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Menarche age and the risk of diabetes: A cross-sectional study in South-Eastern Iran

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Abstract

Background and Aims: Diabetes is a major public health problem worldwide. This study aimed to determine the relationship between menarche age and overt diabetes in southeast Iran.

Methods: This cross-sectional study was conducted on 6094 eligible women between the ages of 35 and 70 participating in the Zahedan Adult Cohort Study. Demographic and background data, fertility, anthropometry, and disease history were collected based on a questionnaire. Menarche age was classified into five categories (under 12 years, 12, 13, 14, 15 years and more). Diabetes is defined as a blood sugar of 126 or more according to the definition by the American Diabetes Association. Data analysis was done using SPSS 26 software. Descriptive analysis was performed with frequency, percentage, mean, and standard deviation; and analytical analysis using chi-square and logistic regression tests. The significance level in this study was $p < 0.05$.

Results: The participants' mean age was 49.41 ± 8.88, and the mean age at menarche was 13 ± 1.49. 22.8% (1389 women) of participants with diabetes and 77.2% (4705 women) did not have diabetes. The findings showed that the chance of developing diabetes in women with a menarche age <12 years was significantly higher than in women with a menarche age of 13 years (reference) (OR = 1.23, 95% CI: 0.96, 1.51). This relationship was significant after adjusting variables such as body mass index, education level, fertility factors, history of diabetes, and reproductive diabetes (OR = 1.21, 95% CI: 0.90, 1.44, $p = 0.04$).

Conclusion: Our findings suggest that young age at menarche may be a risk factor for diabetes in adulthood. Further prospective studies are needed to confirm our findings. However, it is suggested to pay attention to it in diabetes screening so that, if possible, by identifying people at risk and implementing prevention programs, the adverse consequences of diabetes can be reduced.

KEYWORDS
diabetes, menarche, Persian cohort, risk factors, women's health

1 | BACKGROUND

Diabetes is a major public health problem worldwide,[1] which, together with cardiovascular diseases, cancer and respiratory diseases, accounts for more than 80% of premature deaths from non-communicable diseases (NCDs) and is one of the 10 leading causes of death in is the world.[2] This disease is associated with increased mortality from infections, cardiovascular diseases, stroke, chronic kidney disease, chronic liver disease and cancer.[3] In this disease, a set of heterogeneous metabolic disorders occurs, the main finding of which is chronic hyperglycemia. Absence of insulin secretion, impaired secretion, or both conditions may occur in affected people.[4] Although progress has been made in improving the health of the population and increasing life expectancy, diabetes is the second factor with a negative effect on reducing life expectancy adjusted by the World Health Organization.[5] According to the report of the International Diabetes Federation, 451 million people were diagnosed with diabetes in 2017, and the number of patients is expected to increase to 693 million by 2045.[1] In the meantime, the Middle East and North Africa (MENA) region has the highest global prevalence of diabetes in the 20–79-year-old population with a prevalence of 10.9%.[6] According to the report of the World Health Organization, the prevalence of diabetes in Iran in the age group of 20–74 years is 9.6% in men and 11.1% in women, and 10.3% of the adult population of Iran are suffering from diabetes in general.[7,8] It is predicted that nearly 9.2 million Iranians will have diabetes by 2030.[9] With the increasing prevalence of diabetes, identifying the risk factors that cause it is one of the health priorities.[10] Biological factors are considered to be one of these risk factors that underlie the risk of type 2 diabetes, and its effect began years ago in the form of a disorder in blood sugar control.[11] The biological processes involved in the development of puberty may also be an example of the primary determinants of life in later diseases.[12]

Obesity is a known risk factor for impaired glucose tolerance and diabetes, which seems to be related to childhood.[13,14] Obesity likely effective the circulating levels of insulin, testosterone, and insulin-like growth factors also the metabolism by the secreting of hormones, glycerol, leptin, and the release of nonesterified fatty acids (NEFAs), and increases insulin resistance.[15,16] Insulin resistance is a key factor in the development of type 2 diabetes and metabolic syndrome.[12] It is said that early menstruation and longer exposure to estrogen and steroids may maintain a predisposition to obesity.[17] Therefore, it appears that early menarche is associated with obesity risk, which can be associated with increased blood glucose levels and insulin resistance.[11,17] Studies on the relationship between the age of menstruation and the risk of diabetes have conflicting findings, so some of them confirm this relationship[12,18,19] and others reject it.[20,21] Considering the contradictory results of the studies, the need for a comprehensive and supplementary study seems necessary. Because the age of menarche is considered one of the important phenomena in the stages of female puberty and it seems to be related to the level of glucose and insulin resistance; the present study was conducted to determine the relationship between menarche age and risk of diabetes in women of Zahedan city.

