

## History of menstrual disorders associated with gestational diabetes mellitus

Shahnaz Barat<sup>1</sup>, Zinatossadat Bouzari<sup>2,\*</sup>, Shahla Yazdani<sup>1</sup>, Rahil Moslemi<sup>3</sup>,  
Karimollah Hajian-Tilaki<sup>4</sup>

<sup>1</sup>Infertility and Reproductive Health Research Center, Health Research Institute & Department of Obstetrics and Gynecology, Clinical Research Development Unit of Rouhani Hospital, Babol University of Medical Sciences, Babol, Iran

<sup>2</sup>Cellular & Molecular Biology Research Center & Department of Obstetrics and Gynecology, Babol University of Medical Sciences, Babol, Iran

<sup>3</sup>Clinical Research Development Unit of Rouhani Hospital, Pathology Department-Rohani Hospital of Babol, Babol University of Medical Sciences, Babol, Iran

<sup>4</sup>Social Medicine department, Babol University of Medical Sciences, Babol, Iran

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### Abstract

**Background:** Despite the fact that many studies have been published about the risk factors associated with gestational diabetes mellitus, its prevalence remains high. The aim of this study was to examine the relationship between the history of irregular menses and gestational diabetes mellitus among pregnant women.

**Methods:** This case-control study was conducted on 51 pregnant women with gestational diabetes mellitus in prenatal clinics of Ayatollah Rouhani hospital in Babol, Mazandaran, from January 1, 2014 to December 31, 2015. At first, women with family history of diabetes mellitus, pre-pregnancy diabetes mellitus, previous gestational diabetes mellitus, age >35 years, weight >110 kg were excluded from the study. Then, one random control was systematically selected for each case, which was matched for age. All statistical analyses were performed through SPSS (Version 22). P-values less than 0.05 were considered statistically significant.

**Results:** Irregular menses was not associated with gestational diabetes. The mean menarche at age was lower among the women with gestational diabetes ( $p=0.03$ ). There was a significant association between menarche at age and gestational diabetes (OR, 6.74; 95% CI, 1.41-32.17). Dysmenorrhea did not differ between subjects with and without menstrual irregularities.

**Conclusion:** We concluded that early menarche at age (<12 years) could be an important consideration for obstetricians, who adopt a selective screening approach to gestational diabetes.

**Keywords:** Gestational diabetes mellitus Irregular menses, Menarche at age

### Introduction

Gestational diabetes is the most common metabolic disorder during pregnancy (2).

Approximately, 4% of pregnancies are complicated by diabetes, 90% of which are gestational diabetes (3) with severe maternal and fetal complications such as preeclampsia, premature rupture of membranes, preterm delivery, cesarean section, hydramnios, fetal macrosomia, hypoglycemia and the low-birth weight of

\*Corresponding author: Dr. Zinatossadat Bouzari, Department of obstetrics & gynecology, Babol University of Medical Sciences, Ganjafroz, Babol, Iran Tel: +98-11-32360714, Email: z\_b412003@yahoo.com

the infant (3-10). The prevalence of gestational diabetes varies from 1-14% in different parts of the world (2, 11). The review study on the prevalence of gestational diabetes in Iran in 2008 was as follows: the prevalence in different parts of Iran was 1.3 to 8.9; its prevalence among women with no risk factor in Tehran was 4.4%; and in women having at least one risk factor in Sari city was reported to be 10% (12). The known risk factors for gestational diabetes include age, history of diabetes in first-degree relatives, obesity, and polycystic ovarian syndrome (4, 5, 13-15). One of the common manifestations of PCOs is irregular menstruation (48- 49). Therefore, we hypothesized that irregular menstrual could predict gestational diabetes mellitus because of the association of PCOs with oligo-ovulation. A few studies have shown a significant association between menstrual irregularity and gestational diabetes (17), menorrhagia and gestational diabetes (18), oligomenorrhea and amenorrhea with hyperinsulinemia (19), menstrual cycles longer than 40 days or so, and irregular and type 2 diabetes (20, 21). Since the discoveries of new risk factors require extensive studies and can also increase the sensitivity of screening programs, the aim of this study was to evaluate the relationship between the history of irregular menses and gestational diabetes mellitus among pregnant women.

### Materials and Methods

This case-control study was conducted on pregnant women with gestational diabetes mellitus in prenatal clinics of Ayatollah Rouhani hospital in Babol, Mazandaran, from January 1, 2014 to December 31, 2015. All patients in the study were given written consents. This study was approved by the Ethics Committee of the University of Medical Sciences. This sample number can identify 95% confidence level and 80% test power the 0.5 size of variables of menstrual disorder for the incidence of gestational diabetes.

