Ultrasound Evaluation of Visceral Fat Thickness for Prediction of Metabolic Syndrome in the First Trimester of Pregnancy in a Sample of Non-obese Iranian Women

Firoozeh Ahmadi, Somayeh Moukhah, Roya Hosseini, and Amirhossein Maghari

OBJECTIVES: Ultrasonography is a noninvasive and safe modality for assessing body fat and is routinely performed in developed countries. Although pregnant women with obesity are at risk for many unfavorable outcomes, the relationship between abdominal fat distribution and metabolic syndrome (MS) is evident in some studies. Therefore, it is important to evaluate fat thickness in non-obese women and predict MS using fat thickness measurement.

METHODS: A total of 132 pregnant women completed anthropometric and demographic questionnaires. All women were scanned for visceral fat thickness (VFT) via ultrasound at 11–14 weeks gestation. Body mass index (BMI) and waist circumference (WC) were calculated at the first prenatal visit. MS components were also measured in the same weeks. Results: MS was detected in seven (5.3%) women. There was a statistically significant difference between women with and without MS for weight, WC, anterior and posterior VFT, insulin, lipid profile (total cholesterol, high-density lipoprotein cholesterol, and triglyceride), and systolic and diastolic blood pressure (p < 0.050). The optimal cut-off points determined for predicting MS disorder were an anterior VFT of 43.83 mm and a posterior VFT of 32.50 mm.

CONCLUSIONS: Fat thickness measurement in the first trimester is a good predictor for MS even in women with a normal BMI. Ultrasonography as a safe, simple, and cost-effective modality can be used to assess fat thickness besides the other screening evaluations in the first trimester of pregnancy.

Obesity is a common problem. According to the 2018 World Health Organization (WHO) report, 39% of adults aged 18 years and over (39% of men and 40% of women) were overweight, and 13% (11% of men and 15% of women) were obese. Being overweight before pregnancy increases the risk of adverse pregnancy outcomes such as macrosomia, hypertension, congenital malformations, cesarean section delivery, and late fetal death. Moreover, it results in many health problems, such as metabolic syndrome (MS), in women. MS is a collection of risk factors for type 2 diabetes and cardiovascular diseases. Women with MS have a greater risk of adverse perinatal outcomes.

MS is a clustering of at least three of the five following medical conditions: abdominal obesity, high blood pressure (BP), high blood sugar, high serum triglycerides (TGs), and low high-density lipoprotein (HDL) levels. The prevalence of MS varies based on region, population, and sex according to the developmental status of countries, economic growth, and urbanization rate. Its prevalence also increases with age and is commonly seen in women. In developed and developing countries, MS is related to the rising...
incidence of obesity and it is estimated between 24% and 34% of the US population and up to 36% of Europeans aged 40–55 years have MS resulting from obesity. MS predicts a two-fold increase in cardiovascular disease.

MS has some common risk factors such as central obesity, glucose intolerance, insulin resistance, dyslipidemia, and hypertension. There are several ways to estimate maternal adiposity, but the severity of MS is more related to body fat distribution versus the extent of body fat accumulation. Body fat distribution is commonly categorized into central and peripheral fat. There are different methods to assess central obesity for instance, computed tomography, magnetic resonance imaging (MRI), body densitometry, or waist-to-hip ratio. These are considered better markers to determine central obesity than BMI, but they are impractical as screening tools in pregnancy. Spatially MRI examination is expensive and not readily available in most clinical settings. An alternative method for central obesity evaluation is visceral fat measurement, which can be accurately measured using ultrasound in pregnant women.

Ultrasoundography is a noninvasive and safe modality routinely performed on all pregnant women at 11–14 weeks gestation for nuchal translucency (NT) screening for fetal anomalies. Furthermore, this modality is useful for assessing body fat and several studies concluded that measurement of fat thickness is suitable at this time.