2 | METHODS

2.1 | Study design and sampling

The current study is a cross-sectional (descriptive-analytical) study based on the primary data of the cohort study of Zahedan city (part of the large Persian cohort study) to investigate the relationship between menarche age and diabetes in 6099 women participants who had registered from October 2015 to January 2019. The sampling was done in a multistage stratified manner. In this method, the city of Zahedan was divided into three regions (outskirts, city center and upper city) according to municipal areas and socio-economic class. Then it was randomly selected from among the classes of a comprehensive health service center. In the next step, several clusters were selected from each center and in each household from the cluster of all eligible women aged 35–70 years. This study's aims, foundation, and design have been previously published.[22]

All women between 35 and 70 years of age who had Iranian citizenship and had lived in Zahedan for at least 9 months and consented to participate in the study were included in the study. And women who could not cooperate in the study due to any disability and physical or mental disability, and incomplete questionnaires were excluded from the study.[22]

After selecting the eligible people to participate in the study, they were invited to attend the cohort center in Zahedan through a phone call. Then the necessary explanations on how to conduct the research and the high value of cooperation in it were explained. In case of consent to participate in the study, the questionnaire was completed by a trained person.

2.2 | Data collection tools

The measurement tools in this study include questionnaires that were previously validated and confirmed in the Persian cohort study.[22,23] These questionnaires are divided into three sections: general information, medical information, and nutritional information, and they contain 482 questions. The questionnaires of the public sector include questions related to demographic factors, economic and social status, employment status, exposure to fuels, lifestyle, physical activity level, circadian rhythm of sleep, use of mobile phones and exposure to toxins and pesticides. The questionnaire related to the medical part also includes questions to check the medical history of people, drug records, history of family medical records, women's fertility history, oral and dental health status and behavioral habits of people (alcohol, opium, smoking and hookah consumption), blood pressure measurement and physical examinations. The questionnaire of the nutrition department also includes the questionnaire on food frequency, current eating habits, food preparation and storage technique. Anthropometrics and a 25 mL blood sample were also collected, with 15–25 mL taken from each participant after a 12-h fast before sampling. A return link to the test was then sent to the participant via his SMS within 24 h of study entry. In addition, subjects with abnormal tests were referred by the cohort study physicians to the hospital for specific tests as needed.[22,23]

2.3 | Data analysis

The statistical analysis was performed in SPSS 26. Descriptive analysis was performed with frequency, percentage, mean, and standard deviation; and analytical analysis using chi-square and logistic regression tests (forward method). The significance level in this study was $p < 0.05$.

2.4 | Ethical considerations

The study design of the Persian cohort has been approved by the ethics committee of the Ministry of Health and Medical Education, the Institute of Gastrointestinal Diseases, the Tehran University of Medical Sciences, and every medical university participating in this study. The ethics committee of Zahedan University of Medical Sciences approved the study protocol (approval numbers: IR. ZAUMS. REC.1393–96451). Also, the current study has been approved by the ethics committee of Zahedan University of Medical Sciences with code IR. ZAUMS. REC.1402.112. Regarding the ethical considerations, the information was kept confidential, and informed written consent was obtained from the participants; moreover, they were allowed to leave the study at any stage.

3 | RESULTS

Among 6094 participants, 1389 women had diabetes. Demographic characteristics showed the mean (standard deviation) women's age, and first menstruation age were 49.41 ± 8.88, 13 ± 1.49 respectively. 2281 (37.7%) women were overweight and 4948 (81.2%) were inactive. The percentage of diabetes, overweight, and number of children were higher in people who reported the onset of menarche as less than 12 years (Table 1). According to the obtained results, there was a significant increase in the chance of diabetes in women with menarche onset age less than 12 years, compared to women with menarche age 13 years (reference) (OR = 1.23, 95% CI: 0.96, 1.51). In the next step, the effect of body mass index (BMI) in the model was evaluated. The results showed that there was a significant increase in the chance of developing diabetes again in women whose menarche age was less than 12 years compared to the reference (13 years) (OR = 1.25, 95% CI: 0.94, 1.48).

