

# Prediction of Gestational Diabetes Mellitus By Different Obesity Indices

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## Research Article

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# Abstract

**Background:** The incidence rate of obesity and gestational diabetes mellitus (GDM) is increasing in parallel. This study aimed to evaluate the relationship between different obesity indices including pre-pregnancy body mass index (preBMI), the first trimester abdominal circumference (AC), the first trimester abdominal circumference/height ratio (ACHtR) and GDM, and the efficacy of these three indices in predicting GDM.

**Methods:** A total of 15472 pregnant women gave birth to a single child at the Obstetrics and Gynecology Hospital of Fudan University, Shanghai, China. Weight before pregnancy, height and AC were asked and measured at the first prenatal examination at 11-13<sup>6</sup> gestational weeks. GDM was diagnosed through a 75g oral glucose tolerance test at 24-28 gestational weeks. Using receiver operator characteristic (ROC) curve analysis, we evaluated the association between the obesity indices and GDM.

**Results:** Multivariate logistic regression analysis showed that AC, the ACHtR and preBMI  $P < 0.001$  were all independent risk factors for the development of GDM. In the normal BMI population, the higher the AC or the ACHtR, the more likely the pregnant women were to suffer from GDM. The area under the ROC curve (AUC) was 0.63 (95% CI 0.62-0.64) for AC, 0.64 (95% CI 0.63-0.65) for the ACHtR and 0.63 (95% CI 0.62-0.64) for preBMI. An AC  $\geq 80.25$ cm (sensitivity 61.6%, specificity 57.9%), an ACHtR of  $\geq 0.49$  (sensitivity 67.3%, specificity 54%), and a preBMI  $\geq 22.74$  (sensitivity 48.4%, specificity 71.8%) were determined to be the best cut-off levels for identifying subjects with GDM.

**Conclusions:** AC, the ACHtR and preBMI had value in predicting GDM. The increase in AC and the ACHtR in the first trimester of pregnancy and preBMI could be independent risk factors for GDM. Even in the normal BMI population, the higher the AC is, the more likely the pregnant women are to suffer from GDM.

## Background

Gestational diabetes mellitus (GDM) is the first occurrence or discovery of abnormal glucose metabolism during pregnancy. It is a carbohydrate-intolerant state and one of the fastest growing pregnancy complications. The cause of the disease is complex [1]. Obesity is an independent high-risk factor for GDM [2, 3]. The incidence of GDM in China is as high as 17.5% [2]. Obese pregnant women are more likely to have GDM, preeclampsia, gestational hypertension, depression, instrument deliveries and caesarean sections, as well as surgical site infections. GDM is also related to the risk of premature delivery, large for gestational age infants, foetal defects and perinatal death. From 1993 to 2009, the overweight and obesity rates of Chinese women increased to 10.4% and 10.1%, respectively, showing a significant growth trend [4]. The definition of obesity in pregnancy has not been standardized. On the one hand, due to physiological changes during pregnancy, a woman's weight increases significantly in a relatively short period of time, and most of the weight gains (the foetus, amniotic fluid, blood, etc.) in pregnancy immediately decreases after delivery; on the other hand, due to different regions and ethnic groups, there are differences in the diagnostic standards of obesity. Therefore, it is often used to define whether

pregnant women are obese according to their body mass index (BMI) before pregnancy. Based on the differences in weight between the Chinese population and Western population, according to the recommendation of the Chinese adult body mass index classification published by the China Obesity Working Group in 2001, mothers are categorized into four groups: low weight (BMI <18.5), normal weight ( $18.5 \leq \text{BMI} < 24$ ), overweight ( $24 \leq \text{BMI} < 28$ ) and obese (BMI  $\geq 28$ ) [5]. However, the evaluation of obesity during pregnancy using BMI has certain limitations. It cannot distinguish whether body weight comes from fat, muscle or other components and cannot accurately reflect the fat content and fat distribution of the human body, which is of great significance for clinical evaluation. Therefore, in addition to BMI, other indicators of obesity, such as the waist circumference, neck circumference, waist height ratio, waist hip ratio, and body fat ratio, are also used to evaluate and predict the occurrence of GDM. Different obesity indicators are different in measuring and predicting gestational diabetes [6, 7]. According to the current research evidence, the incidence rate of obesity and GDM is rising in parallel. It is meaningful to explore the relationship between obesity and GDM. The international guidelines on gestational diabetes or gestational obesity are mostly based on Western race characteristics, considering the race, regional environment, and environment in China. The differences between lifestyle and diet and other regions, along with the trend of economic development and the increasing obesity and GDM incidence caused by the creation of the two-child policy, result in the need to better prevent and manage gestational obesity and gestational diabetes mellitus through large data research based on the Chinese population