Pregnant women with obesity are at risk for many unfavorable outcomes, and the relationship between abdominal fat distribution and MS has been investigated in some studies. Therefore, it is important to evaluate fat thickness in non-obese pregnant women.

This study aimed to evaluate visceral fat thickness (VFT) for prediction of MS in the first trimester.

**METHODS**

We conducted a cross-sectional prospective study at the Royan Institute, Tehran, Iran, between June 2015 and June 2017. The study was approved by the Ethical Committee of Royan Institution and informed consent for participation was obtained from each subject. Singleton pregnant women with a gestational age of 11–14 weeks were included in the study. Pregnant women with hypertension, on chronic drug therapy, with glucose intolerance or diabetes (or gestational diabetes mellitus in previous pregnancy), and those with a BMI < 30 were excluded.

A total of 132 pregnant women completed anthropometric and demographic questionnaires at 11–14 weeks gestational age, and all women were scanned for VFT via ultrasound. BMI was calculated by measuring the height (meters) and weight (kg) at the first prenatal visit. Waist circumference (WC) was determined by measuring from the middle point of the border of iliac crest to the last rib after normal expiration with the participant in the standing position. Morning fasting blood was drawn at the first prenatal visit for biochemical assessment. Fasting blood sugar (FBS), total cholesterol (TC), low-density lipoprotein (LDL), HDL, TG, and insulin levels were measured. The homeostasis model index (HOMA-IR) was used to evaluate insulin resistance. HOMA-IR was calculated using the following formula: HOMA-IR = (fasting insulin × fasting glucose) / 400.

MS was diagnosed according to the Adult Treatment Panel III method as the presence of three or more of the five criteria: high WC (> 88 cm in women), high BP (> 130/80 mm/Hg), high TG (> 150 mm/dL), high glucose (FBS > 100 mg/dL), and low HDL (< 50 mg/dL in women) levels.

We used SPSS Statistics (SPSS Inc. Released 2007. SPSS for Windows, Version 16.0. Chicago, SPSS Inc.) for descriptive statistics, independent sample t-test, area under the curve and receiver operating characteristic curve, and logistic regression. A statistically significant level was considered < 0.050.

We used the technique described by Armellini et al. to measure VFT. Ultrasonography measurements were performed with the peripheral probe over the abdomen using a high-resolution ultrasound system and 7–13 MHz linear transducer. All measurements were taken with the patient in a supine position. Ultrasonography measurements were taken by one expert radiologist three times and the average calculated.

Application of the transducer on the body surface was done without undue pressure that would alter the body layer contour and thickness. VFT was measured by a convex probe, from the inner border of the rectus abdominis muscle at the level of the linea alba to the anterior wall of the abdominal aorta.
RESULTS

Our study included 150 pregnant women with a gestational age of 11–14 weeks. Eighteen participants refused to continue the study giving a study population of 132 women. MS was detected in seven (5.3%) of these pregnant women.

The average of age, weight, height, BMI, WC, anterior and posterior VFT, FBS, insulin, lipid profile (TC, LDL-C, HDL-C, TG), systolic and diastolic BP were reported in women with and without MS [Table 1]. We found a statistically significant difference between women with and without MS for these variables (p < 0.050). In this study, age was detected as a confounding variable. We used logistic regression to determine the relationship between anterior and posterior VFT and MS in women with and without adjusted confounding variable (age).

The results showed that with and without adjusted confounding variables, MS with anterior and posterior VFT is predictable. In other words, for each unit increase in anterior VFT, there is a 1.10 times (without adjusted confounding variable) and 1.11 times (with adjusted confounding variable) increase in the MS rate, and a unit increases in posterior VFT 1.10 times (without adjusted confounding variable) and 1.10 times (with adjusted confounding variable) the MS rate [Table 2].

The correlation between MS components and both ultrasonographic and anthropometric measurements were evaluated [Table 3].

