

Association between History of Induced Abortion and Subsequent Risk of Gestational Diabetes Mellitus

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Abstract

Background: Some studies have indicated a potential link between a history of induced abortion (IA) and the subsequent risk of gestational diabetes mellitus (GDM), but the relationship is not fully understood, and the aim of this study was to further elucidate the association. **Methods:** The case-control study was conducted at 2 hospitals in central China from April 2018 to October 2020. GDM was diagnosed by an oral glucose tolerance test (OGTT). Information on history of IA was obtained through a face-to-face interview. **Results:** Among 396 GDM cases and 904 controls, the proportion of participants with history of IA in the case group was 30.6%, which was higher than that in the control group (23.1%), and the difference was statistically significant ($p = 0.005$). After adjusting for potential confounders, women with a history of IA had an increased subsequent risk of GDM compared with women without (OR, 1.24, 95% CI, 1.10 - 1.40, $p = 0.002$). The subsequent risk of GDM in pregnant women increased as the number of previous IAs increased (p for trend was equal to 0.004). Stratified analysis showed that women with a history of medical abortion (OR, 1.28, 95% CI, 1.01 - 1.62, $p = 0.048$) or surgical abortion (OR, 1.20, 95% CI, 1.04 - 1.38, $p = 0.024$) both had an increased subsequent risk of GDM compared with women without. **Conclusion:** History of IA, either medical or surgical, was related to an increased risk of GDM in subsequent pregnancy. The greater the number of previous IAs, the greater the subsequent risk of GDM.

Keywords

Gestational Diabetes, Diabetes, Induced Abortion, Abortion, Pregnancy

1. Introduction

Gestational diabetes mellitus (GDM) refers to any degree of glucose intolerance diagnosed during pregnancy that did not occur prior to pregnancy. GDM is one of the most common adverse outcomes during pregnancy. It is reported that the prevalence rates of GDM in most countries and regions are high, and the global incidence is increasing year by year for various reasons, such as the increase in obesity rate [1] [2]. GDM is very harmful to the health of mothers and their fetuses, and can lead to a significantly increased risk of preeclampsia, stillbirth, macrosomia and preterm birth [3] [4]. In addition, GDM can lead to an increased risk of noncommunicable diseases, such as diabetes and serious liver disease, among mothers later in life [5]-[7].

There are many risk factors affecting the incidence of GDM, and identifying risk factors for GDM, especially those that can be managed, is important for implementing early prevention and protecting pregnant women and their fetuses from GDM. Several studies have noted an association between induced abortion (IA) and insulin resistance, finding that IA can lead to impaired blood sugar and metabolic syndrome [8] [9]. Recently, a retrospective cohort study showed that history of IA was related to an increased risk of GDM in subsequent pregnancy, but the difference was not statistically significant [10]. Another Finnish study conducted a survey among first-time mothers and found that the prevalence of GDM among women with a history of IA was significantly higher than that among women without; however, the multivariate analysis showed that the impact of IA history on subsequent GDM risk was not statistically significant [11]. To our knowledge, only the two studies mentioned above have explored the relationship between history of IA and subsequent GDM risk; the association is still not fully understood and requires further research to clarify.

We conducted a case-control study in two hospitals in central China, aiming to explore the association between history of IA and the subsequent risk of GDM. In addition, we also observed whether different types or numbers of IAs were associated with subsequent GDM risk differently.

2. Methods

2.1. Study Population

A case-control study design was adopted in this study. The inclusion of study participants was carried out between April 2018 and October 2020 in Anhui Province Women and Children Health Hospital and Ji'an Women and Children Health Hospital of Jiangxi Province, and pregnant women who attended antenatal visits in both hospitals were invited to participate in this study. The inclusion criteria of the participants were as follows: 1) GDM screening has been completed; 2) Singletons. The exclusion criteria of the participants were as follows: 1) A history of GDM or diabetes mellitus; 2) A history of stillbirth, large baby delivery or fetal malformation; 3) Polycystic ovary syndrome. Pregnant women diagnosed with

GDM were included in the case group, and pregnant women attending antenatal visits during the same period who had non-GDM were invited into the control group. Participating pregnant women underwent a face-to-face interview immediately after being included in the study. This study was reviewed by the Medical Ethics Committee of Jinggangshan University (the serial number of the ethical approval document: 201801, approval date: 2018-02-21), and informed consent was acquired from participants.