In model number 3, after entering education, the chance of diabetes in this group of women was slightly but significantly adjusted (OR = 1.19, 95% CI: 0.95, 1.51). In model 4, family history of diabetes and gestational diabetes were investigated. The results showed that in the presence of these factors, people with a menarche age of less than 12 years have a 23% higher chance of developing diabetes than the reference group (13 years) (OR = 1.23, 95% CI: 1.03, 1.46). In model 5, the effect of fertility factors such as the age of the first pregnancy, the number of children, and the use of birth control pills were evaluated. In the presence of these factors, there was no significant relationship between the menarche age and the chance of diabetes ($p = 0.08$), but People who had more children (≥5) compared to the reference class (≥ 1) independently had a significantly increased chance of diabetes (OR = 2.25, 95% CI: 1.37, 3.84, $p = 0.02$).

In the next step, from the sum of variables entered into the final model (menarche age, education, body mass index, family history of diabetes, history of gestational diabetes, number of children, age of first pregnancy and use of birth control pills), menarche age, education, body mass index, History of family diabetes and gestational diabetes had a significant effect on the chance of developing diabetes. People who reported a menarche age of less than 12 years had a 21% higher chance of developing diabetes than 13 years (reference) (OR = 1.21, 95% CI: 0.99, 1.44, $p = 0.048$). In people who had a higher level of education (higher than a bachelor's), the chance of developing diabetes was 67% lower than that of uneducated people (reference) (OR = 0.33, 95% CI: 0.21, 0.52, $p = 0.001$). People with a body mass index (BMI) of 30 or more had a significantly increased chance of developing diabetes compared to people with a body mass index of less than 18.5 (reference) (OR = 3.38, 95% CI: 2.06, 5.52, $p = 0.001$). Finally, people who reported a history of family diabetes (OR = 2.63, 95% CI: 2.03, 3.40) and gestational diabetes (OR = 2.80, 95% CI: 2.44, 3.21) compared to people who had a history of family diabetes or gestational diabetes did not have a significantly higher chance of developing diabetes ($p = 0.67$) (Table 2).

Based on having or not having diabetes, it showed that the chance of having diabetes increases with increasing age and BMI. So that the age of 65 years and more increased eight times (OR = 8.08, 95% CI: 6.06–10.74, $p < 0.001$) and BMI 30 and more, six times compared to the reference group (OR = 6.15), 95% CI: 3.11–12.15, $p < 0.001$). On the other hand, people with university education were 64% less likely to develop diabetes compared to the reference group (OR = 0.36, 95% CI: 0.27–0.48, $p < 0.001$). The history of taking birth control pills and smoking had no effect on diabetes ($p > 0.05$) (Table 3).

4 | DISCUSSION

This study, which was conducted to investigate the effect of menarche age on the chance of developing diabetes in women aged 35–70 in Zahedan, showed that the age of menarche can be effective in increasing the chance of developing diabetes. In women who reported menarche at the age of 12 and under, after controlling for

TABLE 1 Baseline characteristics of participants according to menarche age; number (%).

