



## Original Article

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## Incidence and Risk Factors Related to Gestational Diabetes Mellitus among Women in Yazd: A Prospective Cohort Study

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### ABSTRACT

**Background:** The incidence of Gestational diabetes mellitus (GDM) is increasing worldwide. The exact prevalence of GDM in Iran is unknown. This study aimed to identify the incidence of GDM and the risk factors based on a cohort study in Yazd.

**Methods:** This is a prospective cohort study involving 3110 pregnant women attending prenatal clinics in Yazd, Iran between 2015 and 2020. GDM was diagnosed using an Oral Glucose Tolerance Test (OGTT) for each participant at 24-28 weeks of gestation. Demographic information was collected at enrollment and during pregnancy. The multivariate logistic regression models were used to identify risk factors for GDM.

**Results:** The overall incidence of GDM was 10.93% in this study. The incidence of GDM in the first, second and third trimesters were 5.65, 2.25 and 3.11%, respectively. The mean age of mothers was calculated to be  $28.64 \pm 5.53$  years. By logistic regression, significant factors associated with GDM were age, Preeclampsia, Pregnancy High blood pressure, history of diabetes mellitus (DM) and obesity.

**Conclusion:** In this population, the incidence of GDM was 10.93%, which was high. The significant risk factors for GDM were age, BMI, smoking, smoking exposure in the current pregnancy and history of GDM and DM. Also, GDM pregnancies have a higher risk of preeclampsia and gestational hypertension. Therefore, considering the high incidence of GDM in Yazd, general screening is highly recommended and more studies are needed in other parts of Yazd province.

## Introduction

Gestational diabetes mellitus (GDM) is a global public health concern with potential consequences for the health of a mother and her offspring.<sup>1</sup> GDM is impaired glucose tolerance that first occurs or is diagnosed after pregnancy.<sup>2</sup> The prevalence of GDM is increasing year after year globally, particularly in low-income and developing countries.<sup>2</sup> Globally, the average estimate of GDM is between 6 and 13%. In the United States, recent estimates suggest that up to 9% of all pregnancies are complicated by GDM. In Central and South America, the recent overall prevalence of GDM has been estimated at 11%.<sup>1</sup> The prevalence of GDM reported in Europe varies considerably, occurring in more than 20% of pregnancies in certain populations.<sup>3</sup> A meta-analysis showed that the prevalence of GDM was 20.9% in Asia, and 14.8% in China.<sup>4</sup>

In Iran, in previous studies conducted in different regions, the prevalence of GDM was between 1-18%.<sup>5</sup> Moreover, this difference is related to race, lifestyle, and differences in data collection methods, non-random selection, and diagnostic criteria. In a review article conducted in 11 provinces of Iran (2009), the prevalence of GDM was reported in the range of 1.3 to 8.9%.<sup>6</sup>

GDM can cause maternal and neonatal complications such as premature rupture of membranes, preeclampsia, and preterm labor and increase the risk of long-term endocrine disorders.<sup>2</sup> GDM is also associated with an increased risk of perinatal morbidity including malformations, neonatal hypoglycemia, shoulder dystocia, and perinatal mortality.<sup>1,7</sup> Women who develop GDM have an elevated lifetime risk of type 2 diabetes mellitus. Currently, a series of studies have shown that women with GDM are also at risk of developing cardiovascular diseases (CVD).<sup>8</sup> However, limited information is available about genetic and environmental factors that are implicated in the progression from GDM to T2DM.<sup>9</sup> Generally risk factors for GDM

include overweight and obesity, advanced maternal age, family history of diabetes, nonwhite race, previous unexplained stillbirth, hypertension, polycystic ovary syndrome (PCOS), and hyperlipidemia.<sup>10</sup> Obesity and a family history of diabetes have been consistently identified as major risk factors for GDM in previous studies.<sup>1</sup> Also, women who conceive at an older age are likely to have a higher body mass index (BMI).<sup>4</sup> In 2010, the IADPSG developed a consensus statement for a new strategy to diagnose GDM. The chosen cut-off point for glucose on a 75 g OGTT conveyed adverse outcomes of  $\geq 1.75$  compared with women with mean glucose levels at 24-28 weeks.<sup>3</sup>

GDM is the most common metabolic disorder in pregnancy, which is caused by insulin resistance and carries many risks for the mother and the fetus. Therefore, it is important to update its prevalence data in different geographical areas.<sup>11</sup> The exact estimate of the incidence of GDM in pregnant women in Yazd is still unknown. We aimed to calculate the incidence of GDM and report the critical risk factors for the development of GDM, in a cohort study on mothers in 5 centers, during 5 years in Yazd using IADPSG/WHO 2013 diagnostic criteria.