## Methods

### Study population

The Human Research Ethics Committee of the Obstetrics and Gynecology Hospital of Fudan University approved this retrospective study. The data were collected from the Obstetrics and Gynecology Hospital of Fudan University from January 1, 2017, to June 30, 2019. A total of 15472 singleton pregnant women with complete prenatal care services and delivery in this hospital had data available for analysis. Patients with pregestational diabetes mellitus, severe medical complications and tumors were excluded.

### Clinical Characteristics

All of the data were extracted from medical charts and the Hospital Information System. Clinical characteristics (including age, gravidity, parity and weight) were registered by self-report and measured at the first prenatal visit at 11-13<sup>+6</sup> gestational weeks and delivery data were recorded in the electronic medical record system.

### Anthropometric Measurements

All participants underwent a physical examination at 11-13<sup>+6</sup> gestational weeks. Body weight was registered by self-report, height was measured, and BMI was calculated by the weight (kg) divided by height (m<sup>2</sup>). BMI was divided into four groups according to the recommendation of the Chinese adult body mass index classification published by the China Obesity Working Group in 2001. Before the measurement of abdominal circumference (AC), the pregnant women emptied their bladders, lay on their backs, and straightened their legs, and a soft ruler was used to measure the length of the abdomen at the navel level for one circle. The minimum circumference was recorded to the nearest 0.1 cm. Two trained physicians who had completed a training program obtained the anthropometric measurements and the abdominal circumference/height ratio (ACHtR) was calculated by abdominal circumference (m) divided by height(m).

The pregnant women were assigned to one of three groups according to the AC quartiles (low-AC, Q1 [AC <74cm, *n* =3270], normal-AC, Q2/Q3 [74 cm ≤ AC ≤ 86 cm, *n* = 8687] and high-AC, Q4 [AC > 86 cm, *n* = 3515]) or ACHtR quartiles (low ACHtR, Q1 [ACHtR <0.46, *n* =3985], normal ACHtR, Q2/Q3 [0.46 ≤ ACHtR ≤ 0.53, *n* = 7776] and high ACHtR, Q4 [ACHtR >0.53, *n* = 3711]). The low AC or ACHtR group was defined as the participants in Q1, the normal AC or ACHtR group was defined as those in Q2 and Q3, and the high AC or ACHtR group was defined as those in Q4. Because the normal range of AC or ACHtR has not yet been established, the cut-off value of AC or ACHtR was not clearly defined.

## Gdm Diagnosis

All subjects returned to the hospital between 24 and 28 weeks of gestation and underwent a 75g oral glucose tolerance test (75g OGTT) as a standard practice in our institution. 75g OGTT was defined as the gold standard of GDM diagnosis, and the diagnosis criteria were based on the International Association of Diabetes and Pregnancy Study Groups (IADPSG) that any 1 or more of the following values equaling or exceeding the thresholds ( FPG:5.1mmol/L, 1-h plasma glucose:10.00 mmol/L and 2-h plasma glucose:8.50 mmol/L)[8]. Subjects were divided into the GDM group (*n*=1912) or the control group (*n*=13560)