Gestational diabetes was diagnosed based on the presence of  $\geq 2$  of the following abnormal plasma glucose in a 3-hour of 100 gram oral glucose tolerance testing: fasting  $\geq 105$  mg/dL, 1-hour  $\geq 190$  mg/dL, 2hour  $\geq 165$  mg/dL, and 3-hour  $\geq 145$  mg/dL. About sixty pregnant women referring to routine prenatal care clinics were diagnosed with gestational diabetes during the two years.

In order to determine the associated gestational diabetes accurately, women with a history of family diabetes mellitus, pre-pregnancy diabetes mellitus, previous gestational diabetes mellitus, age  $>35$  years, weight  $>110$  kg were excluded because these are known as traditional risk factors for gestational diabetes.

Then, initially, information on age, a family history of diabetes mellitus, pre-pregnancy diabetes mellitus, previous gestational diabetes mellitus, and weight were recorded, according to which 9 cases (17.6 %) were excluded and 51 cases remained for the study. After the selection of the case group, for each case, one random control was systematically selected, which was matched in terms of age. Variables of this study included anthropometry variables (weight, height, and body mass index), socioeconomic variables (education level, economic status), alcohol intake, smoking, menarche age, and pre-gestational menstrual histories. Menstrual status was divided into two categories known as regular and irregular menses. The women who reported their menstrual cycle  $\geq 40$  days were categorized as irregular menstrual cycles. None of the

Table 1. Characteristics of women with and without gestational diabetes

Variables	With gestational diabetes N= 51 Mean $\pm$ SD	without gestational diabetes N= 51 Mean $\pm$ SD	P value
Age (years)	28.0(5.0)	28.0(4.6)	0.653
Weight (Kg)	75.8(14.0)	76.3(13.9)	0.832
Height (Cm)	161.5(5.9)	160.8(5.8)	0.927
Body mass index (kg/m <sup>2</sup> )	29.0(4.9)	29.5(5.6)	0.469
Menarche age (years)	13.2(1.3)	12.7(1.3)	0.03
Education level (years)			
<9	23(45.1)	22(43.1)	0.137
9-11	17(33.3)	10(19.6)	
$\geq 12$	11(21.6)	19(37.3)	
Economic status			
Good	21(41.2)	23(45.1)	0.917
Moderate	25(49.0)	23(45.1)	
Bad	5(9.8)	5(9.8)	

women reported alcohol use, cigarette smoking, and hormonal drugs within and before the pregnancy period. The base-line demographics, body mass index, and menstrual history were compared between the two groups.

All analyses were performed with SPSS (Version 22.0). Chi-Square and independent t-test were used for the qualitative and quantitative variables. P values less than 0.05 were considered significant.

## Results

The average age of the participants was  $27.1 \pm 4.9$  (minimum age 18 years and maximum age 35 years). The groups were similar in age, weight, height, body mass index, education level, parity, and economic status. The mean menarche at age was lower among the women with gestational diabetes ( $p=0.03$ ) (Table 1), and the lower menarche was more frequent among the women with gestational diabetes ( $p=0.008$ ). There was a significant association between menarche at age and gestational diabetes (OR, 6.74; 95% CI, 1.41-32.17). Irregular menses was not associated with gestational diabetes. Dysmenorrhea did not differ between subjects with and without menstrual irregularities (Table 2).

## Discussion

According to the findings of this case-control study, irregular menstruation was not associated with gestational diabetes. Haver et al. found that women with menstrual disorder were more likely to get gestational diabetes, 75.3 times (CI 95%=1.28-11.51)

diagnosis of diabetes according to World Health Organization criteria or the Carpenter and Kastan criteria in different studies.

In our study, the age of first menarche is associated with gestational diabetes, which is consistent with the results of Liwei Chen et al. who represented early age of menarche as a novel risk factor for gestational diabetes (47). However, this is incongruous with the result of a study by Karimian et al. in 2006 (39). This discrepancy can be attributed to differences in the age distribution of the study subjects.

The aims of screening for gestational diabetes mellitus is to prevent its adverse effects on the baby and also to determine the individuals, who are at risk for the development of type 2 diabetes mellitus later in life. Many studies defined risk factors of gestational diabetes. In studies by Seshiah et al. (2003) (29), Boriboonhirunsarn et al. (2006) (30), and Gatahun et al. (2010), it was found that women aged between 25-35 years were at risk of gestational diabetes (31). In a study on risk factors for gestational diabetes in 2014, Sreekanthan et al. found that age was associated with diabetes during pregnancy (28). Therefore, we matched age among the two groups. In addition, Yang et al. in 2009 (35), Kaaja et al. in 2009 (36), Tabak et al. in 2011 (37) and Al-Rowaily et al. in 2010 also found the history of diabetes in first-degree relatives as the risk factor for diabetes during pregnancy (38). Due to genetic similarities, pregnant women with a family history of diabetes are at increased risk of gestational diabetes than other women. Several studies have shown that body mass index of the women before pregnancy can be a predicting factor for gestational diabetes (41, 32, 42, 28). Therefore, it can be realized why we controlled traditional risk factors of gestational diabetes in the two groups in this study.

