 2 diabetes in adults, are determined according to the period of growth restriction during pregnancy[18]. In the present study, fetal biometry was measured during the second trimester, at a mean gestational age of 22 weeks. It is possible that the effect of maternal obesity, and especially gestational diabetes, on fetal growth is more evident later in pregnancy.

One question that arises is whether the increased risk of adverse fetal outcome in obese women is associated with obesity alone or with an increased risk of developing GDM. The Hyperglycemia and Adverse Pregnancy Outcome study included more than 23,000 pairs of mothers and babies and showed a strong linear association between fasting glucose and post-glucose load with the incidence of macrosomia and neonatal adiposity[4]. An European multicenter study involving seven countries also showed that both maternal obesity and the presence of GDM are independent risk factors for perinatal complications. However, maternal obesity has a greater relative influence on the risk of macrosomia[19]. Because of the interrelated effect of obesity and diabetes on fetal growth, in the present study, we compared the correlation coefficients of the obese and gestational diabetic groups with a control group of nonobese and nondiabetic pregnant women, but there was still no statistical difference (data not shown) between the groups.

Considering the determinants of fetal growth, it has also been documented that there is a positive correlation between fetal AC and glucose levels in maternal blood in nonobese and nondiabetic pregnant women[20]. In this regard, there seems to be a trend toward increased fetal AC in fetuses of pregnant women with GDM, when compared to controls at the beginning of the last trimester (p=0.077) and at delivery (p=0.078)[21]. Together, these data suggest that the metabolic determinants of fetal growth would have a more important role in fetal tissues sensitive to insulin, such as adipose tissue, as represented by AC measurement. However, in the present study, maternal visceral adiposity positively correlated with fetal biometric parameters representing tissues that were both sensitive and nonsensitive to insulin. Although there was no statistical difference, in the present study, there was a tendency of greater AC and EFW in the gestational diabetic group. It is possible that in larger studies, and maybe in studies during the third trimester, this difference will become significant.

The distribution of fat is very important when analyzing outcomes associated with obesity[22] and is commonly categorized as central adiposity (visceral) when there is an excess of fat in the thoracoabdominal area and peripheral when the accumulation of fat occurs in the subcutaneous tissue, particularly in the hips, thighs, and legs[23]. Maternal obesity is usually defined as a high pre-pregnancy BMI and is associated with adverse outcomes[24]. However, BMI does not adequately differentiate the contributions of the muscles and the abdominal or visceral fat to body weight[22]. It is known that central visceral fat is more related to the risk of metabolic disease when compared to subcutaneous fat[25].

On this subject, central adiposity predicts more accurately than the BMI the risk for type 2 diabetes[26] and insulin resistance development in adults. On the contrary, peripheral fat seems to have a dampening effect or to shield some risks related to weight[25]. Regarding fetal growth, recent data, including 740 pregnant women, report no correlation between pre-pregnancy BMI and fetal biometric parameters such as HC, AC, BPD, and EFW in the second trimester of pregnancy, although maternal visceral adiposity is positively correlated with all those parameters[14]. In the present study, maternal visceral adiposity positively correlated with CC, CA, DBP, and EFW in the second trimester of obese, nonobese, diabetic, and nondiabetic mothers.

Our study has some limitations. First, it had a sectional design. Visceral fat and fetal biometry were measured only once, although the recommended techniques had been followed. Second, fat distribution during fetal life may be influenced by gender, and we could not identify this variable. In fact, the effect of gender on the fat distribution of the fetus is not completely known. Third, many variables influence fetal growth and can potentially alter the distribution of fetal fat. Unfortunately, we could not control them all. However, our study has strengths. The study addressed a topic not yet studied, and an adequate sample was studied; besides that, validated techniques were used.

Several studies point to an association between maternal nutrition during pregnancy and fetal development, influencing the body composition of the offspring[24]. This body composition in early life may influence the development of obesity in childhood and adulthood. However, little is known about the role of growth trajectories and intrauterine body composition as determinants of adverse metabolic outcomes in extrauterine life.