Systolic BP, FBS, and LDL were not correlated with any of the ultrasonographic and anthropometric measurements while diastolic BP and HDL were separately correlated with WC (p < 0.050). TC was correlated with BMI and WC (p < 0.050), and TG was correlated with WC (p < 0.050). Insulin and HOMA-IR were significantly correlated with anterior and posterior VFT and WC (p < 0.050).

Table 1: Baseline characteristics and ultrasonographic findings of pregnancies.

| Variables          | Metabolic syndrome (-) Mean ± SD n = 125 (94.7%) | Metabolic syndrome (+) Mean ± SD n = 7 (5.3%) | p-value |
|--------------------|--------------------------------------------------|-----------------------------------------------|---------|
| Age, years         | 30.4 ± 4.8                                       | 29.1 ± 3.4                                     | 0.516   |
| Weight, kg         | 61.9 ± 8.8                                       | 73.3 ± 9.7                                     | 0.003*  |
| Height, cm         | 159.6 ± 6.0                                      | 161.8 ± 5.3                                    | 0.399   |
| BMI                | 24.7 ± 5.6                                       | 27.8 ± 2.1                                     | 0.187   |
| WC, cm             | 76.6 ± 7.1                                       | 86.0 ± 7.5                                     | 0.022*  |
| Anterior VFT, mm   | 26.7 ± 10.7                                      | 39.5 ± 14.4                                    | 0.010*  |
| Posterior VFT, mm  | 38.4 ± 11.7                                      | 52.5 ± 13.2                                    | 0.012*  |
| Systolic BP, mmHg  | 102.7 ± 11.8                                     | 122.5 ± 11.7                                   | 0.001*  |
| Diastolic BP, mmHg | 63.1 ± 9.2                                       | 80.0 ± 8.9                                     | 0.005*  |
| TC, mg/dL          | 171.2 ± 30.5                                     | 209.3 ± 30.9                                   | 0.003*  |
| TG, mg/dL          | 120.6 ± 40.7                                     | 195.5 ± 33.3                                   | 0.001*  |
| LDL, mg/dL         | 93.2 ± 27.0                                      | 107.1 ± 32.3                                   | 0.223   |
| HDL, mg/dL         | 68.5 ± 18.3                                      | 53.8 ± 10.4                                    | 0.002*  |
| FBS, mg/dL         | 82.4 ± 9.3                                       | 88.8 ± 4.1                                     | 0.101   |
| Fasting insulin, mIU/L | 10.5 ± 5.2                                         | 16.3 ± 8.3                                     | 0.019*  |

Data given as n (%). SD: standard deviation; BMI: body mass index; WC: waist circumference; VFT: visceral fat thickness; BP: blood pressure; TC: total cholesterol; TG: triglyceride; LDL: low-density lipoprotein; HDL: high-density lipoprotein; FBS: fasting blood sugar.

*There was a statistically significant difference between two groups.

Table 2: Results for logistic regression with adjusted confounding variable.

| Variables  | OR  | 95% CI for OR | p-value |
|------------|-----|---------------|---------|
| Age        | 0.886 | 0.726 - 1.082 | 0.236   |
| Constant   |      | 0.058         |         |
| Anterior VFT | 1.107 | 1.019 - 1.201 | 0.016   |
| Age        | 0.904 | 0.726 - 1.126 | 0.367   |
| Constant   |      | 0.181         |         |
| Posterior VFT | 1.109 | 1.019 - 1.207 | 0.017   |
| Age        | 0.903 | 0.726 - 1.123 | 0.359   |
| Constant   |      | 0.294         |         |

OR: odds ratio; CI: confidence interval; VFT: visceral fat thickness.
DISCUSSION

It is obvious that abdominal fat distribution is associated with MS in healthy weight people. Although WC is often considered a measure of abdominal fat, VFT measurement in pregnant women is impractical. Several researchers showed that MS is related to a worse perinatal outcome. Therefore, the correlation between fat thickness and risk factors of MS is discussed in several studies with some demonstrating that VFT is a major factor for MS.

