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RESEARCH PAPER.

PREDICTION OF GESTATIONAL DIABETES MELLITUS BY MEASURING THE VISCERAL FAT THICKNESS ULTRASONOGRAPHICALLY IN THE FIRST TRIMESTER.

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ABSTRACT

Gestational diabetes mellitus is a common antenatal complication associated with adverse perinatal outcomes. Accurate prediction of GDM will help to implement preventive strategies early during pregnancy. The purpose of this study is to determine whether ultrasonography visceral fat thickness measurement can be performed during early gestation. To assess the correlation between the anthropometric measurement and visceral fat thickness and to define the cutoff value of visceral fat thickness for the development of GDM with optimum diagnostic test accuracy level. Prospective longitudinal study was conducted in antenatal clinic: Teaching Hospital Kandy. Gestational age between 11 to 14 weeks of gestation was included for the study. Multiple gestations, already diagnosed mothers with Diabetes Mellitus and past sections were excluded. Ultrasound Scanning machine, anthropometric measurement scales and interviewer administered data collection sheet were used as study instruments. Sample size was 251 and SPSS version 23.0 was used for data analysis. Visceral fat thickness of the participants positively and significantly correlated with the height (r=141), weight(r=550), BMI(r=533), waist circumference(r=470) and hip circumference(r=558). Most suitable cut off value of visceral fat thickness for predicting GDM among the study participants was 11.75 (Sensitivity: 84.2 Specificity :91.6). According to the other anthropometric parameters, when the subcutaneous fat thickness is more than 12.5cm (sensitivity 89.2 and specificity 39.8), hip circumference is more than 81.5cm (sensitivity 81.1 and specificity94.9), waist circumference is more than 66.5cm (sensitivity 86.5 and specificity 51.5) and BMI is above 21.73 (sensitivity 81.1 and specificity 61.8) GDM can be predicted with above mentioned sensitivities and specificities. Anthropometric measurements which are measured at the early gestational ages can be satisfactorily used for predicting gestational Diabetes Mellitus. But visceral fat thickness is the most suitable measurement for obtaining an accurate prediction.

Key words: Anthropometry, Gestational, Diabetes mellitus

INTRODUCTION

GDM is defined as glucose intolerance that appears or is first recognized during pregnancy (1,2).Gestational diabetes mellitus (GDM) is a common antenatal complication which occurs in about 15%-18% (3) of pregnancies and it is also associated with adverse perinatal outcomes. The prevalence of GDM has increased over the last two decades in Sri Lanka (4)(5). Moreover it has shown to carry a significant long term risk of developing diabetes in both the mother and the offspring.

There are well identified risk factors for GDM, including Obesity (body mass index >30kg/m^2), physical inactivity (6), previous history of macrosomic baby or GDM, first degree relative with diabetes and polycystic ovarian syndrome (7). Out of which obesity represents a major modifiable risk factor for GDM (8). Not surprisingly, obese women have four times and severe obese women have around nine times increased chance of getting GDM than lean women (9). Increase rate of weight gain in pregnancy especially in the early trimester may also increase the risk of developing GDM in women (8,10).

Nevertheless, the risk of diabetes mellitus varies within the obese population, and not every obese pregnant woman is at the same risk of adverse outcomes during pregnancy (9,10). Fat distribution in the visceral component is strongly linked to development of metabolic diseases such as type II diabetes mellitus and hypertriglyceridemia (11,12). Accurate prediction of GDM will help to implement preventive strategies early during pregnancy. Recent studies have suggested that excessive central fat is more important in developing gestational diabetes mellitus, preeclampsia and preterm birth rather than the subcutaneous fat (13–15). Anthropometric measurements such as waist circumference, waist/hip ratio, and the hyperglyceridemia waist phenotype are affected by the amount of subcutaneous fat and have poor correlation with development of GDM (16).

The prevalence of obesity in pregnancy has increased worldwide exponentially in last two decade (17–19). Still early prediction of the development of metabolic disease is a challenge to the field of medicine (20). Ultrasonographic measurement of visceral fat is a better test in early pregnancy prediction of GDM than the other anthropometric measurements (21,22). So this is cost effective and has fewer side effects (23).