One limitation of this study was that the menstrual cycle information was evaluated based on the patient's memory at the time of pregnancy, which is of low accuracy, and another limitation was the size of the sample. Therefore, it is vital to conduct further prospective studies to assess the potential risk factors for the irregular menses and gestational diabetes mellitus with larger samples. It would also be better to obtain information about menstrual cycle before the pregnancy.

Table 2. History of specifications of the menstrual cycle in women with and without gestational diabetes.

Variables	Without gestational diabetes N= 51 N(%)	With gestational diabetes N= 51 N(%)	P value
<i>Menstrual status</i>			
Regular menstrual	44(86.3)	40(78.4)	0.299
Irregular menstrual	7(13.7)	11(21.6)	
<i>Dysmenorrheal</i>			
Yes	15(29.4)	21(41.2)	0.214
No	36(70.6)	30(58.8)	
<i>Menarche at age</i>			
<12	2(3.9)	11(21.6)	0.008
≥12	49(96.1)	40(78.4)	

## Conclusion

This study helped us realize the importance of early menarche age identifying factors affecting the health of pregnant women. The results of this study can persuade midwives, physicians, and health care practitioners to pay attention to menarche age before pregnancy. We did not find any association between irregular menstruations and gestational diabetes.

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## Conflict of interest

None declared.

## References

1. American Diabetes A. Diagnosis and classification of diabetes mellitus. *Diabetes Care*. 2010;33 Suppl 1:S62-69.
2. Xiong X, Saunders LD, Wang FL, Demianczuk NN. Gestational diabetes mellitus: prevalence, risk factors, maternal and infant outcomes. *Int J Gynaecol Obstet*. 2001;75(3):221-228.
3. Hirst JE, Tran TS, Do MA, Morris JM, Jeffery HE. Consequences of gestational diabetes in an urban hospital in Viet Nam: a prospective cohort study. *PLoS Med*. 2012;9(7):e1001272.
4. Deierlein AL, Siega-Riz AM, Chantala K, Herring AH. The association between maternal glucose concentration and child BMI at age 3 years. *Diabetes Care*. 2011;34(2):480-484.
5. Aulinas A, Biagetti B, Vinagre I, Capel I, Ubeda J, Maria MA, et al. [Gestational diabetes mellitus and maternal ethnicity: high prevalence of fetal macrosomia in non-Caucasian women]. *Med Clin (Barc)*. 2013;141(6):240-245.
6. Katon J, Reiber G, Williams MA, Yanez D, Miller E. Antenatal haemoglobin A1c and risk of large-for-gestational-age infants in a multi-ethnic cohort of women with gestational diabetes. *Paediatr Perinat Epidemiol*. 2012;26(3):208-217.
7. Fuchs F, Bouyer J, Rozenberg P, Senat MV. Adverse maternal outcomes associated with fetal macrosomia: what are the risk factors beyond birthweight? *BMC Pregnancy Childbirth*. 2013;13:90.
8. Parhofer KG, Hasbargen U, Ulugberdiyeva A, Abdullayewa M, Melebayewa B, Annamammedov A, et al. Gestational diabetes in Turkmenistan: implementation of a screening program and first results. *Arch Gynecol Obstet*. 2014;289(2):293-298.
9. Di Cianni G, Volpe L, Lencioni C, Miccoli R, Cuccuru I, Ghio A, et al. Prevalence and risk factors for gestational diabetes assessed by universal screening. *Diabetes research and clinical practice*. 2003;62(2):131-137.
10. Khoshnniat Nikoo M, Abbaszadeh Ahranjani S, Larijani B. A review on the prevalence of gestational diabetes mellitus (GDM) in different regions of Iran. *Iranian Journal of Diabetes and Lipid Disorders*. 2009;8(1): 47-56.
11. Crete JE, Anasti JN. Diagnosis of gestational diabetes mellitus: can we avoid the glucose challenge test? *J Am Assoc Nurse Pract*. 2013;25(6):329-333.
12. Corrado F, Pintaudi B, Di Vieste G, Interdonato ML, Magliarditi M, Santamaria A, et al. Italian risk factor-based screening for gestational diabetes. *J Matern Fetal Neonatal Med*. 2014;27(14):1445-1448.
13. Godwin M, Muirhead M, Huynh J, Helt B, Grimmer J. Prevalence of gestational diabetes mellitus among Swampy Cree women in Moose Factory, James Bay. *CMAJ*. 1999;160(9):1299-1302.
14. Esmacilzadeh S, Delavar MA, Amiri M, Khafri S, Pasha NG. Polycystic ovary syndrome in Iranian adolescents. *Int J Adolesc Med Health*. 2014;26(4):559-565.
15. Kulshreshtha B, Arora A, Pahuja I, Sharma N, Pant S. Menstrual cyclicity post OC withdrawal in PCOS: Use of non-hormonal options. *J Obstet Gynaecol*. 2016 Mar 16:1-6.
16. Haver MC, Locksmith GJ, Emmet E. Irregular menses: an independent risk factor for gestational diabetes mellitus. *Am J Obstet Gynecol*. 2003;188(5):1189-1191.
17. Heidari T, Kariman N, Afrakhteh M, Alavi Majd H. The study of relationship between menorrhagia and gestational diabetes. *koomesh*. 2008;9(2):147-154.
18. Weiss DJ, Charles MA, Dunaif A, Prior DE, Lillioja S, Knowler WC, et al. Hyperinsulinemia is associated with menstrual irregularity and altered

