



# Maternal Fasting Plasma Glucose, Age and Body Mass Index as Prediction of Gestational Diabetes Mellitus in Iran

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## Abstract

**Background:** Gestational diabetes mellitus (GDM) is a common complication of pregnancy that can lead to adverse outcomes. In this retrospective cohort study, maternal fasting blood sugar (FBS) in the second trimester of pregnancy, body mass index (BMI), and age were assessed as potential screening indicators of later GDM.

**Methods:** The study population included information on 4007 Iranian pregnant women documented by the Integrated Health Record System (SIB) record system (2019-2020).

**Results:** In the adjusted analysis, FBS maintained a significant relationship with GDM ( $P \leq 0.001$ ). In the simple ROC analysis, the AUC (SE) of FBS for the prediction of GDM was 0.905(0.09), and considering the cut-off point as 85.95, sensitivity (Se) and specificity (Sp) were equal to 0.81 and 0.71, respectively, but by stillbirth, abortion, prematurity, neonatal weight, height, and head circumference not obtained acceptable AUC ( $\geq 0.60$ ) for detection of FBS cut-off point. The cut-off point of FBS in the presence of maternal age (AUC $>0.6$ ) and BMI (AUC $>0.6$ ) by GDM was 83.75(Se= 86.4%, Sp= 80.0%).

**Conclusion:** Based on the evidence presented, maternal weight and BMI are important in predicting hyperglycemia leading to GDM. It is necessary to conduct more precise national studies to standardize the FBS cut-off point by controlling age and BMI variables.

**Keywords:** Gestational diabetes mellitus; Fasting blood sugar; Body mass index; Birth weight; ROC curve

## Introduction

Pregnancy is a critical period in a woman's life, during which the health and well-being of both the mother and the developing fetus are of utmost importance. Maternal glucose levels play a

significant role in determining birth outcomes and can have long-lasting implications for the health of the child (1, 2). Globally, hyperglycemia in pregnancy and gestational diabetes prevalence



are increasing (1). According to the International Diabetes Federation (IDF), 16.9% of pregnancies globally are affected by hyperglycemia in pregnancy duration; this proportion was reported as 19% in Iran (1). It is not only women diagnosed with GDM who are at risk; even mild glucose intolerance or high normal glucose levels can impact birth outcomes (2). The mechanisms through which maternal glucose levels influence birth outcomes are multifaceted. Elevated glucose levels can lead to fetal hyperinsulinemia, stimulating excessive growth and resulting in macrosomia (3). Additionally, high glucose levels can impair placental function, leading to inadequate nutrient and oxygen supply to the fetus, thereby increasing the risk of intrauterine growth restriction (4). Moreover, maternal hyperglycemia can contribute to oxidative stress and inflammation, further compromising fetal development (5), cesarean section, and infant macrosomia (1). There is no cut-off point of maternal glucose levels for predictions of maternal and fetus outcomes and the investigation and determination of the blood sugar cut-off point in the Iranian women community can lead to timely screening and diagnosis, correct and optimal care, and plan health and treatment.

Body mass index (BMI) and age are two crucial factors that determine insulin resistance in individuals. Understanding the factors that contribute the most to the current rise in GDM rates among pregnant women can help in developing effective prevention and intervention strategies, especially in areas where this female endocrine disorder is prevalent. Therefore, it is essential to control their effects while determining the maternal glucose cut-off point for predicting gestational diabetes (6-8).

While several studies have examined the association between maternal glucose levels and birth outcomes, conflicting results have been reported. Some studies have found a clear relationship between elevated maternal glucose levels and adverse birth outcomes, while others have failed to demonstrate significant associations. These discrepancies may be attributed to variations in study design, population characteristics, diagnos-

tic criteria for GDM, and differences in the management of glucose levels during pregnancy (2, 9-14).

Various review and meta-analysis studies have explored the link between gestational diabetes, and maternal and neonatal outcomes (15-19). However, research into the relationship between hyperglycemia and maternal-neonatal outcomes, as well as determining the threshold for it, is limited. In a meta-analysis on up 207 000 women, there is a direct relationship between glucose concentration and a wide range of clinically significant perinatal complications, and this association remains consistent without any specific threshold limit for high-income countries. However, for low and middle-income countries, they suggest that further research is necessary to understand the nature of the relationship between gestational glucose and perinatal outcomes. They believe that conducting studies in low and middle-income countries is crucial for gaining a better understanding of this topic (20).