Several methods are used to measure the visceral fat thickness such as bioelectrical impedance (BEI), computerized tomography (CT), dual-energy X-ray absorptiometry and ultrasonography (24). Compared to ultrasonography, other methods are expensive (25). Body water distribution during pregnancy is different and this will affect the use of ionizing radiation related investigations (26). Radiation risk to fetus also play a main role to choose

ultrasound rather than CT during pregnancy(26). Ultrasound is the safer and cost effective method compared to the others and it is objective as well as reproducible (23). The sensitivity of ultrasonographic measurement of fat thickness is similar to that of CT scan (25).

METHODS

Prospective longitudinal study design was conducted in antenatal Clinic: Teaching Hospital Kandy during 2019. All the admissions to the antenatal clinic in the study setting was used as the sampling frame. Gestational age between 11 to 14 weeks of gestation was included for the study. Multiple gestations, already diagnosed mothers with Diabetes Mellitus and past sections were excluded. This study was conducted on women who attend antenatal clinic in Teaching hospital Kandy. Pregnant mothers who were attending ANC clinic during the study period was included into the study.

Detailed medical history and physical examination were performed including anthropometric measurement such as BMI, Waist circumference (WC)-measuring from the middle point of the border between the lower margin of last palpable rib and the top of the iliac crest.(WHO,2008b),Hip circumference(HC)-measurement taken from the widest portion of the buttocks and Waist Hip ratio(27). At the end of dating scan, measurement of pre peritoneal visceral fat thickness and subcutaneous fat thickness were taken according to the previously noted method by Hamawaga et al, by using high-resolution ultrasound system with linear-array transducer 7.5 MHz.

All eligible participants were under follow-up and their routine OGTT values at POA of 24-28 weeks were analyzed. GDM was defined according to the HAPO criteria (FBS >92mg/dl, 1st hour > 180 mg/dl, 2nd hour >153mg/dl.) and the criteria published by SLCOG. The correlation between the visceral fat thickness and development of GDM were analyzed at the end of study period. Initially 271 patients were recruited as there can be non-respondents and loss to follow ups during the study. A specific code number was given to all the selected mothers and a sticker with a specific colour containing the code number was pasted. During the follow up visits after 28 weeks of gestation; participants were identified by using this sticker and code number.

Data was entered into an Excel 2010 data sheet by the principal investigator. Data was analysed by SPSS 25:0 statistical software. Initially a univariate analysis was conducted and for selected variables a bivariate analysis was done. Pearson's correlation co efficient was applied to determine the associations of continuous variables. Receiver Operative Characteristic curve was applied to determine the predictive ability of selected exposure variables. 95% confidence interval 0.05 probability cut off was used for statistical

significance. All statistical tests used will be two-sided. A receiver operating characteristic (ROC) curve analysis will be used to define the cutoff value. Pearson's correlation coefficient (r) will be used for determine the associations between continuous variables.

RESULTS

All collected data was taken for the analysis. Anthropometric measurements were described by using measures of central tendency. Outcome variables were categorised according to standard guidelines. Because of all predictive variables are in continuous scale, Receiver Operative Characteristic curve (ROC) was applied to obtain predictability. 95% confidence interval and 0.05 probability cut off value were applied for statistical significance. Mean value of the height of the participants was 153.33cm and the mean of the weight of the participants was 51.87 kg. Body mass index ranged from 12.98 to 37.55 (mean 24.05). Mean value of the waist circumference was 69.58 cm and the mean of hip circumference was 82.82cm. Subcutaneous fat thickness ranged from 2.3 mm to 61mm. main exposure variable of the study was the visceral fat thickness and it varied in a range from 1mm to 21 mm its mean value was 8.64 mm (SD=3.72)(Table 1).

Table 1 Distribution of anthropometric measurement of study participants

	Minimum	Maximum	Mean	SD
Height (mm)	130.00	180.00	153.33	6.26
Weight(kg)	30.00	101.00	51.87	11.97
BMI(kg/m^2)	12.98	37.55	22.05	4.82
WC(cm)	50.00	100.00	69.58	9.26
HC(cm)	55.00	120.00	82.82	11.05
Subcutaneous fat (mm)	2.30	61.00	15.40	6.04
Visceral Fat(mm)	1.10	21.0	8.64	3.72