Increased insulin resistance has been proposed as the relationship between VFT and MS.

Ultrasonography is commonly used for NT assessment in the first trimester of pregnancy at 11–14 weeks gestational age as a screening test. For convenience, we evaluated VFT coincidently accompanied by NT evaluation. We used Armellini’s technique to measure VFT, but Gur et al. preferred to apply the method described by Hamagawa et al. We measured VFT three times as did Liu and colleagues.

We detected MS in 5.3% of pregnant women and found a significant predictive relationship between VFT and MS similar to other studies. A 2007 study found the prevalence of MS was 25% in adult men and 15% in women. Another study performed in 2016 found a high prevalence of MS. The overall prevalence of MS (29.2%) in pregnant Angolan women is similar to that observed in the Nigerian general population (27.9%) and USA (34.1%), and is higher than the overall prevalence in Angola (17.6%) and Canada.

Our results showed that VFT was only correlated with insulin level and HOMA-IR. This finding was in contrast to other studies in which VFT was correlated with hyperglycemia, dyslipidemia, and insulin resistance. Also, there was a statistically significant correlation between BMI, WC, and TC levels. Another study found a correlation between VFT and WC with insulin levels, but this relationship was not seen between BMI and insulin level.

We found that VFT is no more effective than other anthropometric measurements (BMI and WC) to predict MS. Other studies concluded that VFT measurement is more effective as an indicator than WC or BMI.

The strengths of our study include its acceptable sample size, limitation of BMI for non-obese women, and evaluation of VFT in two parts (anterior and posterior) in contrast to other studies. Unfortunately, we had no control group (such as women with spontaneous pregnancy). Therefore, we recommended conducting a similar study including this group.

CONCLUSION

MS has unfavorable outcomes for pregnant women, and its diagnosis is important in early pregnancy. VFT measurement in the first trimester is a good predictor for MS even in women with normal BMI. The use of ultrasonography is a safe, simple, and cost-effective modality, which can be used to assess fat distribution.

| Parameters       | Anterior VFT, mm | p-value | Posterior VFT, mm | p-value | BMI   | p-value | WC, cm | p-value |
|------------------|------------------|---------|-------------------|---------|-------|---------|--------|---------|
| Systolic BP, mmHg| 0.05             | 0.540   | 0.06              | 0.438   | 0.10  | 0.176   | 0.15   | 0.052   |
| Diastolic BP, mmHg| 0.10             | 0.176   | 0.11              | 0.142   | 0.06  | 0.400   | 0.11   | 0.154   |
| TC, mg/dL        | 0.12             | 0.115   | 0.13              | 0.101   | 0.16  | 0.033*  | 0.16   | 0.032*  |
| TG, mg/dL        | 0.12             | 0.114   | 0.12              | 0.134   | 0.13  | 0.088   | 0.16   | 0.029*  |
| LDL, mg/dL       | 0.04             | 0.618   | 0.05              | 0.489   | 0.12  | 0.103   | 0.10   | 0.197   |
| HDL, mg/dL       | 0.17             | 0.034   | 0.15              | 0.063   | 0.08  | 0.281   | 0.18   | 0.019*  |
| FBS, mg/dL       | 0.07             | 0.404   | 0.07              | 0.355   | 0.05  | 0.505   | 0.08   | 0.271   |
| Insulin, mIU/L   | 0.16             | 0.037*  | 0.17              | 0.026*  | 0.13  | 0.081   | 0.32   | 0.001*  |
| HOMA-IR, %       | 0.17             | 0.038*  | 0.18              | 0.024*  | 0.12  | 0.115   | 0.33   | 0.001*  |

Receiver operating characteristic curve analysis was used to determine the cut-off value. The optimal cut-off points for predicting disorders of metabolic syndrome were anterior visceral fat thickness (VFT) 43.83 mm (area under the curve (AUC) = 0.792, p = 0.027) and posterior VFT 32.50 mm (AUC = 0.755, p = 0.047). BMI: body mass index; WC: waist circumference; BP: blood pressure; TC: total cholesterol; TG: triglyceride; LDL: low-density lipoprotein; HDL: high-density lipoprotein; FBS: fasting blood sugar; HOMA-IR: homeostasis model index (insulin resistance index).