The sample size was calculated based on the following settings. The study design was a nonmatched case-control study, the power of the test was set at 0.90, and the type one error of the hypothesis test was set at 0.05. According to the pilot survey, the proportion of women with history of IA in the control group was set at 25%, and the odds ratio (OR) value was set at 1.8. The hypothesis test was conducted by a two-sided test. After calculation, a minimum of 287 pregnant women were required to be enrolled in the case group, while the minimum sample size of the control group was required to be equal to or greater than that of the case group.

2.2. History of IA

Information on the IA history of participants was obtained through a face-to-face interview through a structured questionnaire by trained investigators. Given that IA is often a sensitive and private issue, the interviews were conducted in a closed office. In the present study, IA was defined as the termination of a viable pregnancy within 24 weeks of conception by surgical or medication techniques to detach the undeveloped embryo and placenta from the mother. Pregnant women were asked if they had a history of IA and, if so, they were asked to list the number of previous IAs and the type (surgical or medical) of each.

2.3. GDM Definition

Diagnostic information for GDM was derived from a routine oral glucose tolerance test (OGTT) between 24 and 28 weeks of gestation. According to the GDM screening standards proposed by the National Health Commission of China, pregnant women were required to fast after 20:00 the night before the OGTT test, and fasting venous blood was collected first on the morning of the OGTT test. Then, an aqueous glucose solution (75 g glucose dissolved in 300 ml warm water) was taken orally, and venous blood was collected immediately after 1 hour and 2 hours after the oral glucose aqueous solution to measure blood glucose [12]. The diagnosis of GDM was based on the criteria proposed by the International Association of Diabetes and Pregnancy Study Group: fasting blood glucose ≥ 5.1 mmol/L and/or 1-hour postprandial blood glucose ≥ 10.0 mmol/L and/or 2-hour postprandial blood glucose ≥ 8.5 mmol/L [13].

2.4. Control for Confounding Bias

To effectively control for potential confounding bias, the following information

of participants was collected as adjustment variables for statistical analysis later: age, ethnicity (Han Chinese/others), educational level (senior high or below/college or bachelor's/master's or above), smoking, drinking, gestational age at OGTT, height, prepregnancy weight, family history of diabetes, and sleep quality during early pregnancy. The gestational age at OGTT was calculated according to the date of the last menstrual period reported by the women and the date of the OGTT test. Height was measured by trained investigators, and prepregnancy weight was reported by the women. Prepregnancy body mass index (BMI) was further calculated according to height and prepregnancy weight, and the calculation formula was $\text{weight}/\text{height}^2$. Sleep quality was measured by the Chinese version of the Pittsburgh Sleep Quality Index scale, which has been used widely to measure sleep quality and is recognized as having good validity and reliability [14].

2.5. Statistical Analysis

The Shapiro-Wilk test was adopted to describe whether the continuous data followed a normal distribution. If the data followed a normal distribution, the mean and standard deviation were used for statistical description; otherwise, the median and interquartile range were used. The statistical description of categorical data adopts frequency and percentage. Comparisons of basic characteristics and IA history between the case and control groups were performed using the Pearson Chi-square test or unpaired Student's *t* test. Multivariate binomial logistic regression analysis was conducted to explore the association of IA history with subsequent GDM risk, and the results were expressed by OR and 95% confidence interval (CI). Stratified analysis was used to investigate whether different types of IA were associated with subsequent GDM risk differently. R software version 4.1.2 was used for all statistical analyses. The significance level was set at 0.05.

3. Results

A total of 396 and 904 pregnant women were included in the case group and the control group, respectively. The Shapiro-Wilk test shows that all the continuous data follow a normal distribution. The age and prepregnancy BMI among GDM women were higher than those among controls, and the proportion of poor sleep quality during early pregnancy, family history of diabetes or drinking among GDM women were all higher than those among the controls; the differences were statistically significant (all $p < 0.05$). See **Table 1**.