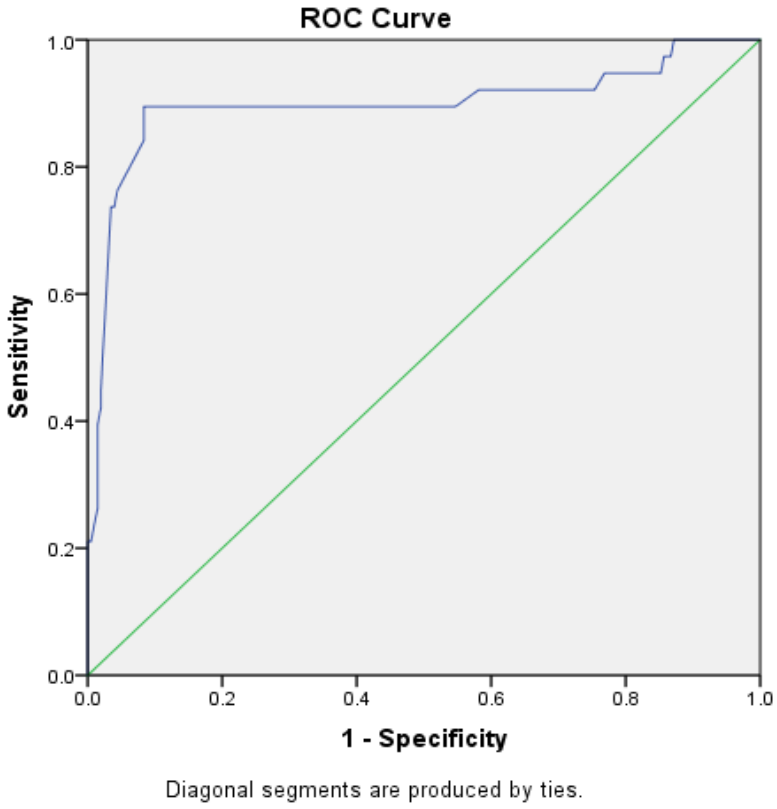
All the anthropometric parameters show a significantly positive correlation between the visceral fat thickness measurements. Among them, highest Pearson's correlation coefficient was shown by the visceral fat thickness and the body weight. A Minimum Pearson's correlation coefficient was depicted between the visceral fat thickness and the height of the participants. Mean value of PPBS was 112.43 mg/dl and the mean value of the FBS was 87.01mg/dl. OGTT values of the first hour ranged from 75mg/dl to 212.4 mg/dl and the OGTT values of the second hour were included into a ranged from 65mg/dl to 181.7 mg/dl (Table 3).

Table 3 : Distribution of blood sugar values among participants

Blood Sugar values	Minimum	Maximum	Mean	SD
PPBS	60.5	196.0	112.43	18.16
FBS	62.0	120.0	87.01	9.1
OGTT -1st hour	75.0	212.4	156.32	25.9
OGTT-2nd hour	65.0	181.7	123.93	20.72

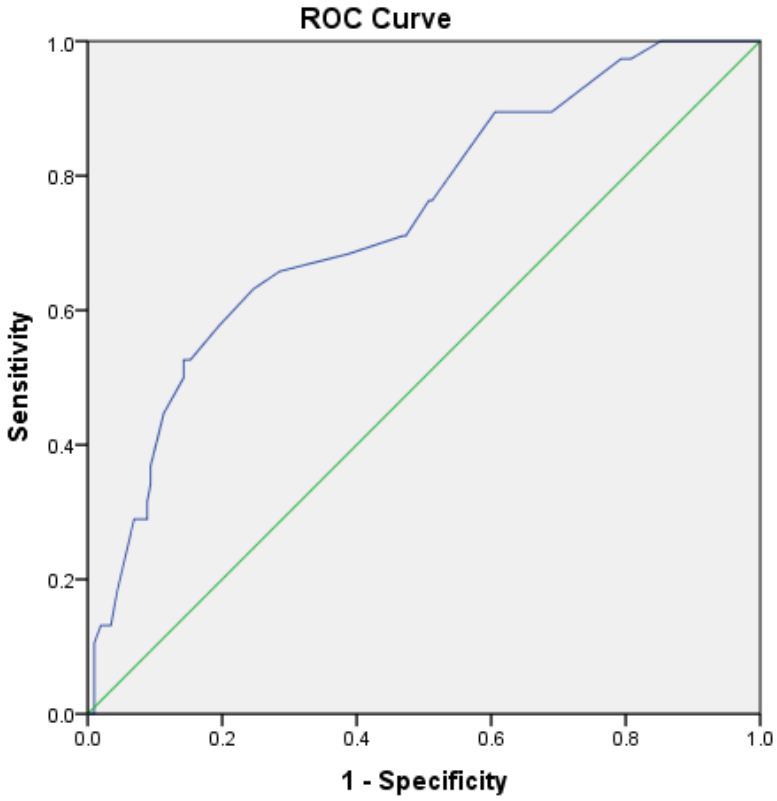
Based on the ROC curve, calculation of providing true positive predictions with relevance to false positive results was done. According to the findings of this study, there is a significant ability of predicting GDM by using the visceral fat thickness measurements (AUC=0.898;95% CI=0.823-0.973). At this, the left uppermost value of the ROC curve can be considered as 11.75mm. Therefore, when the visceral fat thickness is more than 11.75mm, occurrence of GDM during the third trimester can be predicted with an 84.2% sensitivity and a 91.6% specificity (Figure 1).

