

ISFHAC as a novel predictor of macrosomia in gestational diabetes mellitus and normal pregnancy

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Abstract

Background Macrosomia is a major adverse pregnancy outcome of gestational diabetes mellitus (GDM). Although BMI, symphysis-fundal height (SFH) and abdominal circumference (AC) are associated with fetal weight, there are some limitations to their use, especially for the prediction of macrosomia. This study aimed to identify a novel predictive methodology to improve the prediction of high-risk macrosomia. Methods Clinical information was collected from 3730 patients. The association between the ISFHAC (the index of SFH algorithm multiplied by the square of AC) and fetal weight was performed and validated. A new index, the ISFHAC, was evaluated by area under the curve (AUC) analysis. Results A total of 1087 GDM and 657 normal singleton pregnancies were analyzed. ISFHAC was positively correlated with fetal weight in GDM pregnancies and normal pregnancies (NPs). The AUCs of the ISFHAC were 0.815 in the GDM group and 0.804 in the NP group. The ISFHAC cutoff points were 41.7 and 37 in the GDM and NP groups, respectively. The sensitivity values for the prediction of macrosomia with high ISFHAC were 75.9% and 81.3% in the GDM and NP groups, respectively, which were higher than that for the prediction of BMI. Regarding the validation data, the sensitivity values for prediction with a high ISFHAC were 78.9% (559 GDM pregnancies) and 78.3% (1427 NPs). Conclusions The ISFHAC can be regarded as a new predictor and risk factor for macrosomia in GDM pregnancy and NP.

Introduction

The increasing prevalence of overweight/obesity during pregnancy has increased the risk of adverse pregnancy outcomes by increasing the prevalence of GDM. Gestational diabetes mellitus (GDM) is defined as glucose intolerance that is first diagnosed during pregnancy [1]. Women with GDM have high levels of blood sugar and IGF. In the relatively long period of pregnancy, fetuses are in a state of rapid growth with high levels of nourishment, especially in middle and late pregnancy. Nutritional counseling and exercise intervention are suitable noninvasive therapeutic options that can be readily applied to manage weight gain and improve the pregnancy outcomes of women with GDM [2–6]. The incidence of fetal macrosomia and cesarean delivery is also significantly higher for GDM pregnancies [7]. Fetal macrosomia, defined as a birth weight $\geq 4,000$ g, affects 12% of newborns from non-GDM pregnancies and 15–45% of newborns from GDM pregnancies [8–9]. Thus, in the context of GDM, fetal growth assessment is an important part of antenatal care. BMI, obesity and waist circumference are the conventional risk factors for pregnancy outcomes. B-ultrasonography, the symphysis-fundal height (SFH) chart and abdominal circumference (AC) measurements are monitoring approaches that are used routinely in departments of obstetrics and gynecology. Several studies have revealed that BMI, obesity, SFH and AC are associated with fetal weight, and these parameters are commonly used to predict fetal size and select a safe delivery method [10–12]. However, BMI, SFH and AC are not powerful enough for the diagnosis of macrosomia. The aim of this study was to develop a new index to predict macrosomia. The index of symphysis-fundal height and abdominal circumference (ISFHAC) combines SFH and AC, which are used to evaluate fetal birth weight, and this index has great potential for use in predicting macrosomia in normal pregnancies (NPs) and GDM pregnancies.

Materials And Methods

Study design

The cross-sectional study was conducted from 2013–2016 at the Department of Obstetrics and Gynecology in Zhongnan Hospital of Wuhan University. All participants provided informed written consent prior to taking part. This process, together with all other aspects of the study, was approved by the Research Ethics Committee of Wuhan University. Women ≥ 16 years of age and with a singleton pregnancy with or without GDM were randomized to either standard antenatal care or physical activity and dietary behavioral intervention superimposed on standard antenatal care[13]. The patients were divided into two sets. One set was used to analyze the relationship between several clinical parameters and macrosomia and comprised 1744 patients with complete data. The other set was used to validate the results derived from the first set. The validation set comprised data from another 1986 patients. (Fig. 1)

Participants

Patients were enrolled according to the diagnostic criteria for GDM of WHO 2013 [14]. All pregnant women received a 75-g OGTT between 24 and 28 weeks. Two individuals were excluded: one had a hypertensive disorder of pregnancy and other diseases and the other had a complication of diabetes mellitus (DM) during pregnancy.