The proportion of pregnant women with a history of IA among GDM women was 30.6%, which was higher than that among controls (23.1%), and the difference was statistically significant ($p = 0.005$). See **Table 2**. After adjusting for a series of potential confounding factors, the subsequent risk of GDM increased by 24% in pregnant women with a history of IA compared with those without, and the difference was statistically significant ($p = 0.002$). With the increase in the number of previous IAs, the risk of GDM in pregnant women gradually increased significantly (p for trend was equal to 0.004). See **Table 3**.

Table 1. Maternal characteristics in the GDM and control groups.

Characteristics	Total (n = 1300)	GDM		
		Yes (n = 396)	No (n = 904)	p-value
Age (years)	28.07 ± 3.38	28.91 ± 3.65	27.71 ± 3.19	<0.001
Age category (years)				<0.001
≤30	1032 (79.4%)	283 (71.5%)	749 (82.8%)	
30 - 35	225 (17.3%)	88 (22.2%)	137 (15.2%)	
>35	43 (3.3%)	25 (6.3%)	18 (2.0%)	
Ethnicity				0.174
Han Chinese	1269 (97.6%)	390 (98.5%)	879 (97.2%)	
Others	31 (2.4%)	6 (1.5%)	25 (2.8%)	
Education				0.165
Senior high or below	234 (18.0%)	80 (20.2%)	154 (17.0%)	
College or bachelor's	808 (62.2%)	248 (62.6%)	560 (61.9%)	
Master's or above	258 (19.8%)	68 (17.2%)	190 (21.1%)	
Prepregnancy BMI (kg/m ²)	21.70 ± 2.92	22.66 ± 3.24	21.28 ± 2.66	<0.001
BMI category (kg/m ²)				<0.001
<18.5	163 (12.5%)	36 (9.1%)	127 (14.0%)	
18.5 - 24.9	960 (73.8%)	267 (67.4%)	693 (76.7%)	
25.0 - 30.0	165 (12.7%)	86 (21.7%)	79 (8.7%)	
≥30.0	12 (0.9%)	7 (1.8%)	5 (0.6%)	
Parity				0.021
Nulliparous	1135 (87.3%)	333 (84.1%)	802 (88.7%)	
Parous	165 (12.7%)	63 (15.9%)	102 (11.3%)	
Family history of diabetes				<0.001
Yes	137 (10.5%)	62 (15.7%)	75 (8.3%)	
No	1163 (89.5%)	334 (84.3%)	829 (91.7%)	
Drinking				<0.001
Yes	23 (1.8%)	15 (3.8%)	8 (0.9%)	
No	1277 (98.2%)	381 (96.2%)	896 (99.1%)	
Smoking				0.058
Yes	33 (2.5%)	15 (3.8%)	18 (2.0%)	
No	1267(97.5%)	381 (96.2%)	886 (98.0%)	

Continued

Sleep quality					<0.001
Good	1044 (80.3%)	287 (72.5%)	757 (83.7%)		
Poor	256 (19.7%)	109 (27.5%)	147 (16.3%)		
Gestational age at OGTT	25.52 ± 1.89	25.82 ± 3.09	25.38 ± 0.95	0.006	

Values are presented as the means ± SDs for continuous variables and numbers (percentages) for categorical variables. Abbreviations: GDM: gestational diabetes mellitus; BMI: body mass index; OGTT: oral glucose tolerance test.

Table 2. Comparison of history of IA between GDM and control groups.

Previous IA	Total (n = 1300)	GDM		χ^2	<i>p</i> -value
		Yes (n = 396)	No (n = 904)		
Never	970 (74.6%)	275 (69.4%)	695 (76.9%)	8.039	0.005
Ever	330 (25.4%)	121 (30.6%)	209 (23.1%)		

Values are presented as numbers (percentages). Abbreviations: GDM: gestational diabetes mellitus; IA: induced abortion.