Figure 1 : Prediction of GDM by visceral fat thickness-ROC



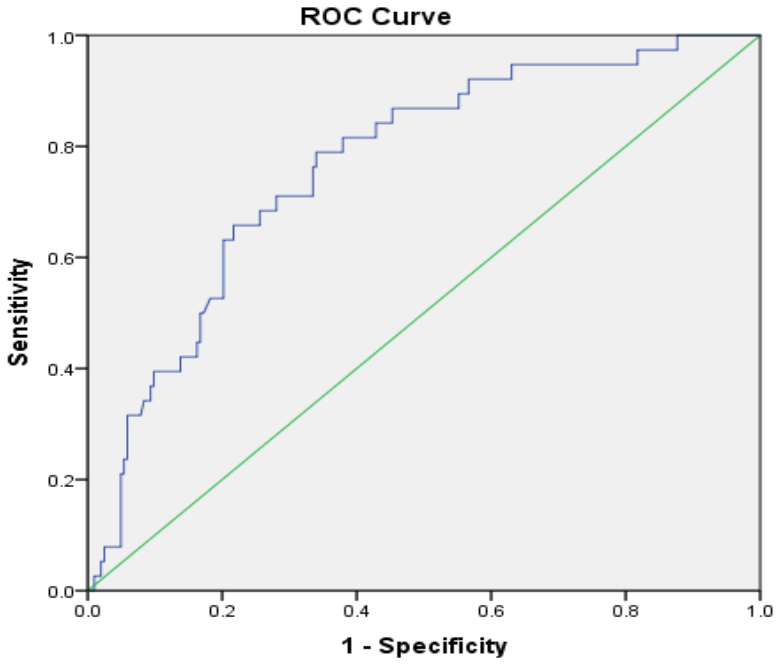
Based on the ROC curve, calculation of providing true positive predictions with relevance to false positive results was done. According to the findings of this study, there is a significant ability of predicting GDM by using the subcutaneous fat thickness measurements (AUC=0.733;95% CI=0.642-0.823). At this, the left uppermost value of the ROC curve can be considered as 12.5mm. Therefore, when the subcutaneous fat thickness is more than 12.5mm, occurrence of GDM during the third trimester can be predicted with an 89.2 % sensitivity and a 39.8% specificity (Figure 2).