Procedures

Data on characteristics including medical and family history of DM and pregnancy-related information, such as gestational age (GA), age, parity, prepertum height and weight, mode of delivery, SFH, AC, and fetal birth weight were collected for each study group. The validation set was mainly missing prepertum BMI data, but the other clinical data were sufficient.

GA was confirmed by means of the specific last menstrual period (LMP) or B-ultrasonography. Infant weight was measured by an obstetrician or midwife after delivery.

SFH was measured from the superior border symphysis to the highest uterine fundus. AC was defined as the length of the navel round belly. We assumed that a pregnant woman's belly was cylindrical, obtained the height and perimeter, and multiplied height by the square of the perimeter to determine the volume. We examined our proposed method, namely, the ISFHAC, a new index with the algorithm of SFH (cm) multiplied by the square of AC (m), for its ability to serve as a means to predict fetal birth weight with GDM.

First, logistic regression was used to analyze the relationship between macrosomia and the data parameters. Then, ROC curve analysis was carried out with the ISFHAC and macrosomia. We determined the cutoff points for NP and GDM pregnancy. To verify the predictiveness of the ISFHAC for macrosomia, the ISFHAC was applied in the analysis set (1744) and the validation set (1986).

Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics version 20.0. For measurement data, an independent-sample t-test was used. Afterward, ROC curve analysis was performed with the ISFHAC and macrosomia. We determined the ISFHAC of the correct index (sensitivity- (1-specificity)) with the maximal value. To compare the effect of the predictive value of BMI for macrosomia, we examined the effect of its prediction of macrosomia in the NP and GDM groups in the analysis cohort. Sensitivity, specificity and accuracy were determined in the analysis.

Validation of the prediction model

To further evaluate the predictive effect of the ISFHAC for macrosomia, data from another 1986 additional patients were used for the clinical trial evaluation. Sensitivity, specificity and accuracy were estimated.

Results

Study characteristics

A total of 1744 participants (1087 GDM and 657 controls) with complete clinical data were screened for analysis (Fig. 1). According to the data we collected, the ages of the participants ranged from 16 to 54, and women with GDM were older than women in the control group. The mean prenatal BMI in the GDM group was higher than that in the control group. Obesity in the GDM group was 3.27-fold that in the control group, while the number of patients with normal weight in the control group was 2.53-fold that in the GDM group. There were statistically significant differences in BMI categories between the control and GDM groups. The ratio of multiparas with GDM was 2.17-fold that of multiparas in the NP group, and the family history of DM was higher in the GDM group than in the control group. The percentage of cesarean sections was 75.6% in the GDM group, which was higher than that in the control group (69.9%) (Table 1).

Table 1
Characteristics of NP and GDM pregnancy groups.

	NP (N = 657)	GDM (N = 1087)	P-value
Mean (SD) age at delivery (y)	28.86 (3.96)	29.62 (4.76)	P = 0.001 ^a
Mean (SD) gestational weeks (w)	38.81 (1.80)	38.91 (1.22)	P = 0.175 ^a
Women with BMI			
Mean (SD) BMI (kg/m ²)	26.36 (3.04)	29.1 (3.95)	P < 0.0001 ^a
Pregnancy BMI categories (%)			P < 0.0001 ^b
≥ 18.5&< 25	213 (32.4%)	139 (12.8%)	
≥ 25&<30	358 (56%)	536 (49.3%)	
≥ 30	76 (11.6%)	412 (37.9%)	
Parity (%)			P < 0.0001 ^b
Nulliparous	535 (81.4%)	649 (59.7%)	
Parous	122 (18.6%)	438 (40.3%)	
Family history (%)			P < 0.0001 ^b
No DM	646 (98.3%)	954 (87.8%)	
With DM	11 (1.7%)	133 (12.2%)	
Mode of delivery (%)			P = 0.009 ^b
Vaginal	195 (30.1%)	266 (24.4%)	
Cesarean section	453 (69.9%)	824 (75.6%)	