## Statistical analysis

All analyses were performed using SPSS for Windows version 24.0 (SPSS Inc., Chicago, IL, USA) with statistical significance set at 2-sided *p* < 0.05, continuous variables are presented as the mean (SD) and skewed variables are described as the median (interquartile range). We use student's *t* test for independent samples which were normally distributed continuous variables and the Chi squared ( $\chi^2$ ) test was used for categorical variables. Receiver operator characteristic (ROC) curve analysis was performed to evaluate the ability of the ACHtR, AC and preBMI in predicting GDM, and the Youden index formula, equivalent to the maximum sum of the sensitivity and specificity for all possible values of the cut-off point, which was defined as  $J = \text{sensitivity} + \text{specificity} - 1$ [9]. Multivariate logistic regression analysis

was carried out to explore the independent factors associated with GDM (the backwards method) and the odds ratios (ORs) with 95% confidence intervals (CIs) of different obesity indices.

## Results

Our study included 15472 women, with 1912 women with GDM and 13560 women without GDM. The clinical characteristics of the participants are shown in Table 1. The GDM group was older, presented greater gravidity and parity, and delivered earlier ( $P < 0.001$ ). The mean AC (84.2 vs. 80.2 cm) ACHtR (0.52 vs. 0.50) and preBMI (22.9 vs. 21.5 kg/m<sup>2</sup>) were higher in the GDM group than in the control group ( $P < 0.001$ ). However, neonatal birth weight and the postpartum haemorrhage were similar in the 2 groups ( $P > 0.05$ ).

Multivariate logistic regression analysis (Table 2) showed that in the normal BMI population ( $n=10382$ ), the risk of GDM increased with increasing AC. The risk of GDM in the high AC group was 1.5 times than that in the normal AC group (OR = 1.50; 95% CI, 1.26-1.80), and the risk of GDM in the low AC group was 0.52 times than that in the normal AC group (OR = 0.52; 95% CI, 0.43-0.65); The results of the ACHtR were similar. The incidence risk of GDM in the high ACHtR group was 1.5 times higher than that in the normal group (OR = 1.54; 95% CI, 1.31-1.83), while the incidence risk of GDM in the low ACHtR group was 0.5 times than that in the normal ACHtR group (OR = 0.48; 95% CI, 0.40-0.58).

The ROC curve determined the ability of the ACHtR, AC and preBMI to identify GDM. The AUCs were 0.64 (95% CI 0.63-0.65) for the ACHtR, 0.63 (95% CI 0.62-0.64) for AC, and 0.63 (95% CI 0.62-0.64) for preBMI (Fig. 1).

The results showed that the ACHtR and AC were similar to preBMI and had the value in predicting GDM.

The optimal cut-off point was the point on the ROC curve closest to the (0, 1) point. An AC of 80.25 cm yielded the highest combination of sensitivity (61.6%) and specificity (57.9%), and an ACHtR of 0.49 (sensitivity 67.3% and specificity 54%), and a preBMI of 22.74 yielded the highest combination of sensitivity (48.4%) and specificity (71.8%) (Table 3).

Multivariate logistic regression analysis showed that, considering confounders in early gestation (including the ACHtR, maternal age, parity and height), the ACHtR, age and parity were independent risk factors for GDM development.

The incidence risk of GDM in the high ACHtR group was 1.7 times higher than that in the normal group (OR = 1.70; 95% CI, 1.53-1.89), while the incidence risk of GDM in the low ACHtR group was 0.6 times than that in the normal ACHtR group (OR = 0.55; 95% CI, 0.48-0.64). The same multivariate logistic regression analysis was applied to the AC and preBMI, the risk of GDM in the high AC group was 1.7 times than that in the normal AC group (OR = 1.73; 95% CI, 1.55-1.93), and the risk of GDM in the low AC group was 0.6 times than that in the normal AC group (OR = 0.57; 95% CI, 0.48-0.66); The results of the preBMI were similar. The incidence risk of GDM in the obese group was 3.1 times higher than that in the normal weight

group (OR = 3.08; 95% CI, 2.55-3.72), while the incidence risk of GDM in the low weight group was 0.8 times than that in the normal weight group (OR = 0.82; 95% CI, 0.69-0.98) and the incidence risk of GDM in the overweight group was 1.9 times than that in the normal weight group (OR = 1.88; 95% CI, 1.67-2.12) (Table 4).