Figure 2 : Prediction of GDM by subcutaneous fat thickness-ROC



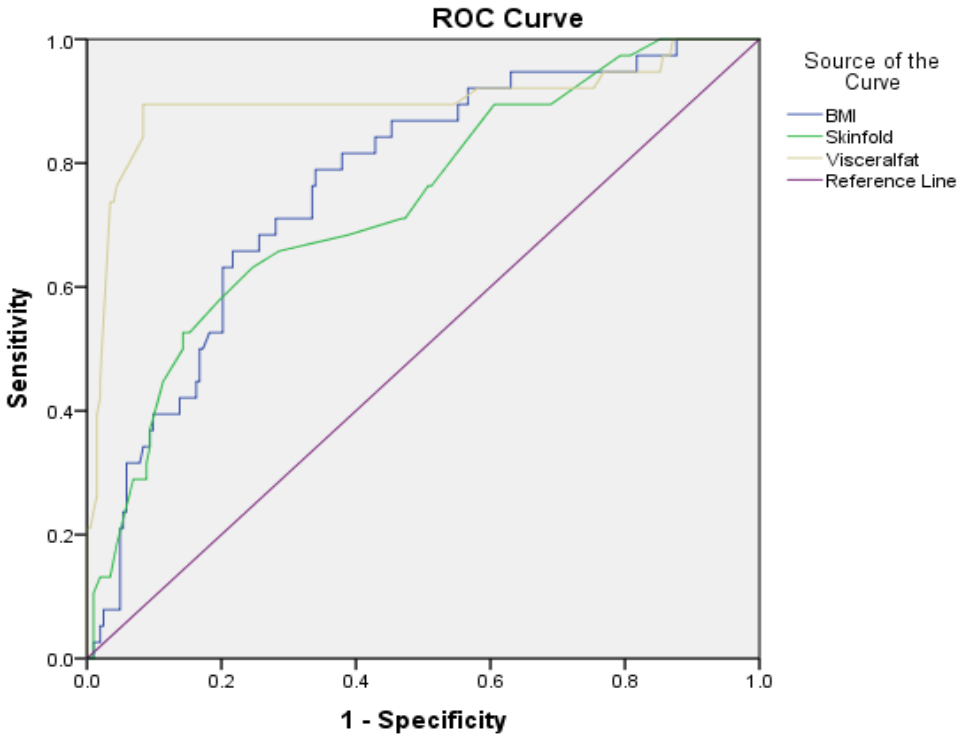
Based on the ROC curve, calculation of providing true positive predictions with relevance to false positive results was done. According to the findings of this study, there is a significant ability of predicting GDM by using the Body Mass Index measurements (AUC=0.735; 95% CI=0.639-0.806). At this, the left uppermost value of the ROC curve can be considered as 21.73kg/m^2. Therefore, when the Body Mass Index is more than 21.73kg/m^2, occurrence of GDM during the third trimester can be predicted with an 81.1 % sensitivity and a 61.8% specificity (Figure 3).

Figure 3 : Prediction of GDM by Body Mass Index-ROC



Body Mass Index, Subcutaneous fat thickness and the visceral fat thickness show significant predictive abilities (AUC>0.5) when true positives against false positive predictions are considered. But a maximum area under curve is shown by the visceral fat thickness (Figure 4).

Figure 4 : ROC curves for all anthropometric measurements



Same cut off value is considered with relevance to visceral fat thickness for diagnosing GDM according to the HAPO guideline which is used around the world and the SLCOG guideline which is used in Sri Lanka. But the sensitivity and the specificity values achieved with the SLCOG guidelines appear higher (Table 4).

Table 4: Summary of cut off values- for visceral fat thickness

	Cut off	Sensitivity	Specificity
HAPO			
Overall values	11.75	81.1	90.7
FBS Only	11.75	84.4	89.9
OGTT 1st hour only	12.8	86.2	95.3
OGTT 2nd hour only	12.8	84.6	89.5
SLCOG			
Overall values	11.75	84.2	91.6
FBS Only	12.8	80.0	89.8
OGTT 1st hour only	12.8	86.2	95.3
OGTT 2nd hour only	12.25	81.5	92.5

DISCUSSION

Although prevalence of GDM is relatively less at present, its prevalence is expected to increase with the existing lifestyle and dietary modifications. Although reported GDM associated mortality is less, obstetrics and perinatal complications can occur due to GDM. Adverse outcomes of probable complications can be minimised by early detection and implication of primary prevention activities. Nowadays, both GDM prediction and confirmation are done by blood sugar measurements. There are many practical difficulties of obtaining most accurate blood sugar measurements such as need of a fasting period before taking blood samples and overlapping with meals. On the other hand, blood sugar measuring procedures are not popular among most of the patients. Therefore, there is a practical need of non-invasive screening procedures which are easy to apply and less expensive in order to predict GDM.

According to the current study findings, there is a possibility of predicting GDM by using the maternal anthropometric measurements taken during the early stage of pregnancy. There is a possibility of identifying 88% of high-risk pregnancies for developing GDM by using the visceral fat measurements. As it is a measurement taken by ultrasonography it does not produce the discomfort of drawing blood and the measurement value is available at the time of performing the examination. As there is a routine booking visit during the first trimester in which a dating scan is essentially done, special arrangements are not required to obtain visceral fat measurements. Therefore, taking ultrasonographic visceral fat measurements appears to be relatively cost effective as additional time and resources are not required.