Table 3. Association between history of IA and subsequent GDM risk.

	n	Crude		Adjusted ^a	
		OR (95% CI)	<i>p</i> -value	OR (95% CI)	<i>p</i> -value
Previous IA					
Never	970	1.00 (1.00, 1.00)	1.000	1.00 (1.00, 1.00)	1.000
Ever	330	1.19 (1.04, 1.36)	0.005	1.24 (1.10, 1.40)	0.002
Number of IA					
0	970	1.00 (1.00, 1.00)	1.000	1.00 (1.00, 1.00)	1.000
1	166	1.16 (0.95, 1.42)	0.102	1.16 (0.97, 1.39)	0.086
2	99	1.18 (0.88, 1.58)	0.179	1.28 (0.98, 1.67)	0.061
≥3	65	1.26 (0.87, 1.82)	0.167	1.44 (1.01, 2.05)	0.047
<i>p</i> for trend			0.034		0.004

Abbreviations: GDM: gestational diabetes mellitus; IA: induced abortion. ^aAdjusted for age, ethnicity, education, parity, family history of diabetes, smoking, drinking, gestational age at OGTT, prepregnancy BMI category and sleep quality during early pregnancy.

We further conducted stratified analysis according to the type of IA to explore whether surgical abortion (SA) and medical abortion (MA) were related to subsequent GDM risk differently. Compared to women with no IA history, women with a history of MA only had a subsequent increased risk of GDM (OR = 1.28, *p* =

0.048); women with a history of SA only had a subsequent increased risk of GDM (OR = 1.20, $p = 0.024$). Compared to women with no IA history, women with a history of MA + SA had an increased subsequent risk of GDM; however, the difference was not statistically significant (OR = 1.38, $p = 0.142$). See **Table 4**.

Table 4. Association between history of IA and subsequent GDM risk stratified by type of IA used.

	n	Crude		Adjusted ^a	
		OR (95% CI)	<i>p</i> -value	OR (95% CI)	<i>p</i> -value
Type 1					
None	970	1.00 (1.00, 1.00)	1.000	1.00 (1.00, 1.00)	1.000
MA only	75	1.18 (0.94, 1.48)	0.126	1.28 (1.01, 1.62)	0.048
SA only	237	1.20 (1.02, 1.41)	0.041	1.20 (1.04, 1.38)	0.024
MA + SA	18	1.12 (0.56, 2.24)	0.588	1.38 (0.82, 2.32)	0.142
Type 2					
None	970	1.00 (1.00, 1.00)	1.000	1.00 (1.00, 1.00)	1.000
MA only	75	1.18 (0.94, 1.48)	0.126	1.28 (1.01, 1.62)	0.048
Others	255	1.19 (1.02, 1.39)	0.037	1.23 (1.08, 1.40)	0.012
Type 3					
None	970	1.00 (1.00, 1.00)	1.000	1.00 (1.00, 1.00)	1.000
SA only	237	1.20 (1.02, 1.41)	0.041	1.20 (1.04, 1.38)	0.024
Others	93	1.17 (0.87, 1.57)	0.194	1.32 (1.03, 1.80)	0.037

Abbreviations: GDM: gestational diabetes mellitus; IA: induced abortion; MA: medical abortion; SA: surgical abortion. ^aAdjusted for age, ethnicity, education, parity, family history of diabetes, smoking, drinking, gestational age at OGTT, prepregnancy BMI category and sleep quality during early pregnancy.

4. Discussion

In the present study, we found that history of IA was associated with an increased subsequent risk of GDM, and the risk gradually increased as the number of IAs increased. In addition, no significant association was observed between the type of IA and the subsequent risk of GDM, and women with a history of SA or MA had an increased subsequent risk of GDM compared with women without a history of IA.

IA is a major public health concern worldwide, and approximately one in four women will have an IA in their lifetime [15]. In China, due to the strict implementation of the one-child birth policy over 3 decades, the prevalence of induced abortion is at a very high level [16] [17]. IA is related to a variety of adverse outcomes in subsequent pregnancy and is very harmful to the health of pregnant

women and their fetuses [18].