Variable		Menarche age (year) 12> 669 (11)	12 1890 (31)	13 1446 (23.7)	14 1256 (20.6)	≥15 833 (13.7)	*p*-value[a]	Sum 6094 (100)
Age (year)	35–44	221 (10.6)	567 (27.1)	518 (24.7)	482 (23)	305 (14.6)	<0.001	2093 (34.3)
	45–54	245 (11.7)	649 (30.9)	503 (23.9)	442 (21)	263 (12.5)		2102 (34.5)
	55–65	165 (10)	581 (35.3)	362 (22)	297 (18.1)	240 (14.6)		1645 (27)
	65<	38 (15)	93 (36.6)	63 (24.8)	35 (13.8)	25 (9.8)		254 (4.2)
Diabetes	Yes	169 (12.2)	470 (33.8)	332 (23.9)	243 (17.5)	175 (12.6)	0.001	1389 (22.8)
	No	497 (10.6)	1414 (30.2)	1109 (23.7)	1010 (21.5)	675 (14)		4705 (77.2)
Marriage status	Married	548 (11)	1547 (31)	1189 (23.8)	1014 (20.3)	696 (13.9)	0.006	4994 (81.9)
	Single	17 (11.3)	27 (18)	39 (26)	48 (32)	19 (12.7)		150 (2.5)
	Widow	104 (10.9)	316 (33.3)	218 (22.9)	194 (20.4)	118 (12.4)		950 (15.6)
BMI	18.5>	30 (10.1)	91 (30.7)	63 (21.3)	56 (18.9)	56 (18.9)	0.001	296 (4.9)
	18.5–24.9	117 (8.9)	414 (31.4)	312 (23.7)	293 (22.2)	181 (13.7)		1317 (21.8)
	25–29.9	250 (11)	675 (29.6)	538 (23.6)	475 (20.8)	343 (15)		2281 (37.7)
	≥30	267 (12.4)	695 (32.3)	519 (24.1)	429 (19.9)	241 (11.2)		2151 (35.6)
Education	Unable to read and write	196 (11.3)	624 (35.9)	419 (24.1)	311 (17.9)	187 (10.8)	0.001	1737 (28.5)
	Elementary and high school level 1	259 (12.3)	661 (31.4)	486 (23.1)	430 (20.4)	268 (12.7)		2104 (34.5)
	High school level 2 and diploma	181 (10.4)	494 (28.3)	412 (23.6)	393 (22.5)	268 (15.3)		1748 (28.7)
	Master's and bachelor's degree	17 (8.7)	46 (23.5)	45 (23)	42 (21.4)	46 (23.5)		196 (3.2)
	Master's degree and higher	16 (5.2)	65 (21)	84 (27.2)	80 (25.9)	64 (20.7)		309 (5.1)
Physical activity	Inactive	538 (10.9)	1523 (30.8)	1201 (24.3)	1016 (20.5)	670 (13.5)	0.35	4948 (81.2)
	Active	131 (11.4)	367 (32)	245 (21.4)	240 (20.9)	163 (14.2)		1146 (18.8)
Cigarette smoking	Yes	22 (14.7)	44 (29.3)	42 (28)	24 (16)	18 (12)	0.28	150 (2.5)
	No	647 (10.9)	1845 (31)	1404 (23.6)	1232 (20.7)	815 (13.7)		5943 (97.5)
Family history of diabetes	No	277 (10.9)	812 (31.9)	599 (23.5)	524 (20.6)	333 (13.1)	0.67	2545 (41.8)
	Yes	392 (11)	1077 (30.4)	847 (23.9)	732 (20.6)	500 (14.1)		3548 (58.2)
Child number	0–1	41 (13.1)	80 (25.5)	78 (24.8)	68 (21.7)	47 (15)	0.001	314 (5.3)
	2–3	84 (7.6)	294 (26.7)	255 (23.2)	273 (24.8)	194 (17.6)		1100 (18.5)
	4–5	201 (11.9)	491 (29)	410 (24.2)	325 (19.2)	266 (15.7)		1693 (28.4)
	>5	327 (11.5)	1001 (35.1)	668 (23.4)	546 (19.2)	308 (10.8)		2850 (47.8)
Age of first pregnancy	15>	162 (18.1)	342 (38.8)	258 (28.8)	120 (13.4)	13 (1.5)	<0.001	895 (15.4)
	15–19	221 (10.1)	688 (31.3)	494 (22.5)	508 (23.1)	288 (13.1)		2199 (37.9)
	20–24	176 (9.4)	560 (30)	422 (22.6)	357 (19.2)	349 (5)		1864 (32.2)
	≥25	76 (9.1)	237 (28.3)	202 (24.1)	186 (22.2)	137 (16.3)		838 (14.5)
History of gestational diabetes	Yes	37 (11.8)	85 (27.1)	88 (28)	67 (21.3)	37 (11.8)	0.25	314 (5.2)
	No	632 (10.2)	1805 (31.2)	1358 (23.5)	1189 (20.6)	796 (13.8)		5780 (94.8)