This study may determine the incidence, risk factors and pregnancy outcomes of delivery with GDM in Yazd, which is important for researchers to design more effective intervention measures such as diet, exercise and other early interventions. Understanding the incidence and risk factors in the region will help develop targeted interventions to reduce the adverse outcomes of GDM.

## Materials and Methods

**Data Collection:** This study is a prospective cohort study using the Mother-Infant Study Cohort data. 3110 pregnant women participated in this study. The target population of the study included all pregnant women who participated in the Mother-Infant Study Cohort in Yazd. All pregnant women participating in this research have been

examined for GDM and its related causes. Exclusion criteria included type 1 and 2 diabetes and the use of drugs such as steroids affecting glucose metabolism.

To collect data, a comprehensive data collection form was used in the context of the required information and the investigated variables. The said form included the following information: history of diabetes in the first-degree family, history of pre-diabetes, history of GDM, mother's age, body mass index, body fat percentage, fasting blood sugar, triglycerides, cholesterol, alcohol consumption, smoking, history of previous high-risk pregnancy, history of stillbirth, history of miscarriage, urinary tract infection, history of hypertension, history of abnormality, systolic blood pressure, diastolic blood pressure, history of pre-eclampsia, history of macrosomia.

The diagnosis of GDM was made according to the latest national guidelines for screening and diagnosis of gestational diabetes. Women with GDM are identified through the glucose challenge test (GCT) by measuring 50 grams of glucose and blood sugar one hour later. So values less than 131 are negative and disease-free, but values equal to or higher than 130 are considered positive in this program. In the next step, if the GCT was positive, a 3-hour glucose tolerance test (OGTT) was requested for them. OGTT was performed after three days of a diet without carbohydrate restriction and in a fasting state, first, fasting blood Sugar (FBS) was recorded and then 100 grams of glucose was prescribed. Then the blood glucose level was measured at intervals of one, two, and three hours after consuming the glucose solution. Finally, the diagnosis was made based on the American Diabetes Association criteria (Bs3h > 140, Bs2h ≥ 150, Bs1h > 180, FBS > 95). Diabetes should be proven in at least two glucose tests. In this way, if the result was positive in at least 2 glucose tests, the person was diagnosed with gestational diabetes. After collecting information, the data was analyzed using SPSS software version 19, and statistical tests of chi-square, independent t,

analysis of variance, and logistic regression were used at a significance level of  $1.15 \alpha$ . ( $P < 0.05$ ).

## Results

**Basic information:** We used data from March 2016 and continue until February 2021. The study was approved by the Institutional Ethics Committee of Shahid Sadoughi University of Medical Sciences, and all participants signed written informed consent before testing. We confirmed that the research was performed following relevant clinical technical specifications.

The total number of people studied was 3110. Of the 3110 pregnant women, information on baseline characteristics was missing for a few mothers. Participants ranged in age from 15 to 45. The average age of mothers was calculated to be  $28.64 \pm 5.53$  years. More than 50% of the studied people were between 26 and 35 years old. The distribution of pregnant women in the three age groups was 30.6, 57.3, and 12.1%, respectively. Out of those 1494 (48%), people had Higher education. The income of 2320 (78.3%) of the studied people was middle. Two thousand and three hundred twenty (78.3%) of participants belonged to the middle-income group. Most of the surveyed mothers 2427 (79.2%) were housewives. The demographic characteristic of pregnant women shows in Table 1.

**Table 1.** Baseline Sociodemographics Characteristics of the Studied Subjects

Variables	Frequency	Percent (%)
Age		
15-25	951	30.6
26-35	1783	57.3
36-45	376	12.1
Level of education		
Primary	516	16.6
High school	1100	35.4
Higher education	1494	48.0
Income		
Low	302	10.2
Middle	2320	78.3
High	342	11.5
Employment status		
Housewife	2427	79.2
Employed	637	20.8

**Characteristics and history of the study population:** Characteristics of pregnant women are shown in Table 2. The mean pre-pregnancy BMI was 26.6 kg/m<sup>2</sup>. In our population, 53.2% of pregnant women had BMI < 25 (underweight), and 30% had a normal BMI (25- 29.9). Only 16% had BMI > 30 and were overweight (Table 2). More than 60% of the investigated mothers had a history of pregnancy and 34.2% of these mothers had a history of parity (parity = 1). Also, 33.7% had no history of pregnancy and were experiencing their first pregnancy in this study. The frequency of history of GDM in pregnant women was 6.7%, which was close to the frequency of history of GDM in the family of pregnant women (10.6%). Pregnant women with GDM may be more likely to have a history of GDM. The frequency of the history of DM in pregnant women was low (3.7%), While the frequency of a history of diabetes in the families of pregnant women was high (46.2%). The history of pregnancy hypertension was 2.9% and 8% in participants and their families, respectively.