GDM, gestational diabetes mellitus; BMI, body mass index. Regarding pregnancy BMI categories, ≥ 18.5&< 25 means normal weight; ≥25&<30 means overweight; ≥30 means obesity. Regarding gestational weeks, < 37 means premature birth; ≥37&<42 means mature birth; ≥42 means postterm birth. ^a p values were calculated using the independent sample T-test, and ^b p values were calculated using the chi-square test.

ISFHAC is a novel potential predictor for macrosomia

To evaluate the effect of the ISFHAC in predicting the risk of macrosomia, ROC curve analysis was performed on the data for analysis and evaluation (Fig. 2). The area under the curve (AUC) of the ISFHAC was larger (area = 0.803, p < 0.0001) in the control group, and the AUC of the ISFHAC was larger (area = 0.815, p < 0.0001) in GDM. We determined the cutoff points of the different groups (Table 2). The ISFHAC value was higher in the GDM group than in the control group.

Table 2
ROC curve analysis of the utility of clinical parameters for predicting macrosomia

	GDM		NP	
	Area	P-value ^a	Area	P-value ^a
ISFHAC	0.815	< 0.001	0.803	< 0.001
SFH	0.804	< 0.001	0.767	< 0.001
AC	0.753	< 0.001	0.744	< 0.001
BMI	0.707	< 0.001	0.651	< 0.001
GA	0.540	0.07	0.640	< 0.001

^a p values were calculated by ROC curve analysis.

The cutoff points for the ISFHAC in the NP and GDM groups were 37 and 41.7, respectively. The ISFHAC values were divided into three categories according to BMI. Of note, in the GDM and NP groups, 41.7 and 37, respectively, were the lower bounds for the ISFHAC according to obesity (Supplementary Table 1).

ISFHAC can predict macrosomia in GDM pregnancy and NP

Moreover, there were 208 and 64 cases of macrosomia in the GDM (1087, 19.1%) and NP (657, 9.7%) groups, respectively; the rate of macrosomia in the GDM group was 2-fold that in the NP group. Samples were divided into high- and low-ISFHAC groups according to the following cutoff points: less than 41.7 as the low index group and greater than 41.7 as the high index group in the GDM group and less than 37 as the low index group and greater than 37 as the high index group in the NP group. We further predicted macrosomia in our study. The cutoff point was 41.7 in the GDM group, with a sensitivity of 75.9%, specificity of 72.9%, and accuracy of 73.5%. The cutoff point was 37 in the NP group, with a sensitivity of 81.3%, specificity of 66.4%, and accuracy of 67.9% (Table 3). A high ISFHAC value could predict 75.9% of macrosomia cases, but with BMI, the prediction for macrosomia was only 60.1% in the GDM group. In the NP group, the high ISFHAC and BMI prediction values were 81.3% and 25%, respectively (Table 3).

Table 3
Macrosomia with ISFHAC and BMI analysis

	GDM (N = 1087)		NP (N = 657)	
	Macrosomia (n = 208)	Normal (n = 879)	Macrosomia (n = 64)	Normal (n = 593)
ISFHAC	158 (75.9%)	238 (27.1%)	52 (81.3%)	199 (33.6%)
BMI ≥ 30	125 (60.1%)	287 (32.7%)	16 (25%)	60 (10.1%)

Validation results

To evaluate the predictive power of the ISFHAC, 559 (GDM pregnancy) and 1427 (NP) women were screened for validation and used for the clinical trial evaluation. A high ISFHAC value could predict macrosomia in the NP group with a sensitivity of 78.9%, specificity of 71.3%, and accuracy of 72.1%. In the GDM group, the sensitivity was 78.3%, specificity was 82.8%, and accuracy was 82.3% (Table 4).