This original research paper aims to investigate the association between maternal glucose levels during pregnancy and birth outcomes in a large population as well as the determination of blood glucose level cut-off points for prediction of outcomes. The findings from this study have the potential to inform clinical practice guidelines and interventions aimed at optimizing maternal glucose control during pregnancy. Ultimately, by identifying modifiable risk factors and implementing appropriate interventions, we can strive to improve birth outcomes and reduce the long-term health risks associated with maternal hyperglycemia.

## **Methods**

This study was a retrospective cohort study. We used the Integrated Health Record System (SIB) dataset (Sep 2019, Mar 2020) (21), SIB is one of the most important information systems for recording public health information in the Iranian population (21).

The study utilized convenience sampling to select eligible research units whose pregnancy and childbirth information were recorded in the integrated system (SIB) and met the criteria for entering the study. Overall, 4007 people were included in the study after being fully registered in the SIB system and meeting the inclusion criteria. This was a census study, encompassing all eligible mothers.

The inclusion and exclusion criteria for the study are as follows: 1) Pregnant women aged 18 to 40 yr, 2) Iranian race, 3) Not using blood glucose-lowering medications, 4) No smoking and alcohol consumption, 5) Not taking neuropsychiatric drugs, 6) Not having diabetes and other related diseases, 7) Availability of mothers and infants information.

In this retrospective cohort study, the medical and demographic information documented by the SIB record system was used for comparison. These variables included: blood glucose levels in the second trimester of pregnancy (24-28 wk of pregnancy), the mother's demographic-clinical factors, and delivery details (including, education status, BMI, gestational diabetes mellitus (GDM), preterm birth) and neonatal outcomes (stillbirth, and spontaneous abortion) as well as neonatal anthropometric indices. Low birth weight (LBW) was defined as a neonatal birth weight <2500 g and premature birth was defined as a baby born between 28 and 37 gestational weeks.

Data are reported as mean and standard deviations (SD) or frequency (proportions). Continuous data was analyzed for normality using the Shapiro-Wilk test of normality. Logistic regression was used for further analysis. The ROC curve was used to estimate the accuracy of FBS (in the presence of maternal BMI and age) in the second trimester by neonatal-maternal outcomes including GDM, stillbirth, abortion, prematurity, weight, height, and head circumference. The data was analyzed with SPSS-27 software (IBM, Ar-

monk, NY, USA) and a  $P$ -value of  $\leq 0.05$  was considered significant.

### *Ethical Approval*

This article was the result of a research project approved by the Tehran university of medical sciences (code: 99-3-152-50691) and the Ethics Committee (code: IR.TUMS.IKHC.REC.1399.440)

### **Results**

Of the 4007 pregnant women were included in this study, the average (SD) age of pregnancy was 29.5 (5.9) yr, the average (SD) BMI in early pregnancy was 24.76 (5.04), and mean (SD) fasting blood sugar (FBS) in the second trimester was 80.20(10.84) (Table 1). Participant characteristics with full details are accessed in Table 1.

Prevalence of GDM was 16.0% (571 patients). Considering GDM, prematurity, neonatal weight, height and head circumference as dependent variables, univariate and multiple logistic regressions was executed on FBS (in the second trimester) for each of them. Effect of maternal age, BMI and educational status was controlled. Neonatal height (B (SE)=0.005(0.005);  $P=0.30$ ) and prematurity (B (SE)=-0.006(0.004);  $P=0.20$ ) did not have association with maternal FBS in the univariate logistic regression and did not have the condition to enter the multiple model ( $P<0.2$ ). As shown as Table 2, association between neonatal weight and FBS was not maintained in the adjusted logistic regression in the presence of maternal BMI ( $P=0.051$ ). Moreover, head circumference didn't significant relationship with FBS in the presence of maternal age and BMI ( $P=0.408$ ). FBS in the adjusted regression analysis had statistically significant relationship with GDM in the presence of age and BMI ( $P\leq 0.001$ ).