Some studies have examined the impact of IA on blood glucose. A large prospective cohort study found that women with a history of IA had a 7% increased risk of developing diabetes, and the risk of diabetes increased gradually with the number of IAs [19]. Another study found that women who had more than 2 abortions had a significantly higher risk of developing diabetes [20]. Few studies have investigated the relationship between history of IA and blood glucose during pregnancy; to our knowledge, only two studies have assessed the relationship between history of IA and subsequent risk of GDM. One study was conducted in Shanghai, China, based on a retrospective cohort study design. They found a significant 18% increased subsequent risk of GDM in pregnant women with a history of IA; however, after adjusting for age, age at menarche, number of pregnancies, prepregnancy BMI, family history of diabetes and use of assisted reproductive technology, the association between history of IA and subsequent risk of GDM was not statistically significant [10]. Another study examined the relationship between history of IA and GDM risk in first-time mothers, and the results showed that the prevalence of GDM was significantly higher among women with a history of IA than women without; however, after adjusting for age, cohabiting, smoking and weight, the effect of IA history on GDM risk was not significant [11]. In this study, women with a history of IA were observed to have a significantly increased subsequent risk of GDM, which was inconsistent with the conclusions of the previous 2 studies. We believe that one of the possible explanations for this observation is that more abundant covariates were collected to adjust for potential confounding bias in the present study.

This is the first study to observe the relationship between the type and number of IAs with subsequent GDM risk. We found that the subsequent GDM risk in pregnant women increased gradually with the increase in the number of IAs, suggesting that pregnant women who had many previous IAs are at high risk of GDM, and special attention should be given to the prevention and control of GDM in these pregnant women. Compared with previous studies, this study better demonstrates the association between history of IA and subsequent GDM risk and provides a higher level of evidence due to the significant dose-effect association we observed [10] [11] [21]. In the stratified analysis, we found that women with a history of both SA or MA had an increased subsequent GDM risk compared with women without a history of IA. These findings have significant clinical and public health implications. Women with a history of IA should be informed of their potentially increased risk of developing GDM and encouraged to adopt preventive measures, including maintaining a healthy lifestyle both before and during pregnancy. Clinicians should recognize pregnant women with a history of IA as a high-risk group for GDM and adjust screening protocols accordingly in prenatal care management. Furthermore, the public health sector may develop policies and initiatives based on these findings, such as enhancing public education to promote more informed decision-making regarding IA. These findings need to be validated

by more studies in the future.

The biological mechanism of the association between history of IA and gestational diabetes remains unclear. Studies have reported that IA will lead to sudden interruption of processes such as immunity that regulate the coexistence of the body and the fetus during pregnancy, which have a lasting impact on endocrine function and metabolism; these impacts can even gradually lead to hormonal and immune disorders in the body, resulting in the occurrence of GDM [22]. In addition, women who choose IA often face additional stress, which puts them at a higher-than-average risk of depression, anxiety, and other mental health problems, which is related to elevated levels of proinflammatory markers that lead to the development of GDM [23]-[26].

This study has several limitations that should be noted. First, the case-control study design used in this study may lead to recall bias, and the validation power of causality is lower than that of prospective epidemiological study designs such as cohort studies. Second, the sample size was not large, especially the number of pregnant women who had a history of SA combined with MA, which was small. Third, the IA history collected in this study was self-reported by pregnant women, some of whom may have been unsure whether the pregnancy termination they received was due to a missed miscarriage. Fourth, although the abundant covariates have been adjusted in statistical models, there are still unknown confounding factors that may exist, such as the lifestyles of the pregnant women, which may change after IA [27].

5. Conclusion

This study found that women with a history of IA had a higher subsequent risk of GDM than women without, and the greater the number of previous IAs was, the greater the subsequent risk of GDM. Our findings suggest that pregnant women who have had a history of IA, especially those who have had a high number of IAs, should pay special attention to blood glucose monitoring and prevention during pregnancy to minimize the subsequent risk of GDM.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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