Table 4
The validation of ISFHAC for predicting macrosomia in the GDM pregnancy and NP groups

	GDM (N = 559)		NP (N = 1427)	
	Macrosomia (n = 60)	Normal (n = 499)	Macrosomia (n = 147)	Normal (n = 1280)
ISFHAC	47 (78.3%)	86 (17.2%)	116 (78.9%)	367 (28.7%)
ISFHAC 41.7<	13 (21.7%)	413 (82.8%)	31 (21.1%)	913 (71.3%)

Discussion

In recent decades, China has witnessed rapid lifestyle and socioeconomic changes characterized by changes in dietary intake and decreased physical activity [15]. The report released in China shows that 148.2 million people, comprising 72.1 million female patients, have prediabetes. Among women between the ages of 20 and 39 years, approximately 5.6 million have DM (3.2%) and 15 million have prediabetes (9%) [16]. Prediabetes is defined as impaired glucose tolerance and/or abnormal fasting glucose levels.

The dramatic increase in GDM can be attributed to parity and age. In our study, the average maternal age in the GDM group was 29.6 years, which was markedly higher than that in the control NP group. The percentage of multiparas in the GDM group was 40.3%, which was obviously higher than that in the control group. Moreover, patients of advanced maternal age were prone to GDM, and the GDM group has a higher percentage of multiparas.

Regarding the specific eating habits of Chinese people and the lack of sufficient exercise during pregnancy, obesity in the GDM group (37.9%) was 3.27-fold that in the NP group (11.6%) (Table 1). A previous study revealed that normal weight accounted for most NPs [17]. In this study, however, 56% and 49.3% of the patients in the NP and GDM groups, respectively, were overweight.

A higher BMI, AC, and fasting glucose in the first trimester of pregnancy increased GDM risk [18]. Excessive gestational weight gain, according to the targets set by the Institute of Medicine (IOM), was associated with cesarean section, LGA and macrosomia. Modification of the IOM criteria, including more restrictive

targets, did not improve perinatal outcomes [19]. Our results confirm that obesity in pregnancy can lead to adverse pregnancy outcomes. There was a high percentage of obesity in the GDM group, and the rate of macrosomia in the GDM group was 1.96-fold that of the control group.

In a previous study, the incidence of fetal macrosomia (the main outcome) was significantly higher in the GDM group (20.0%) than in the control group (3.6%) [20]. In our research, fetal macrosomia was observed in 9.7% of women in the control group and 19.1% of women with GDM.

SFH and AC are used in obstetrical departments and are two routine measurements. They have clinical significance for predicting infant size and as a reflection of the pregnant woman's nutritional status for reference. The SFH chart shows high performance in predicting both SGA and LGA newborns of DM-2, GDM and MGH mothers. These findings support the internal validation of the SFH chart, which may be implemented in the prenatal care of patients with diabetes and pregnancy [12]. The SFH measurement is primarily practiced to detect fetal intrauterine growth restriction (IUGR). Undiagnosed IUGR may lead to fetal death, as well as increased perinatal mortality and morbidity [21].

To our knowledge, this is the first time that the notion of combining SFH and AC to calculate the ISFHAC was put forth as a new indicator of pregnancy outcome.

Regarding the AUCs of different parameters, the AOC for the ISFHAC is the largest among the NP and GDM groups. Thus, we think that the relationship between the ISFHAC and macrosomia is relevant. In this study, the cutoff points for the ISFHAC are 37 and 41.7 in the control and GDM groups, respectively; women in the high bin of the index were prone to adverse pregnancy outcomes. Interestingly, 41.7 was the lower bound of the ISFHAC, which is in accordance with obesity in GDM, and 37 was the lower bound of the ISFHAC in the control group, which is also in accordance with obesity.