## Discussion

With the development of the economy and the improvement of national living standards, the incidence rates of GDM and obesity are increasing year by year. BMI before pregnancy, weight gain at different stages of pregnancy, and gestational weight gain are clearly associated with adverse pregnancy outcomes [10]. Previous studies have shown that an increase in maternal obesity (BMI and other obesity-related indicators) increases the risk of GDM. The increase in BMI before pregnancy is linearly related to the incidence rate of GDM, the probability of occurrence of GDM increased by 0.92% after a 1 kg/m<sup>2</sup> increase in BMI, and obese older women (BMI > 23 and age > 35) were more likely to be attacked by GDM [3, 11, 12]. The average annual weight gain between 20 and 24 years old more than 1.5% with a BMI within the range is also an important risk factor for GDM [13]. An increase in body weight  $\geq 2.5$  kg/year before the 5 years of being pregnant may increase the risk of GDM by 2.5 times [14]. With a previous pregnancy with a normal BMI and a second pregnancy with a BMI of obese, the risk of gestational diabetes increased by 3 times, and weight loss during the two pregnancies could reduce the risk of gestational diabetes mellitus [15]. In addition to BMI, other obesity evaluation indices are also used to evaluate and predict the occurrence of GDM. The increase in neck circumference in early pregnancy may be one of the independent risk factors for GDM. When NC  $\geq 33.8$  cm in early pregnancy, the incidence of GDM increased significantly [16, 17]. Abdominal subcutaneous fat thickness (ASFT) was measured by ultrasound at 10<sup>+6</sup> to 13<sup>+6</sup> weeks of gestation, if the ASFT is  $\geq 2.4$  cm, it can be used to predict the risk and prognosis of GDM in middle and late pregnancy [18]. Visceral adipose tissue thickness (VAT) and total adipose tissue thickness (TAT) by ultrasonography in early pregnancy can independently predict the risk of abnormal blood glucose in late pregnancy: with the increase in VAT and TAT, the incidence of diabetes increases [19].

In our present study, we demonstrated that AC and the ACHtR in the first trimester could be used as novel indicators to predict GDM. Obesity, especially abdominal obesity (AO), has been considered a risk factor for diabetic complications. Abdominal obesity may be defined as excess deposits of fat in the abdominal region. It is positively related to noncommunicable diseases, such as cardiovascular diseases, diabetes, hypertension, cancer, kidney diseases and nonalcoholic fatty liver disease, the latest guidelines for South Asians define AO as large waist circumference (WC)  $\geq 90$  cm in men and  $\geq 80$  cm in women independent of BMI [20]. According to a recent study, the waist-to-height ratio (WHtR) is better than WC in predicting AO [21]. However, pregnant women generally do not have waist circumference measured during pregnancy but abdominal circumference is measured to accurately estimate the size of the foetus. Therefore, we used abdominal circumference and the abdominal circumference/height ratio to evaluate the pregnant women's abdominal obesity. Our research suggests that pregnant women with a higher AC

or ACHtR and normal BMI also have a higher risk of GDM, which shows that even in women with a normal BMI, the prevalence of GDM is higher in individuals with abdominal obesity. The diagnostic accuracy of AC and the ACHtR in the first trimester for predicting GDM was similar to that of preBMI. An AC of 80.25 cm and ACHtR of 0.49 might be the optimal cut-off points for predicting GDM. Whether AC and the ACHtR are correlated with GDM remains unclear, and studies are lacking. In this study, the AUC was 0.63 for AC and 0.64 for the ACHtR in predicting GDM, and this was better than the traditional predictor of a preBMI of 0.63 in predicting GDM. Because abdominal circumference and height are objective data measured by doctors, they are more objective measures than that when pregnant women recall their weight before pregnancy and can avoid memory errors or subjective errors. In fact, some women cannot accurately state their pre-pregnancy weight.