CONCLUSION

The present study found no significant difference between the correlation of maternal visceral adiposity and fetal biometric parameters when comparing obese and nonobese mothers, or gestational diabetic and nondiabetic mothers in the second trimester of pregnancy. Larger studies that investigate these correlations in the second and third trimesters may contribute to a better understanding of the exact role and timing of each factor in determining fetal growth.

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AUTHORS' CONTRIBUTIONS

KRML: Conceptualization, Data curation, Investigation, Project administration, Resources, Writing – original draft, Writing – review & editing. **JGA:** Conceptualization, Formal Analysis, Methodology, Resources, Supervision, Writing – review & editing. **ASRS:** Conceptualization, Data curation, Formal Analysis, Investigation, Methodology, Resources, Supervision, Writing – review & editing.

REFERENCES

1. Reece EA, Leguizamón G, Wiznitzer A. Gestational diabetes: the need for a common ground. Lancet. 2009;373(9677):1789-97. https://doi.org/10.1016/S0140-6736(09)60515-8
2. Giacca A, Xiao C, Oprescu AI, Carpentier AC, Lewis GF. Lipid-induced pancreatic β-cell dysfunction: focus on in vivo studies. Am J Physiol Endocrinol Metab. 2011;300(2):E255-62. https://doi.org/10.1152/ajpendo.00416.2010
3. Tan HC, Roberts J, Catov J, Krishnamurthy R, Shypailo R, Bacha F. Mother's pre-pregnancy BMI is an important determinant of adverse cardiometabolic risk in childhood. Pediatr Diabetes. 2015;16(6):419-26. https://doi.org/10.1111/pedi.12273
4. Riskin-Mashiah S, Younes G, Damti A, Auslender R. First-trimester fasting hyperglycemia and adverse pregnancy outcomes. Diabetes Care. 2009;32(9):1639-43. https://doi.org/10.2337/dc09-0688
5. Logan KM, Gale C, Hyde MJ, Santhakumaran S, Modi N. Diabetes in pregnancy and infant adiposity: systematic review and meta-analysis. Arch Dis Child Fetal Neonatal Ed. 2017;102(1):F65-72. https://doi.org/10.1136/archdischild-2015-309750
6. Hull HR, Thornton JC, Ji Y, Paley C, Rosenn B, Mathews P, et al. Higher infant body fat with excessive gestational weight gain in overweight women. Am J Obstet Gynecol. 2011;205(3):211.e1-7. https://doi.org/10.1016/j.ajog.2011.04.004
7. Hull HR, Dinger MK, Knehans AW, Thompson DM, Fields DA. Impact of maternal body mass index on neonate birthweight and body composition. Am J Obstet Gynecol. 2008;198(4):416.e1-6. https://doi.org/10.1016/j.ajog.2007.10.796
8. Martin AM, Berger H, Nisenbaum R, Lausman AY, MacGarvie S, Crerar C, et al. Abdominal visceral adiposity in the first trimester predicts glucose intolerance in later pregnancy. Diabetes Care. 2009;32(7):1308-10. https://doi.org/10.2337/dc09-0290
9. Cisneiros RM, Dutra LP, Silveira FJ, Souza AR, Marques M, Amorim MM, et al. Visceral adiposity in the first half of pregnancy predicts newborn weight among adolescent mothers. J Obstet Gynecol Can. 2013;35(8):704-9. https://doi.org/10.1016/S1701-2163(15)30860-4
10. American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care. 2011;34(Suppl 1):S62-9. https://doi.org/10.2337/dc11-S062
11. Arcaro G, Zamboni M, Rossi L, Turcato E, Covi G, Armellini F, et al. Body fat distribution predicts the degree of endothelial dysfunction in uncomplicated obesity. Int J Obes Relat Metab Disord. 1999;23(9):936-42. https://doi.org/10.1038/sj.ijo.0801022
12. Ribeiro-Filho FF, Faria AN, Azjen S, Zanella MT, Ferreira SR. Methods of estimation of visceral fat: advantages of ultrasonography. Obes Res. 2003;11(12):1488-94. https://doi.org/10.1038/oby.2003.199
13. Mauad FM, Chagas-Neto FA, Benedeti ACGS, Nogueira-Barbosa MH, Muglia VF, Carneiro AAO, et al. Reprodutibilidade da avaliação da gordura abdominal pela ultrassonografia e tomografia computadorizada. Radiol Bras. 2017;50(3):141-7. https://doi.org/10.1590/0100-3984.2016.0023
14. Lopes KRM, Souza ASR, Figueiroa JN, Alves JGB. Correlation between pre-pregnancy body mass index and maternal visceral adiposity with fetal biometry during the second trimester. Int J Gynaecol Obstet. 2017;138(2):133-7. https://doi.org/10.1002/ijgo.12202
15. Grivell RM, Yelland LN, Deussen A, Crowther CA, Dodd JM. Antenatal dietary and lifestyle advice for women who are overweight or obese and the effect on fetal growth and adiposity: the LIMIT randomised trial. BJOG. 2016;123(2):233-43. https://doi.org/10.1111/1471-0528.13777
16. Canavan TP, Deter RL. The effect of maternal body mass index on fetal growth: use of individualized growth assessment and two-level linear modeling. J Clin Ultrasound. 2014;42(8):456-64. https://doi.org/10.1002/jcu.22158
17. Breij LM, Steegers-Theunissen RP, Briceno D, Hokken-Koelega AC. Maternal and fetal determinants of neonatal body composition. Horm Res Pædiatrics. 2015;84(6):388-95. https://doi.org/10.1159/000441298
18. Pilgaard K, Hammershaimb Mosbech T, Grunnet L, Eiberg H, Van Hall G, Fallentin E, et al. Differential nongenetic impact of birth weight versus third-trimester growth velocity on glucose metabolism and magnetic resonance imaging abdominal obesity in young healthy