**Table 1:** Maternal characteristics of study participants

<i>Variables</i>	<i>cofactors</i>	<i>n (%)</i>	<i>Variables</i>	<i>cofactors</i>	<i>n (%)</i>
Mother age; (yr)	Mean(SD)	29.5(5.9)	The interval between pregnancies; (yr)	≤2	981(24.52)
				>2	3019(75.47)
Mother age; (yr)	16-18	190(48.9)	Parity	0	2133(53.2)
	18.1-30.0	1094(27.3)		1	1122(28.0)
	30.1-35	910(22.7)		2	461(11.5)
	≥35.1	43(1.1)		≥3	290(7.2)
Residence	Urban& suburban	2215(55.3)	Abortion number	0	3060(76.4)
	Rural& nomads	1792(44.7)		1	745(18.6)
Education status	Illiterate	227(5.84)		2	153(3.8)
	High school diploma college degree	2986(76.83)	≥3	49(1.2)	
Gravidity	1	2464(63.33)	BMI ( at early pregnancy)	mean(SD)	24.76(5.04)
	2	609(16.88)	Weight (at early pregnancy)	mean(SD)	62.75(12.85)
	>2	533(14.78)	Weight (at the second trimester)	mean(SD)	70.54(13.84)
Amniotic fluid	Normal	2774(97.95)	Weight (gain at pregnancy)	mean(SD)	7.75(6.68)
	Polyhydramnios	34(1.2)	FBS (second trimester)	mean(SD)	80.20(10.84)
	Oligohydramnios	24(0.84)	Multi gestational	No	2776(97.95)
			Yes	58(2.04)	

BMI Body Mass Index; FBS Fast Blood Sugar

**Table 2:** Univariate and multiple regression logistic analysis of maternal FBS, age, BMI, and educational status on GDM, prematurity, neonatal weight, height and head circumference as dependent variables

<i>Dependent variables</i>	<i>Independent variables</i>	<i>Univariate</i>			<i>Adjusted</i>		
		B(SE)	OR(CI95%)	P-Value	B(SE)	OR(CI95%)	P-Value
Neonatal weight	Maternal FBS	0.012(0.006)	-	0.037	0.013(0.007)	-	0.051
	Maternal BMI	0.05(0.013)	-	≤0.001	0.045(0.013)	-	0.01
	Maternal age	0.001(0.01)	-	0.906	-	-	-
	Educational status:						
	Illiterate	-	-	-	-	-	-
	≤Diploma	-	0.794(0.48, 1.32)	0.371	-	-	-
	Collage	-	0.689 (0.39,1.19)	0.184	-	-	-
	Maternal FBS	0.01(0.004)	-	0.021	0.004(0.005)	-	0.408
	Maternal BMI	0.059(0.01)	-	≤0.001	0.052(0.011)	-	≤0.001
	Maternal age	0.025(0.007)	-	0.001	0.012(0.009)	-	0.18
	Educational status;						
Neonatal head circumference	illiterate	-	-	-	-	-	-
	≤Diploma	-	0.697(0.478,1.02)	0.06	-	0.713(0.467,1.09)	0.118
	Collage	-	0.986(0.646,1.51)	0.949	-	0.882(0.546,1.43)	0.608
	Maternal FBS	0.267(0.01)	-	-	0.274(0.013)	-	≤0.001
	Maternal BMI	0.09(0.01)	-	-	0.011(0.013)	-	0.468
	Maternal age	0.063(0.008)	-	-	0.058(0.013)	-	≤0.001
	Educational status:						
GDM	Illiterate	-	-	-	-	-	-
	≤Diploma	-	0.772(0.529,1.13)	0.21	-	-	-
	Collage	-	1.02(0.721,1.65)	0.667	-	-	-

BMI Body Mass Index; FBS Fast Blood Sugar; GDM Gestational Diabetes Mellitus

In the simple ROC analysis, AUC of FBS for prediction of GDM was calculated 0.905 (SE=0.09), and considering the cut-off point as 85.95, the sensitivity and specificity were estimated 0.806 and 0.71, respectively. Its noticeable still birth, abortion, prematurity, weight, height and head circumference variables did not access acceptable AUC ( $\geq 0.60$ ) for detection of FBS cut-off point.

We used of predicted probabilities by multiple logistic regression for determination of accuracy and cut-off point of FBS in the presence of maternal age (AUC>0.6) and BMI (AUC>0.6) by GDM. AUC by these three variables (FBS, age and BMI) for prediction of GDM was obtained 0.915 (SE=0.009). Based on this, the FBS cut-off point for mothers over 30 and BMI over 25.80 was equal to 83.75 (SE=86.4%, SP=80.0%) (Table 3) (Fig. 1).