Table 3: Comparison between correlations of metabolic syndrome components and ultrasonographic measurements and anthropometric measurements.
thickness alongside other screening evaluations in the first trimester of pregnancy.

Disclosure
The authors declared no conflicts of interest. No funding was received for this study.

REFERENCES
1. World Health Organisation (WHO), Global Database on Body Mass Index. [cited 2018 February 16]. Available from http://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight.
2. Cnattingius S, Bergström R, Lipworth L, Kramer MS. Prepregnancy weight and the risk of adverse pregnancy outcomes. N Engl J Med 1998 Jan;338(3):147-152.
3. Ehrenberg HM, Mercer BM, Catalano PM. The influence of obesity and diabetes on the prevalence of macrosomia. Am J Obstet Gynecol 2004 Sep;191(3):964-968.
4. Shenier E, Levy A, Menes TS, Silverberg D, Katz M, Mazor M. Maternal obesity as an independent risk factor for caesarean delivery. Paediatr Perinat Epidemiol 2004 May;18(3):196-201.
5. Thadhani R, Stampfer MJ, Hunter DJ, Manson JE, Solomon CG, Curhan GC. Body mass index and hypercholesterolemia: risk of hypertensive disorders of pregnancy. Obstet Gynecol 1999 Oct;94(4):543-550.
6. Garcia-Patterson A, Erdozain L, Ginovart G, Adelantado JM, Cubero JM, Gallo G, et al. In human gestational diabetes mellitus congenital malformations are related to pre-pregnancy body mass index and to severity of diabetes. Diabetology 2004 Mar;47(3):509-514.
7. Stephansson O, Dickman PW, Johansson A, Cnattingius S. Maternal weight, pregnancy weight gain, and the risk of antepartum stillbirth. Am J Obstet Gynecol 2001 Feb;184(3):463-469.
8. Bartha JL, Marín-Segura P, González-González NL, Wagner F, Aguilera-Diosdado M, Hervias-Vivancos B. Ultrasound evaluation of visceral fat and metabolic risk factors during early pregnancy. Obesity (Silver Spring) 2007 Sep;15(9):2233-2239.
9. Dos Prazeres Tavares H, Dos Santos DC, Abbade JF, Negrato et al. Sonographic measurement of mesenteric fat thickness is a good correlate with cardiovascular risk factors: comparison with subcutaneous and preperitoneal fat thickness, magnetic resonance imaging and anthropometric indexes. Int J Obes (Lond) 2002 Nov;26(5):364-376.
10. Alberti KG, Zimmet P, Shaw J; IDF Epidemiology Task Force Consensus Group. The metabolic syndrome—a new worldwide definition. Lancet 2005 Sep;366(9491):1099-1106.
11. Matsuzawa Y. Pathophysiology and molecular mechanisms of visceral fat syndrome: the Japanese experience. Diabetes Metab Rev 1997 Mar;13(1):3-13.
12. Hamdy O, Porramatikul S, Al-Ozairi E. Metabolic obesity: the paradox between visceral and subcutaneous fat. Curr Diab Rep 2006 Nov;2(4):367-373.
13. Klein S. The case of visceral fat: argument for the defense. J Clin Invest 2004 Jun;113(11):1530-1532.
14. Lapidus L, Bengtsson C, Larsson B, Pennert K, Rybo E, Sjöström L. Distribution of adipose tissue and risk of cardiovascular disease and death: a 12 year follow up of participants in the population study of women in Gothenburg, Sweden. Br Med J (Clin Res Ed) 1994 Nov;208(654):1257-1261.
15. Kady S, Wyldes M. Professional opinion of nuchal translucency screening in West Midlands. Ultrasound Obstet Gynecol 2004;24:269-372.