We were interested in the high index group. Here, the high ISFHAC predicted (75.9%) most of the macrosomia cases in the GDM group, and this rate was higher than that of the obesity-based grouping (60.1%).

In the NP group, the high ISFHAC predict 81.3% of macrosomia cases, and obesity predicted 25% of macrosomia. The high ISFHAC prediction ability for macrosomia was better than that of the obesity-based grouping.

In another validation dataset, the high ISFHAC predicted most of the macrosomia cases in the NP and GDM groups. High ISFHAC was a risk factor for macrosomia.

All measures used should aim to prevent excessive SFH and AC, and the high ISFHAC group needs exercise or dietary intervention. Chinese GDM prevention and treatment programs should target overweight and obese adults with central obesity. Interpregnancy SFH and AC control is an important target to reduce the risk of an adverse perinatal outcome in a subsequent pregnancy.

Further studies are needed to determine whether the ISFHAC can predict fetal weight in different GA groups. We hope to provide the ISFHAC chart using the index at different GAs to predict fetal weight.

Abbreviations

ISFHAC:the index of SFH algorithm multiplied by the square of AC; GDM:Gestational diabetes mellitus; DM:Diabetes mellitus; BMI:Body mass index; OGTT:Oral glucose tolerance test; WHO:World Health Organization; AC:Abdominal circumference; SFH:Symphysis-fundal height; IUGR:intrauterine growth restriction; GA:gestational age; AUC:area under the curve.

Declarations

Acknowledgments

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Author Contributions

LW and ZGC: study design and revision of the manuscript. YTX, ZGC and HYH: data analysis and draft of the manuscript. ZGC, YTX, LLJ, XJC, RL, XLZ, CW, YLW and HYH: follow-up patient's information. All authors read and approved the final manuscript.

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Competing Interests

The authors have declared that no competing interests exist.

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Figures

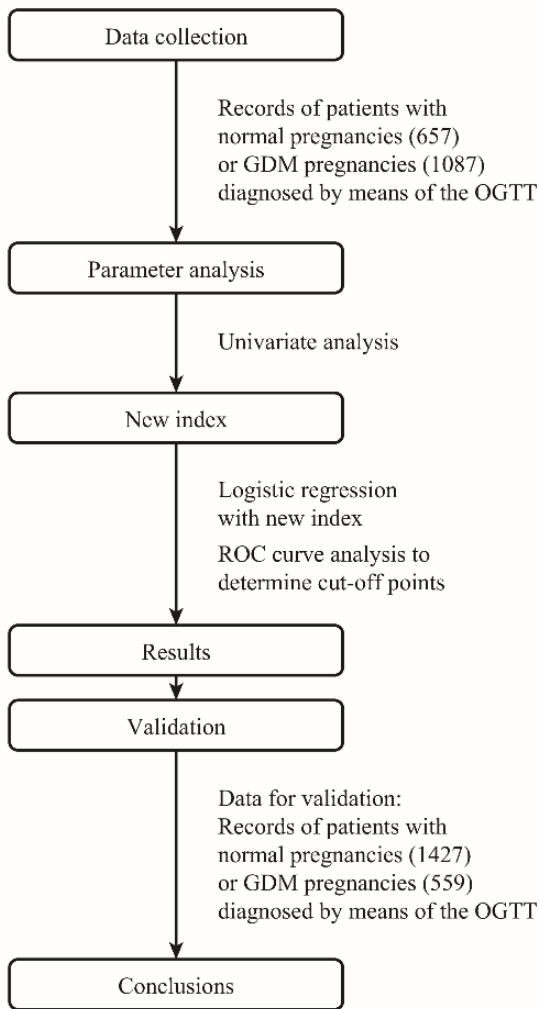


Figure 1

A total of 1744 participants (1087 GDM and 657 controls) with complete clinical data were screened for analysis.