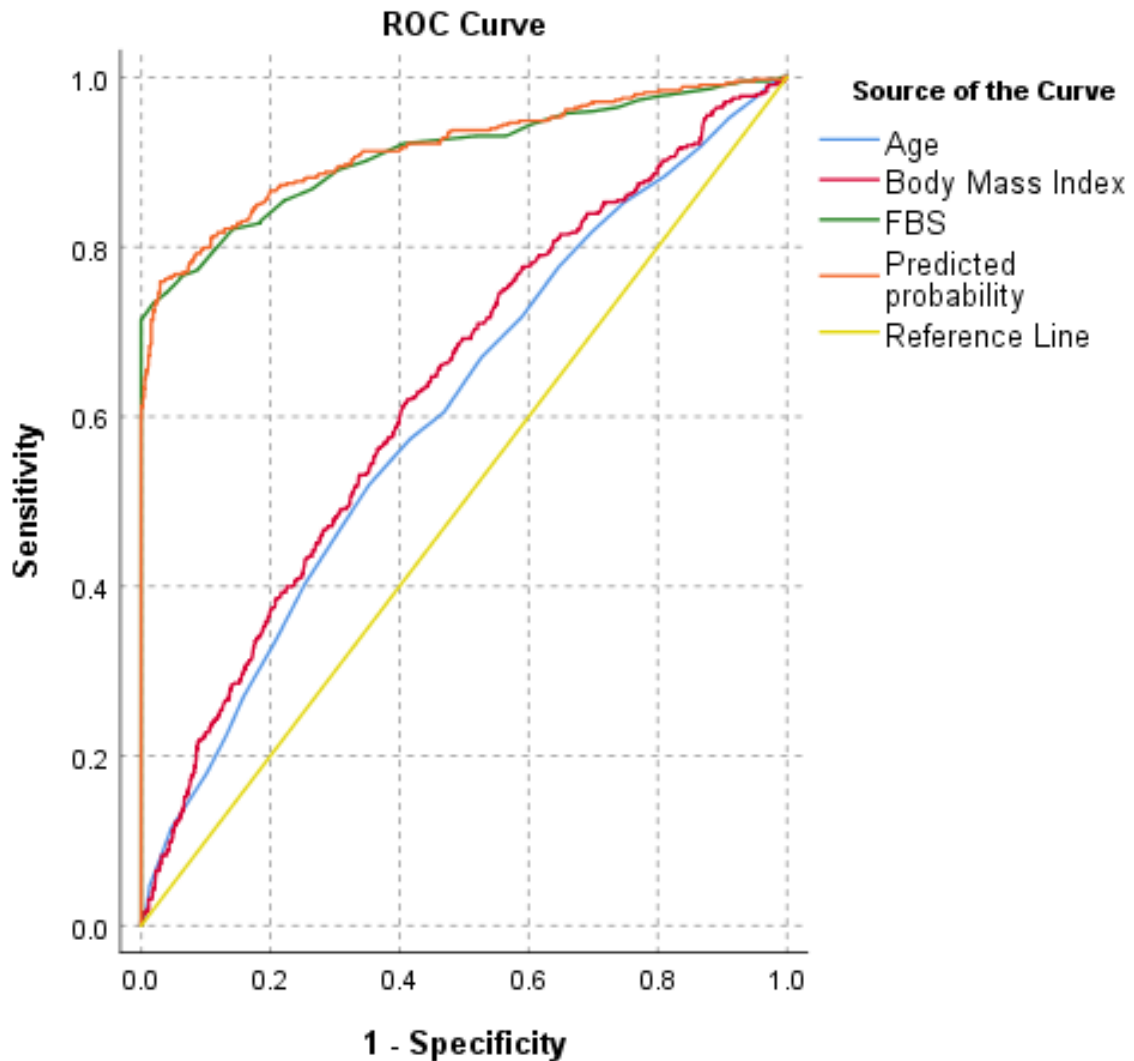


Fig. 1: ROC curves of maternal FBS, age, BMI and combined FBS-age-BMI by GDM

**Table 3:** Accuracy of FBS in prediction of gestational diabetes and other neonatal- maternal

<i>Dependent variable</i>	<i>Independent variables</i>	<i>AUC(SE)</i>
Gestational diabetes mellitus	FBS	0.915(0.009)
	Age	
	BMI	
Still birth	FBS	0.384(0.016)
	Age	
	BMI	
Abortion	FBS	0.370(0.014)
	Age	
	BMI	
Prematurity	FBS	0.417(0.018)
	Age	
	BMI	
Neonatal birth weight	FBS	0.42(0.018)
	Age	
	BMI	
Neonatal head circumference	FBS	0.41(0.015)
	Age	
	BMI	
neonatal Height	FBS	0.457(0.024)
	Age	
	BMI	

Outcomes in the presence of maternal age and BMI

BMI Body Mass Index; FBS Fast Blood Sugar; GDM Gestational Diabetes Mellitus; AUC Area under Curve

## Discussion

The purpose of this study was to investigate the relationship between maternal glucose levels during the second trimester and maternal-neonatal outcomes in a large population. The study also aimed to determine the optimal FBS levels that can accurately predict GDM. To achieve these objectives, the study conducted multiple logistic regression analyses to examine the association between maternal FBS levels and maternal and neonatal health outcomes such as GDM, prematurity, neonatal weight, height, and head circumference. The adjusted analyses indicated that only FBS had a significant association with GDM. The study also identified the cut-off point for FBS levels that can predict GDM while controlling for maternal age, BMI, and education. Therefore, the study provided a comprehensive finding that could assist

healthcare providers in managing and preventing GDM.