twins. J Clin Endocrinol Metab. 2011;96(9):2835-43. https://doi.org/10.1210/jc.2011-0577

19. Vellinga A, Zawiejska A, Harreiter J, Buckley B, Di Cianni G, Lapolla A, et al. Associations of body mass index (maternal BMI) and gestational diabetes mellitus with neonatal and maternal pregnancy outcomes in a multicentre european database (diabetes and pregnancy vitamin D and lifestyle intervention for gestational diabetes mellitus. ISRN Obes. 2012;2012:424010. https://doi.org/10.5402/2012/424010
20. Parretti E, Mecacci F, Papini M, Cioni R, Carignani L, Mignosa M, et al. Third-trimester maternal glucose levels from diurnal profiles in nondiabetic pregnancies: correlation with sonographic parameters of fetal growth. Diabetes Care. 2001;24(8):1319-23. https://doi.org/10.2337/diacare.24.8.1319
21. Zornoza-Moreno M, Fuentes-Hernández S, Prieto-Sánchez MT, Blanco JE, Pagán A, Rol MA, et al. Influence of gestational diabetes on circadian rhythms of children and their association with fetal adiposity. Diabetes Metab Res Rev. 2013;29(6):483-91. https://doi.org/10.1002/dmrr.2417
22. Després JP, Lemieux I, Prud'homme D. Treatment of obesity: need to focus on high risk abdominally obese patients. BMJ. 2001;322(7288):716-20. https://doi.org/10.1136/bmj.322.7288.716
23. Hamdy O, Porramatikul S, Al-Ozairi E. Metabolic obesity: the paradox between visceral and subcutaneous fat. Curr Diabetes Rev. 2006;2(4):367-73. https://doi.org/10.2174/1573399810602040367
24. Sebire NJ, Jolly M, Harris JP, Wadsworth J, Joffe M, Beard RW, 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. https://doi.org/10.1038/sj.ijo.0801670
25. Carey DG, Jenkins AB, Campbell LV, Freund J, Chisholm DJ. Abdominal fat and insulin resistance in normal and overweight women: direct measurements reveal a strong relationship in subjects at both low and high risk of NIDDM. Diabetes. 1996;45(5):633-8. https://doi.org/10.2337/diab.45.5.633
26. Bray GA, Jablonski KA, Fujimoto WY, Barrett-Connor E, Haffner S, Hanson RL, et al. Relation of central adiposity and body mass index to the development of diabetes in the Diabetes Prevention Program. Am J Clin Nutr. 2008;87(5):1212-8. https://doi.org/10.1093/ajcn/87.5.1212