As other anthropometric measurements also have shown favourable results for GDM prediction, a GDM prediction criteria with higher sensitivity can be developed by combining several parameters. A specially trained health care specialist's service is essential to obtain ultrasonographic visceral fat measurements. A consultant radiologist's service is rarely taken at the routine set up to do first trimester obstetrics ultrasound scanning. Therefore, ultrasonographic measurements can be taken at the maternity unit itself and in the current study, measurements were taken by the principal investigator himself after a short training period. Present study findings can be used to conduct further extensive studies to predict GDM by combining many parameters with visceral fat measurements such as subcutaneous fat thickness, waist hip circumference and BMI and pay attention on updating the national obstetric guidelines as well.

Special nutritional and lifestyle modification programmes can be conducted targeting the high-risk pregnant mothers identified by the visceral fat measurement method. It helps to reduce adverse perinatal maternal outcomes and maternal obstetric complications. This intervention is extremely important in achieving the sustainable development goal of reducing neonatal mortality rate. It is possible to observe that the results of the study done in Turkey in 2014 overlapped with the results of the presents study (21). In that study a strong positive correlation was identified between subcutaneous and visceral fat thickness and a poor correlation was identified between body mass index and the waist circumference. A significantly positive correlation is identified between visceral and subcutaneous fat thickness in the present study as well. In that study, visceral fat thickness cut off value to predict GDM was taken as 19.5 mm. And in the present study 11.77 mm was calculated as the cut off value. Cut off value for BMI in the present study was 21.76 kgm^2, but in the previous study the value was as high as 34.5kgm2. However anthropometric changes of the general population should be expected between a country such as Turkey which has a Mediterranean climate and a country such as Sri Lanka which experiences a tropical climate. According to the data published by Bartha et al in 2007, variations of plasma glucose levels can be predicted by visceral fat estimation (22). In that study special attention was paid not only on plasma glucose levels, but also on blood pressure, serum cholesterol and insulin resistance. But the present study was focused only on blood sugar level.

CONCLUSIONS

Anthropometric measurements which are measured at the early gestational ages can be satisfactorily used for predicting gestational Diabetes Mellitus. But visceral fat thickness is the most suitable measurement for obtaining an accurate prediction. Primordial and primary prevention activities for GDM can be implemented by the findings of visceral fat thickness measurements.

By frequent and periodical monitoring delaying the onset of GDM and minimizing harmful obstetric complications can be achieved. More extensive and methodical research studies should be planned in the future to decide on predictive values with a higher accuracy. According to the findings of these studies, an opportunity of including the concept "visceral fat thickness for GDM prediction" to the obstetric management guidelines can be acquired.

REFERENCES

1. Diabetes G. Gestational Diabetes Burden Report. 2013;1–20.
2. Turok DK, Ratcliffe SD, Baxley EG. Management of gestational diabetes mellitus. Am Fam Physician. 2003 Nov;68(9):1767–72.
3. Bhavadharini B, Mahalakshmi MM, Anjana RM, Maheswari K, Uma R, Deepa M, et al. Prevalence of Gestational Diabetes Mellitus in urban and rural Tamil Nadu using IADPSG and WHO 1999 criteria (WINGS 6). Clin diabetes Endocrinol. 2016;2:8.
4. Siribaddana SH, Deshabandu R, Rajapakse D, Silva K, Fernando DJ. The prevalence of gestational diabetes in a Sri Lankan antenatal clinic. Ceylon Med J. 1998 Jun;43(2):88–91.
5. Dahanayaka NJ, Agampodi SB, Ranasinghe OR, Jayaweera PM, Wickramasinghe WA, Adhikari AN, et al. Inadequacy of the risk factor based approach to detect gestational diabetes mellitus. Ceylon Med J [Internet]. 2012 Mar;57(1):5—9. Available from: https://doi.org/10.4038/cmj.v57i1.4193
6. Chasan-Taber L, Schmidt MD, Pekow P, Sternfeld B, Manson JE, Solomon CG, et al. Physical activity and gestational diabetes mellitus among Hispanic women. J Womens Health (Larchmt). 2008;17(6):999–1008.
7. Reece EA. The fetal and maternal consequences of gestational diabetes mellitus. J Matern Fetal Neonatal Med. 2010 Mar;23(3):199–203.
8. Hedderson MM, Gunderson EP, Ferrara A. Gestational weight gain and risk of gestational diabetes mellitus. Obstet Gynecol. 2010 Mar;115(3):597–604.
9. Chu SY, Callaghan WM, Kim SY, Schmid CH, Lau J, England LJ, et al. Maternal obesity and risk of gestational diabetes mellitus. Diabetes Care. 2007 Aug;30(8):2070–6.
10. M C. Effects of gestational weight gain and body mass index on obstetric outcome in Sweden. Int J Obs Gynecol. 2006;93:269–74.