The optimal cut-off point of an AC of 80.25 cm yielded the highest combination of sensitivity and specificity; an ACHtR of 0.49 and a preBMI of 22.74 indicated that AC and the ACHtR might be a good anthropometric index to screen for GDM. However, different studies may report different sensitivities and specificities at different cut-off points, possibly due to different study populations, gestational weeks and ethnicities. A recent study supported that the optimal cut-off level of maternal WC in the first trimester of pregnancy was >84.50 cm with a sensitivity of 78% and a specificity of 54%. Another study found that WC can predict GDM in the range of 86-88 cm at 20-24 weeks of gestation[22]. Larger sample studies and multicentre studies are needed to determine the optimal cut-off value for AC and the ACHtR to predict GDM.

There were also some limitations in our study. On the one hand, this study was a single-centre study in Shanghai, China, which may have affected the results and restrict the application of the study conclusions. Further study needs to be conducted to confirm our findings. On the other hand, all subjects were asked to retrospectively report their weight prior to pregnancy, which were used to calculate preBMI. As the study began after delivery, It is difficult to obtain the accurate measurements of pre-pregnancy weight.

## Conclusion

In this study, we found that AC, the ACHtR in the first trimester and preBMI might be new anthropometric indices for predicting GDM. An increase in AC and the ACHtR may be an independent risk factor for GDM in the first trimester of pregnancy. Even in the normal BMI population, the higher the AC and ACHtR are, the more likely a pregnant woman is to suffer from GDM.

## Abbreviations

GDM: gestational diabetes mellitus; preBMI: pre-pregnancy body mass index; AC: abdominal circumference; ACHtR: abdominal circumference/height ratio; ROC: receiver operator characteristic curve analysis; AUC: area under the curve; AO: abdominal obesity; WC: waist circumference; NC: neck

circumference; VAT: visceral adipose tissue thickness; TAT: total adipose tissue thickness; ASFT: abdominal subcutaneous fat thickness.

## **Declarations**

### **Ethics approval and consent to participate**

All procedures in this study were approved by the Human Research Ethics Committee of the Obstetrics and Gynecology Hospital, Fudan University [2015] (grant no. 41). All methods were performed in accordance with the approved guidelines and regulations. All participants gave written informed consent.

### **Consent for publication**

Not applicable.

### **Availability of data and materials**

The datasets generated and/or analysed during the current study are not publicly available due patient privacy but are available from the corresponding author on reasonable request.

### **Competing interests**

The authors declare that they have no competing interests.

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### **Authors' contributions**

HDC and QYZ designed the study. ZMS supervised the laboratory exams and data collection. ZMS and YFF analysed and interpreted the data. ZMS and YC wrote the first draft of the paper. HDC and QYZ edited the paper. All authors contributed to the writing of the paper. All authors read and approved the manuscript.

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## Tables

Table 1. Characteristics of the GDM group and Control group\*

	GDM n=1912	Control n=13560	P
Age (years)	32.0±4.1	30.5±3.8	0.001
PreBMI (kg/m <sup>2</sup> )	22.9±3.6	21.5±3.0	0.001
< 18.5	17.6±0.7	17.6±0.7	0.59
≥18.5 to <24	21.0±1.5	21.4±1.5	0.001
≥ 24 to < 28	25.7±1.1	25.5±1.1	0.001
≥ 28	30.5±2.3	30.0±1.9	0.008
AC Quartile (cm)	84.2±9.4	80.2±8.8	0.001
Q1	70.2±2.7	70.0±2.6	0.45
Q2/Q3	80.3±3.6	79.4±3.6	0.001
Q4	94.3±6.4	93.6±6.2	0.009
ACHtR Quartile (cm/cm)	0.52±0.06	0.50±0.05	0.001
Q1	0.44±0.02	0.44±0.02	0.15
Q2/Q3	0.50±0.02	0.49±0.02	0.001
Q4	0.58±0.04	0.58±0.04	0.09
Parity(%)			0.001
Primiparous	1349(70.6)	10277(75.8)	
Multiparous	563(29.4)	3283(24.2)	
Gravidity(%)			0.001
Primigravid	846(44.2)	7224(53.3)	
Multigravid	1066(55.8)	6336(46.7)	
Gestational week of delivery	38.6±1.5	38.9±1.5	0.001
Neonatal birth weight (kg)	3.32±0.49	3.34±0.45	0.09
Postpartum hemorrhage	53(2.8%)	312(2.3%)	0.12