16. Armellini F, Zamboni M, Rigo L, Todesco T, Bergamo-Andreis IA, Proacci C, et al. The contribution of sonography to the measurement of intra-abdominal fat. J Clin Ultrasound 1990 Sep;18(7):563-567.
17. Metzger BE, Buchanan TA, Coustan DR, de Leiva A, Dunger DB, Hadden DR, et al. Summary and recommendations of the Fifth International Workshop-Conference on Gestational Diabetes Mellitus. Diabetes Care 2007 Jul;30(1)(Suppl 2):S251-S260.
18. Matsuzawa Y, Nakao YM, Masuda I, Higashiyama A, Takegami M, Nishimura K, et al. Risk for metabolic diseases in normal weight individuals with visceral fat accumulation: a cross-sectional study in Japan. BMJ Open 2017 Jan;7(1):e013831.
19. Brambilla P, Bedogni G, Moreno LA, Garon MI, Gutin B, Fox KR, et al. Crossvalidation of anthropometry against magnetic resonance imaging for the assessment of visceral and subcutaneous adipose tissue in children. Int J Obes (Lond) 2006 Jan;30(1):23-30.
20. Gur EB, Ince O, Turan GA, Karadeniz M, Tatar S, Celik E, et al. Ultrasonographic visceral fat thickness in the first trimester can predict metabolic syndrome and gestational diabetes mellitus. Endocrine 2014 Nov;47(2):478-484.
21. Bertoli S, Leone A, Vignati L, Sadafranca A, Bedogni G, Vanzulli A, et al. Metabolic correlates of subcutaneous and visceral abdominal fat measured by ultrasonography: a comparison with waist circumference. Nutr J 2016 Jan;15(1):2.
22. Fujioka S, Matsuzawa Y, Tokunaga K, Tanii S. Contribution of intra-abdominal fat accumulation to the impairment of glucose and lipid metabolism in human obesity. Metabolism 1987 Jan;36(1):54-59.
23. Björntorp P. Metabolic implications of body fat distribution. Diabetes Care 1991 Dec;14(12):1132-1143.
24. Hamagawa K, Matsumura Y, Kubo T, Hayato K, Okawa M, Tanioka K, et al. Abdominal visceral fat thickness measured by ultrasonography predicts the presence and severity of coronary artery disease. Ultrasound Med Biol 2010 Nov;36(11):1769-1775.
25. Liu KH, Chan YL, Chan WB, Kong WJ, Kong MO, Chan JC. Sonographic measurement of mesenteric fat thickness is a good correlate with cardiovascular risk factors: comparison with subcutaneous and preperitoneal fat thickness, magnetic resonance imaging and anthropometric indexes. Int J Obes Relat Metab Disord 2003 Oct;27(10):1267-1273.
26. Panagiotakos DB, Pitsavos C, Das UN, Skoumas Y, Stefanadis C. The implications of anthropometric, inflammatory and glycaemic control indexes in the epidemiology of the metabolic syndrome given by different definitions: a classification analysis. Diabetes Obes Metab 2007 Sep;9(5):660-668.
27. Cunningham FG, Kenneth J, Leveno, MD, Bloom LS, Hauth JC, Rouse JD, Spong YC. Williams obstetrics, 23rd ed. Unite State of America: McGraw-Hill; 2014. p. 108-114.
28. Brisson D, Perron P, Guay SP, Gaudet D, Bouchard L. The “hypertriglyceridemic waist” phenotype and glucose intolerance in pregnancy. CMAJ 2010 Oct;182(15):E722-E725.
29. Gustar J, Elkasabany A, Srinivasan S, Berenson GS. Relation of abdominal height to cardiovascular risk factors in young adults: the Bogalusa heart study. Am J Epidemiol 2000 May;151(9):885-891.