11. Fain JN, Madan AK, Hiler ML, Cheema P, Bahouth SW. Comparison of the release of adipokines by adipose tissue, adipose tissue matrix, and adipocytes from visceral and subcutaneous abdominal adipose tissues of obese humans. Endocrinology. 2004 May;145(5):2273–82.
12. Minocci A, Savia G, Lucantoni R, Berselli ME, Tagliaferri M, Calo G, et al. Leptin plasma concentrations are dependent on body fat distribution in obese patients. Int J Obes Relat Metab Disord. 2000 Sep;24(9):1139–44.
13. Roberts JM, Bodnar LM, Patrick TE, Powers RW. The Role of Obesity in Preeclampsia. Pregnancy Hypertens. 2011 Jan;1(1):6–16.
14. Chatzi L, Plana E, Daraki V, Karakosta P, Alegkakis D, Tsatsanis C, et al. Metabolic syndrome in early pregnancy and risk of preterm birth. Am J Epidemiol. 2009 Oct;170(7):829–36.
15. Butte NF. Carbohydrate and lipid metabolism in pregnancy: normal compared with gestational diabetes mellitus. Am J Clin Nutr. 2000 May;71(5 Suppl):1256S-61S.
16. Neeland IJ, Turer AT, Ayers CR, Powell-Wiley TM, Vega GL, Farzaneh-Far R, et al. Dysfunctional adiposity and the risk of prediabetes and type 2 diabetes in obese adults. JAMA. 2012 Sep;308(11):1150–9.
17. Nishida C, Borghi E, Branca F, Onis M De. Global trends in overweight and obesity. 2014;(May):1–8.
18. Chu S, WM C, Kim S, Schmid C, Lau J, England L, et al. Maternal Obesity and Risk of Gestational Diabetes Mellitus. Diabetes Care. 2007;30(8):2070–6.
19. Rooney BL, Schauberger CW. Excess Pregnancy Weight Gain and Long-Term Obesity : One Decade Later. 2002;100(2):245–52.
20. Nanda S, Savvidou M, Syngelaki A, Akolekar R, Nicolaides KH. Prediction of gestational diabetes mellitus by maternal factors and biomarkers at 11 to 13 weeks. Prenat Diagn. 2011 Feb;31(2):135–41.
21. 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;47(2):478–84.
22. Bartha JL, Marín-Segura P, González-González NL, Wagner F, Aguilar-Diosdado M, Hervias-Vivancos B. Ultrasound evaluation of visceral fat and metabolic risk factors during early pregnancy. Obesity (Silver Spring) [Internet]. 2007;15(9):2233–9. Available from: http://www.ncbi.nlm.nih.gov/pubmed/17890491
23. Nassr AA, Shazly SA, Trinindad MC, El-Nashar SA, Marroquin AM, Brost BC. Utility of ultrasound measurement of maternal visceral and parietal fat for prediction of gestational diabetes. Am J Obstet Gynecol [Internet]. 2016;214(1):S90–1. Available from: http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L72164330%5Cnhttp://resolver.ebscohost.com/openurl?sid=EMBASE&issn=00029378&id=doi:&atitle=Utility+of+ultrasound+measurement+of+maternal+visceral+and+parietal+fat+for+prediction+of+g
24. 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):478–84.
25. Hirooka M, Kumagi T, Kurose K, Nakanishi S, Michitaka K, Matsuura B, et al. A technique for the measurement of visceral fat by ultrasonography: comparison of measurements by ultrasonography and computed tomography. Intern Med. 2005

Aug;44(8):794–9.
26. Wladmiroff J E-NS. Ultrasound in Obstetrics and Gynecology. 1st ed. Elsivier, editor. 2009. chapter 6.
27. WHO. Waist Circumference and Waist-Hip Ratio: Report of a WHO Expert Consultation. World Heal Organ. 2008;(December):8–11.