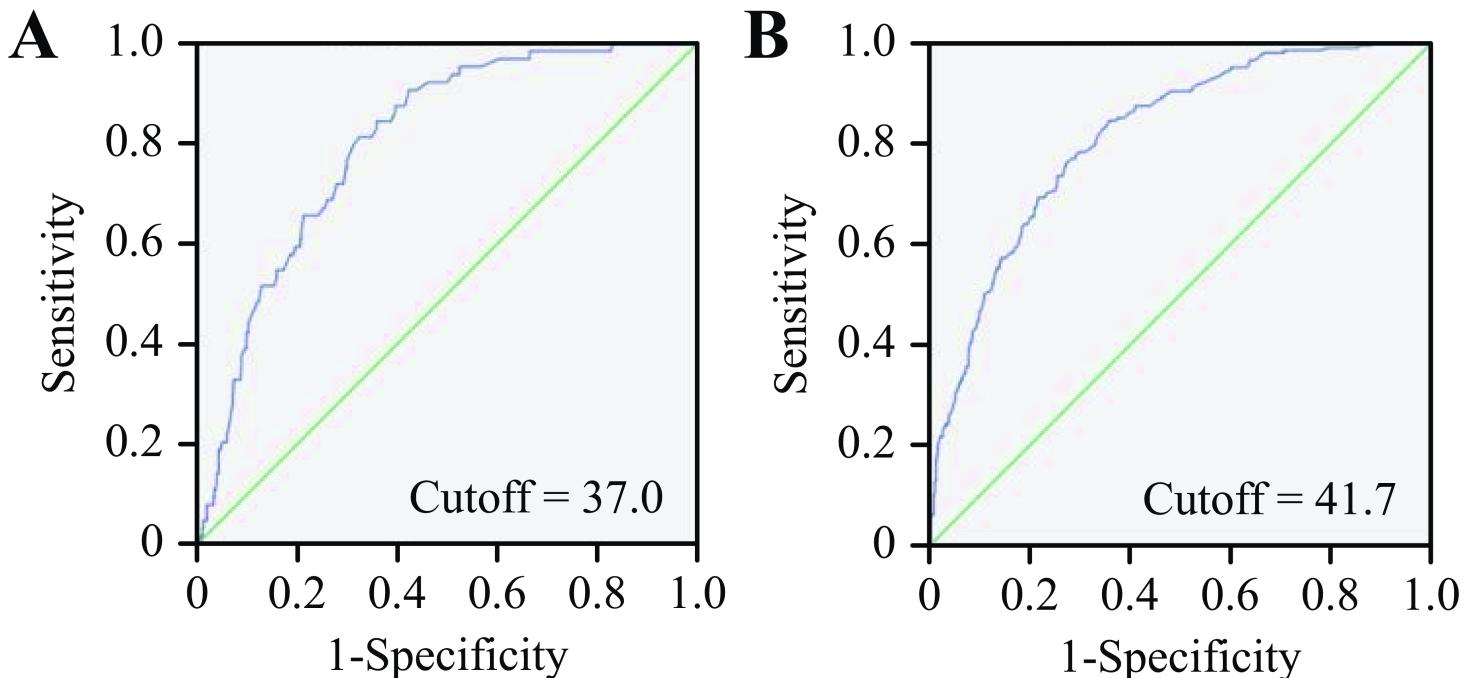


Figure 2

To evaluate the effect of the ISFHAC in predicting the risk of macrosomia, ROC curve analysis was performed on the data for analysis and evaluation. The area under the curve (AUC) of the ISFHAC was larger (area = 0.803, p < 0.0001) in the control group, and the AUC of the ISFHAC was larger (area = 0.815, p < 0.0001) in GDM.

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