**Table 2.** Characteristics of the Study Population and Their Family

Variables	Frequency	Percent (%)
<b>Participants</b>		
BMI (kg/m <sup>2</sup> )		
25 < (underweight)	1656	53.6
25-29.9 (normal)	933	30.3
30 ≥ (overweight)	498	16.1
History of pregnancy		
Yes	2007	66.3
No	1021	33.7
Parity		
0	1021	33.7
1	1034	34.2
2	641	21.2
≤ 3	330	10.9
Preeclampsia		
Yes	42	1.4
No	2994	98.6
History of GDM		
Yes	205	6.7
No	2829	93.3
History of DM		
Yes	115	3.8
No	2917	96.2

**Table 2.** Characteristics of the Study Population and Their Family (Continue)

Variables	Frequency	Percent (%)
History of gestational hypertension		
Yes	89	2.9
No	2940	97.1
High cholesterol		
Yes	78	2.6
No	2977	97.4
Urinary tract infection		
Yes	1325	43.7
No	1707	56.3
Smoking history		
Yes	6	0.2
No	3104	99.8
History of hookah use since three months before pregnancy		
Yes	126	4.1
No	2984	95.9
Exposure to cigarette smoke in recent pregnancy		
Yes	337	10.8
No	2773	89.2
<b>Family</b>		
History of GDM		
Yes	306	10.6
No	2573	89.4
History of DM		
Yes	1437	48.6
No	1521	51.4
History of gestational hypertension		
Yes	230	8
No	2650	92
History of miscarriage		
Yes	968	33.5
No	1922	66.5
History of recurrent miscarriages (≤ 2)		
Yes	335	11.3
No	2622	88.7
History of stillbirth		
Yes	259	9
No	2618	91
History Preterm Delivery		
Yes	325	11.3
No	2547	88.7
Treatment		
Diabetes Treated	54	44
With Insulin		
Diabetes Treated	69	56
Without Insulin		
Family history of diabetes treated with insulin	791	43.9
Family history of diabetes treated Without insulin	1012	56.1

The amount of history of miscarriage in

the family (mother and sister) was 31.1% and the history of recurrent miscarriages was 10.8%. Also, the history of premature birth in the family of pregnant women was 10.5 % (Table 3). In our study, almost all mothers (99.8%) were non-smokers and small percentages (0.02%) were smokers. However, 10.8% of pregnant women were exposed to cigarette smoke during their recent pregnancy (Table 2).

**Incidence of GDM in first, second, and third trimesters:** The study initially included 3110 patients, including 340 with GDM. The overall incidence of GDM in our population of Yazd pregnant women was 10.93% (95% CI: (9.85- 12.08)). Table 3 shows the incidence of GDM by trimesters in first, second, and third. The incidence of GDM in the first, second, and third trimesters were 5.65, 2.25 and 3.11%, respectively. In the first trimester, the risk of GDM in women was higher than in other months (95% CI: (4.78-6.42)). This shows that diagnosis in the first trimester is more valuable.

**Table 3.** The Incidence of GDM in Each Trimester of Pregnancy

	Frequency	Risk (CI)*
Overall	340	1093 (9.85-12.08)
The first trimester	173	5.65 (4.78-6.42)
The second trimester	70	2.25(1.75-2.83)
The third trimester	97	3.11(2.53-3.79)

\* Per 100 people

**Risk factors associated with GDM:** Table 4 shows the results of multiple logistic regression analysis on associations between potential risk factors and GDM. Maternal and family risk factors for GDM development at enrolment are displayed in this Table. The most important risk factors in GDM among our population were analyzed, which include the following. Significant risk factors associated with GDM were age ( $P = 0.003$ , 95% CI (1.184-2.341)), BMI ( $P = \leq 0.001$ , 95% CI (1.210- 2.124)), history of DM, history of GDM, Smoking exposure in the current pregnancy and smoking three months

before pregnancy. Also, GDM pregnancies have a higher risk of preeclampsia ( $P = 0.008$ , 95% CI (1.340-7.277)) and gestational hypertension ( $P = 0.040$ ). The incidence of GDM was strongly associated with a history of previous GDM ( $P \leq 0.001$ , 95% CI: 1.543-3.584) and a history of DM ( $P \leq 0.001$ , 95% CI: 3.408- 9.052).