\*Values are mean (SD) or medians (interquartile ranges). BMI were divided into four groups: low weight (BMI < 18.5), normal weight (18.5 ≤ BMI < 24), overweight (24 ≤ BMI < 28) and obese (BMI ≥ 28). AC were divided into three groups according to the quartile: Q1, low-AC group (< 74 cm); Q2/Q3, normal-AC group (74-86 cm); Q4, high-AC group (> 86 cm).

86cm); Q4, high-AC group(≥86cm); ACHtR were divided into three groups according to the quartile (Q1, Low- ACHtR group(≤0.46);Q2/Q3, Normal-ACHtR group(0.46-0.53); Q4, High-ACHtR group(≥0.53)).

Table 2 The relative risk of GDM in normal BMI(n=10792) between different AC and ACHtR groups\*

		OR(95%CI)	P
AC(cm)	Normal-AC(74-86)	1	0.001
	Low-AC(≤74)	0.52(0.43-0.65)	0.001
	High-AC(≥86)	1.50(1.26-1.80)	0.001
ACHtR	Normal-ACHtR(0.46-0.53)	1	0.001
	Low- ACHtR(≤0.46)	0.48(0.40-0.58)	0.001
	High-ACHtR(≥0.53)	1.54(1.31-1.83)	0.001

\*OR, odds ratio AC were divided into three groups according to the quartile Q1, low-AC group(≤74cm);Q2/Q3, normal-AC group(74-86cm); Q4, high-AC group(≥86cm);

ACHtR were divided into three groups according to the quartile (Q1, Low- ACHtR group(≤0.46);Q2/Q3, Normal-ACHtR group(0.46-0.53); Q4, High-ACHtR group(≥0.53)).

Table3. ACHtR, AC, PreBMI as predictors for gestational diabetes mellitus

	cut-off point	sensitivity	specificity	Youden index
preBMI	22.74	48.4%	71.8%	0.202
AC(cm)	80.25	61.6%	57.9%	0.195
ACHtR	0.49	67.3%	54%	0.213

\* Youden index formula is defined as  $J = \text{sensitivity} + \text{specificity} - 1$

Table 4. Multiple logistic regression analysis ACHtR or AC or preBMI, and maternal age, parity,height as confounders of gestational diabetes mellitus\*

Items	B	Wald	OR[95CI%]	P-value
Normal-ACHtR		218.91	1	<0.001
Low- ACHtR	-0.59	63.18	0.55(0.48-0.64)	<0.001
High-ACHtR	0.53	92.70	1.70[1.53-1.89]	<0.001
Age (years)	0.81	144.39	1.08[1.07-1.10]	<0.001
Parity	-0.11	4.09	0.90(0.80-0.99)	0.043
Normal-AC		196.84	1	<0.001
Low-AC	-0.57	50.91	0.57(0.48-0.66)	<0.001
High-AC	0.55	99.79	1.73(1.55-1.93)	<0.001
Age (years)	0.08	148.42	1.09[1.07-1.10]	<0.001
Parity	-0.11	3.73	0.90[0.81-1.00]	0.053
Height	-0.02	8.73	0.99[0.98-1.00]	0.003
normal weight		232.62	1	<0.001
low weight	-0.19	4.86	0.82(0.69-0.98)	0.027
overweight	0.63	106.69	1.88(1.67-2.12)	<0.001
obese	1.13	136.16	3.08(2.55-3.72)	<0.001
Age (years)	0.08	188.67	1.09(1.08-1.10)	<0.001

\* Backward method was used [B, beta coefficient; CI, confidence interval; OR, odds ratio]