GDM is an increasing healthcare subject, affecting 3% to 25% of pregnancies worldwide (22). The prevalence of GDM in the present study was calculated at 16% (571 patients). The global and regional prevalence of GDM with the criteria of the International Association of the Diabetes and Pregnancy Study Groups (IADPSG), the global standardized prevalence of GDM was estimated at 14%, the regional standardized prevalence in North America and the Caribbean 7.1%, in Europe 7.8%, in South America and Central America 10.4%, in Africa 14.2%, in the Western Pacific 14.7%, in Southeast Asia 20.8% and in the Middle East and North Africa was calculated as 27.6%. The standardized prevalence of gestational diabetes in low, middle, and high- income countries was 12.7%, 9.2%, and 14.2% respectively too (23).

Thus, the prevalence of GDM in the present study is higher than the global standardized prevalence (16% V.S 14%).

In the univariate logistic regression test, there was a statistically significant relationship between the FBS with the neonatal birth weight and head circumference, but this relationship was not maintained in the multiple analysis. In a study with the aim of gestational diabetes and ultrasound-assessed fetal growth in South Asian and White European women, GDM was associated with early fetal size deviations before GDM diagnosis, highlighting the need for novel strategies to diagnose pregnancy hyperglycemia earlier than current methods (24).

Poorly managed GDM can lead to accelerated fetal growth (1) and increase the risk of macrosomic and large-for-gestational-age neonates (25, 26).

In our study information about infants with anthropometric indices higher than normal was not available. Therefore, it was not possible to evaluate infants with anthropometric indices higher than normal based on maternal FBS or GDM.

The results of the ROC analysis in the present study indicated, the cut-off point for FBS in the second trimester (AUC>.90) in the diagnosis of GDM was 85.95 mg/dl (with a sensitivity of 80.6% and a specificity of 71.0%) that was different from standard classification by American Diabetes Association (92 mg/dL or 5.1 mmol/L) (27). While the inability to recognize GDM (high percentage of false negatives in diagnosis) is associated with adverse pregnancy outcomes, the low specificity and high false positive in the diagnosis of GDM lead to psychological stress, unnecessary treatments, and reduction in quality of life [8], so the importance of correct prediction and diagnosis is unavoidable.

Due to the importance of age and BMI in the prediction of GDM (diagnosis accuracy >0.6), the results of multiple logistic regression probabilities were used to determine the accuracy of FBS in the presence of age and BMI, and the cut-off point for FBS obtained 83.75mg/dl. In

this way in women over 30 yr old and BMI above 25.8, FBS above 83.75 predicted the occurrence of GDM.

The best cut-off point for FBS was 85.5 mg/dl (AUC=0.8) with a sensitivity of 71% and a specificity of 69% (28). These results are in agreement with the findings of the present study. However, in Iran, the cut-off point was determined for FBS to be  $\leq 91$  mg/dl with a sensitivity of 63.89% and a specificity of 76.56% (29).

FBS and BMI were used as predictors of GDM in a Chinese population. The increase in the prevalence of GDM was directly related to the increase in maternal age and weight. They reported the FBS level  $\geq 82.8$  as the best threshold for predicting GDM (sensitivity of 53.89%, specificity 70.90%), also a BMI higher than 23.5 kg/m<sup>2</sup> had a sensitivity of 48.5% and a specificity of 73.1% for predicting GDM. The combination of FBS and BMI significantly increased the predictive ability for GDM (30). This finding is consistent with the results of the present study.

It is imperative to conduct further national studies of FBS by controlling some maternal variables as age and BMI variables.

One of the limitations of this study was that the information related to anthropometric indices more than normal in neonates was incomplete, and another limitation was the non-availability of some clinical information of mothers such as, preeclampsia.

## **Conclusion**

The prevalence of GDM was 16%. The cut-off point of FBS in predicting of gestational diabetes is estimated 85.95, which is lower than the standard classification. The FBS cut-off point was lower among women over 30 yr- old and with a BMI over 25.8. This finding is important in terms of screening and control of women with higher age and BMI. Our findings suggest maternal age, and BMI are important in

identifying hyperglycemia-associated pathological effects.

## Journalism Ethics considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

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## Conflict of Interest

The authors declare that there is no conflict of interests.

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