There was no significant difference in the following risk factors, including education, income, number of parity, cystitis, history of gestational hypertension, high blood pressure, and previous pregnancy. There wasn't any significant relation between GDM with family risk factors such as a history of diabetes, history of stillbirth or history of miscarriage. Other non-significant risk factors include a history of familial recurrent miscarriage, gestational hypertension, GDM, preterm delivery, high blood pressure, DM, and gestational hypertension.

## Discussion

GDM is a common health problem during pregnancy and is defined as intolerance of carbohydrate levels in women at the beginning or during pregnancy.<sup>12,13</sup> Women with GDM are more likely to suffer pregnancy complications, and the diagnosis is associated with both immediate and long-term adverse consequences for their offspring.<sup>3</sup> In pregnant women, the excess amounts of blood glucose are transferred to the fetus. This causes several disorders in neonates.<sup>14</sup> The prevalence of GDM has increased in recent decades in parallel with older age at the time of pregnancy and the western lifestyle, which is associated with economic prosperity.<sup>4</sup> GDM affects approximately 15.1% of women worldwide, which, if untreated, has severe consequences for maternal and neonatal outcomes. Gestational diabetes is managed with conventional medications like insulin and oral antidiabetics such as metformin, in addition to diet and exercise.<sup>15</sup> This study estimated the prevalence of GDM in Yazd and determined the risk factors and consequences related to it (and outcomes).

**Table 4.** Risk Factors Associated with GDM by Multivariate Logistic Regression Models

Characteristics	Odds Ratio	95% CI	P
Age.cat	Ref.		0.005
Age.cat(1)	1.665	1.184-2.341	0.003
Age.cat(2)	2.059	1.286-3.296	0.003
BMI1.CAT	Ref		
BMI1.CAT(1)	1.603	1.210- 2.124	0.001
BMI1.CAT(2)	2.089	1.485-2.939	≤ 0.001
Education.cat	Ref		0.827
Education.cat(1)	1.090	0.740-1.605	0.663
Education.cat(2)	1.005	0.671- 1.505	0.981
Incom.cat	Ref		0.055
Incom.cat(1)	1.307	0.846- 2.019	0.228
Incom.cat(2)	0.789	0.429- 1.450	0.445
previous pregnancy	0.717	0.441- 1.166	0.180
Number of parity.cat	Ref		0.777
Number of parity.cat(1)	1.050	0.684- 1.612	0.823
Number of parity.cat(2)	1.149	0.754- 1.752	0.519
Preeclampsia	3.123	1.340- 7.277	0.008
History of GDM	2.352	1.543- 3.584	≤ 0.001
History of DM	5.554	3.408- 9.052	≤ 0.001
Gestational hypertension	0.334	0.117- 0.951	0.040
History gestational hypertension	1.059	0.402- 2.789	0.907
High Blood Pressure	2.381	0.899- 6.309	0.081
Cystitis	1.112	0.868- 1.426	0.400
Daily Smoking	4.760	0.729- 31.062	0.103
Smoking three months before pregnancy	1.953	1.155- 3.303	0.013
Smoking exposure in the current pregnancy	1.607	1.135- 2.276	0.008
Family			
Gestational hypertension	1.120	0.734- 1.710	0.599
History of GDM	1.388	0.965- 1.996	0.077
History of DM	1.212	0.939- 1.564	0.140
Miscarriage	1.045	0.797- 1.370	0.753
Recurrent miscarriage	1.409	0.977- 2.034	0.067
Still birth	1.120	0.741- 1.692	0.591
Preterm delivery	0.832	0.560- 1.237	0.364

In our study, the prevalence of GDM was 10.9%. When we compare our results with the prevalence of diabetes in the world and in Iran, we find that the prevalence of diabetes in Yazd was relatively high. The estimated prevalence of GDM in Yazd (10.93%) is similar to the estimate of the meta-analysis conducted in 2019. Behboudi-Gandevanis et al., in a meta-analysis estimated the worldwide prevalence of GDM. The pooled overall prevalence of GDM in the diagnostic threshold used in IADPSG criteria was 10.93% (95% CI 10.5-10.93%).<sup>16</sup>