## Figures

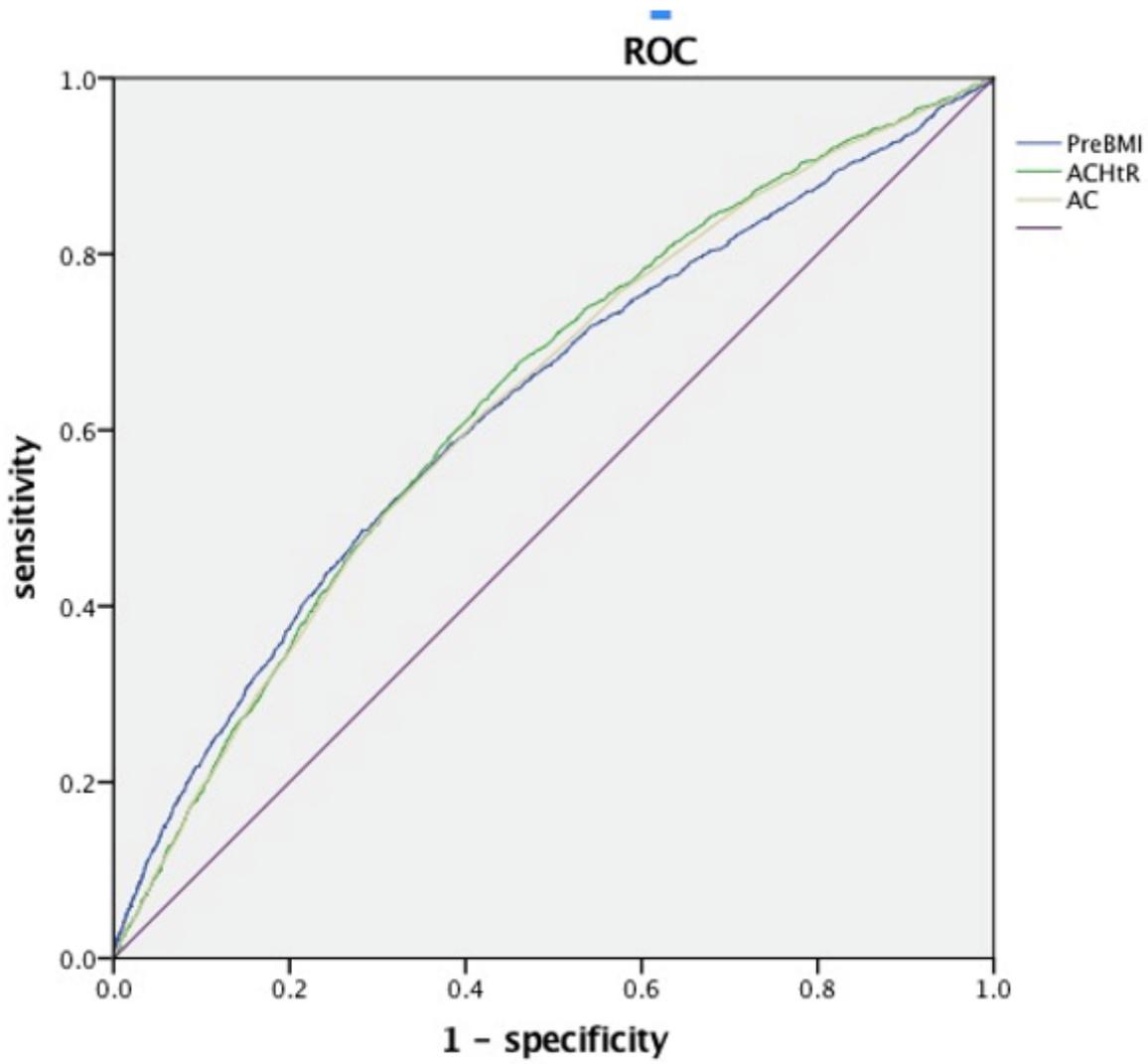


Figure 1

ROC curves for determining ACHtR,AC and preBMI cutoff values for identifying GDM