- serum androgens in Pima Indian women. *Metabolism*. 1994;43(7):803-807.
19. Solomon CG, Hu FB, Dunaif A, et al. Long or highly irregular menstrual cycles as a marker for risk of type 2 diabetes mellitus. *JAMA*. 2001;286(19):2421-2426.
  20. Sreekanthan K, Belicita A, Rajendran K, Vijayakumar A. Prevalence of Gestational Diabetes Mellitus in a Medical College in South India: A Pilot Study. *Indian Journal of Clinical Practice*. 2014;24(4):341-347.
  21. Roumain J, Charles MA, de Courten MP, Hanson RL, Brodie TD, Pettitt DJ, et al. The relationship of menstrual irregularity to type 2 diabetes in Pima Indian women. *Diabetes Care*. 1998;21(3):346-349.
  22. Chen L, Li S, He C, Zhu Y, Buck Louis GM, Yeung E, et al. Age at Menarche and Risk of Gestational Diabetes Mellitus: A Prospective Cohort Study Among 27,482 Women. *Diabetes Care*. 2016;39(3): 469-471.
  23. Seshiah V, Sahay B, Das A, Shah S, Banerjee S, Rao P, et al. Gestational diabetes mellitus-Indian guidelines. *Journal of the Indian Medical Association*. 2009;107(11):799.
  24. Boriboonhirunsarn D, Talungjit P, Sunsaneevithayakul P, Sirisomboon R. Adverse pregnancy outcomes in gestational diabetes mellitus. *J Med Assoc Thai*. 2006;89 Suppl 4:S23-28.
  25. Getahun D, Fassett MJ, Jacobsen SJ. Gestational diabetes: risk of recurrence in subsequent pregnancies. *Am J Obstet Gynecol*. 2010;203(5):467 e1-6.
  26. Yang X, Hsu-Hage B, Zhang H, Yu L, Dong L, Li J, et al. Gestational diabetes mellitus in women of single gravidity in Tianjin City, China. *Diabetes Care*. 2002;25(5):847-851..
  27. Kaaja R, Ronnema T. Gestational diabetes: pathogenesis and consequences to mother and offspring. *Rev Diabet Stud*. 2008 Winter;5(4):194-202.
  28. Tabak AG, Tamas G, Peterfalvi A, Bosnyak Z, Madarasz E, Rakoczi I, et al. The effect of paternal and maternal history of diabetes mellitus on the development of gestational diabetes mellitus. *J Endocrinol Invest*. 2009;32(7):606-610.
  29. Al-Rowaily MA, Abolfotouh MA. Predictors of gestational diabetes mellitus in a high-parity community in Saudi Arabia. *East Mediterr Health J*. 2010;16(6):636-641..
  30. Zargar AH, Sheikh MI, Bashir MI, Masoodi SR, Laway BA, Wani AI, et al. Prevalence of gestational diabetes mellitus in Kashmiri women from the Indian subcontinent. *Diabetes research and clinical practice*. 2004;66(2):139-145.
  31. Sivakumar V, Rajasekeran A, Arummugam A. Assesment of Risk Factors for the Early Detection of Gestational Diabetes Mellitus. *Int J of Pharma Sciences and Research*. 2014;5(3):114-118.
  32. Hadaegh F, Tohidi M, Harati H, Kheirandish M, Rahimi S. Prevalence of gestational diabetes mellitus in southern Iran (Bandar Abbas City). *Endocr Pract*. 2005;11(5):313-318.