In the following, we have given examples of the global prevalence of diabetes, the amount of which is different. In 2018, Stark S

et al. estimated the prevalence of GDM in the United States to be 7.6%, with 19.7% of these women subsequently developing diabetes. They observed that women with a history of GDM, obesity and a family history of diabetes, should be closely monitored for blood sugar.<sup>10</sup> In 2018, Groof Z et al., evaluated the prevalence, risk factors, and fetal outcomes of GDM in Kuwait. They estimated that 12.6% of mothers had GDM in their last pregnancy. The prevalence of GDM increased with maternal age and pre-pregnancy BMI.<sup>17</sup> In Gloria et al., a study in Peru in 2018, the prevalence of GDM was approximately 16% of pregnant women. The most risk factors for the incidence of GDM

were associated with maternal obesity, family history of diabetes, and antepartum depression among Peruvian women.<sup>1</sup> Generally obesity and maternal age are the two most important factors independently affecting the risk of GDM.<sup>4</sup> Stacey et al., evaluated GDM and the risk of late stillbirth in England, UK. They concluded optimal screening and diagnosis of GDM reduces the higher risks of late stillbirth in women "at risk" of GDM and/or with elevated FPG.<sup>18</sup>

Our result was higher than the Iranian meta-analysis done in 2015 by Jafari Shabiri et al. They conducted a systematic review and meta-analysis to evaluate the prevalence and risk factors of GDM in Iran. Their results showed the prevalence of GDM was 3.41% and the highest and lowest prevalence rates were 18.6% and 1.3%, respectively.<sup>19</sup> Perham et al., evaluated the prevalence of GDM in Qom, Iran in 2018. They reported 20.76% of women had gestational diabetes. GDM was significantly associated with maternal age, BMI, history of GDM, a family history of type II diabetes in first-degree relatives, history of preterm labor, history of macrosomia and known hypothyroidism before pregnancy.<sup>11</sup> Vakili et al., evaluated the prevalence of GDM and its risk factors in the city of Maybod, Yazd in 2013-2014. Their results showed that the prevalence of GDM in the mentioned group is 27.1 %, which is considered to be high in comparison with other parts of Iran.<sup>5</sup> In 2012 Vakili et al., evaluated the prevalence of GDM and its risk factors in Yazd. The prevalence of GDM in the present study was 12%.<sup>20</sup> A cross-sectional study was conducted in Yazd province from March 2008 to March 2011 by Rashidi et al. They used logistic regression was used to calculate the Odds Ratio at 95% Confidence Interval to estimate the independent association of different risk factors with GDM. Their results showed the overall prevalence of GDM was 3.3%.<sup>21</sup>

According to most studies overweight and obesity, gestational BMI, older age, having family history of T2DM/GDM, prepregnancy

overweight, and prior history of giving stillbirth/miscarriage were associated with increased risk of GDM. In our study age, preeclampsia, pregnancy HBP, history of DM, BMI, exposure to secondhand smoke during the current pregnancy, and smoking three months before pregnancy, were correlated with an increased risk of GDM. We estimated the incidence of GDM in Yazd to be 10%, which is high. Considering that the incidence of GDM is high in Yazd, there is a need for more studies in this field. Considering the above risk factors, society can strengthen education for high-risk populations, determine effective prevention strategies, and develop and improve early intervention management models for diabetic patients. Also, Public health measures may be helpful to prevent excessive gestational weight gain. In general, timely diagnosis, treatment, intervention, and accurate control of blood glucose levels lead to improved outcomes for mother and baby.

### Conclusion

Our study found that 10.93% of women in Yazd are affected by GDM. Advanced age, pregnancy HBP, history of diabetes mellitus, and BMI were independent risk factors for GDM. Moreover, because of GDM's high incidence in Yazd, general screening is strongly recommended and more studies are needed to be conducted in other parts of Yazd province. In order to better understand the importance and response to GDM in Yazd, there is a need to formulate national strategies, guidelines and policies by gaining empirical knowledge about the current situation. According to the recommendations, general screening is strongly recommended among Yazd women. Also, doctors should refer patients with diabetes to resources related to the risks of diabetes and request a diabetes test after delivery to reduce the burden of diabetes and its complications.

### Conflict of Interest

The authors have no conflict of interest.

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The present study was approved by the Ethics Committee of Islamic Azad University/ Yazd Branch (IR.SSU.SPH.REC.1399.176).

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