TABLE 1 (Continued)

Variable		Menarche age (year) 12> 669 (11)	12 1890 (31)	13 1446 (23.7)	14 1256 (20.6)	≥15 833 (13.7)	*p*-value[a]	Sum 6094 (100)
Menopause	No	288 (10.9)	901 (34)	626 (23.6)	485 (18.3)	351 (13.2)	<0.001	2651 (43.5)
	Yes	381 (11.1)	989 (28.7)	820 (23.8)	771 (22.4)	482 (14)		3443 (56.5)
Taking oral contraceptive pill	Yes	357 (10.3)	1017 (29.5)	872 (25.3)	707 (20.5)	497 (14.4)	<0.001	3450 (56.6)
	No	312 (11.8)	873 (33)	547 (21.7)	549 (20.8)	336 (12.7)		2644 (43.4)

[a]*p* value from χ2 test.

TABLE 2 The odds ratio in the association between age of menarche and risk of diabetes using logistic regression.

Age at menarche Subgroups Variable	<12 OR	95% CI	12 OR	95% CI	13 OR	95% CI	14 OR	95% CI	≥15 OR	95% CI	*p*-value[a]
Model 1	1.23	0.96–1.51	1.21	1.03–1.44	1	Referent	0.86	0.70, 1.05	0.95	0.76–1.19	**0.001**
Model 2	1.25	0.94–1.48	1.20	0.98–1.39	1	Referent	0.89	0.73–1.09	0.826	0.76–1.08	**0.002**
Model 3	1.19	0.95–1.51	1.18	1.03–1.46	1	Referent	0.86	0.71–1.06	0.99	0.79–1.23	**0.04**
Model 4	1.21	0.96–1.53	1.20	1.01–1.44	1	Referent	0.85	0.69–1.04	0.97	0.77–1.21	**0.04**
Model 5	1.22	0.97–1.52	1.20	1.05–1.48	1	Referent	0.86	0.71–1.05	0.97	0.78–1.21	**0.001**
Model 6	1.21	0.99–1.44	1.19	0.96–1.36	1	Referent	0.88	0.72–1.09	0.91	0.83–1.31	**0.05**

Note: Model 1: Unadjusted, Model 2: Results were adjusted for BMI, Model 3: Results were adjusted for BMI and education levels, Model 4: Results were adjusted for Model 3 and family history diabetes and gestational diabetes, Model 5 were adjusted for age of first pregnancy, number of children and use of birth control pills, Model 6: Results were adjusted for models 2, 3, 4 and 5.

[a]Logistic regression test.

education, history of family diabetes and gestational diabetes, body mass index, and so forth, the chance of developing diabetes increased by 21%.

The results of Elks et al.'s study, which was conducted on 9590 women with an average age of 50 years, showed that every 1-year delay in menarche reduces the risk of diabetes by 9%.[24] The results of a meta-analysis study that evaluated a population of about 315,428 women from three cross-sectional studies and seven cohort studies showed that the risk of type 2 diabetes for the lowest age group at the time of menarche is 22% higher than the middle to upper age group.[25] Other studies also reached similar results,[26,27] which are consistent with the present study. It is not known by what mechanism premature menarche can contribute to the occurrence of diabetes in the later stages of life, but the relationship between the low level of insulin-like growth factor-1 (IGF-1) and the increase in type 2 diabetes is known.[28,29] Estrogen modulates the secretory activity of growth hormone through two pathways. Low levels of estrogen stimulate IGF-1 secretion through growth hormone secretion, while high levels inhibit IGF-1 production and the onset of menarche. Therefore, exposure to high levels of estrogen may be a reason for the occurrence of diabetes in the later stages of life,[30,31] but on the other hand, studies also reported an inverse relationship between the age of menarche and diabetes[19] or no relationship.[18,20]

The differences might be explained by many factors, such as study design, sample size, population covered, age of participants, and the age range covered by Menarche. In the present study, after entering BMI, the percentage of diabetes in people who experienced earlier menarche increased slightly. This finding may be partly explained by the dual role of obesity in the development of menarche and type 2 diabetes. According to studies, obesity is associated with the early onset of puberty[31,32] and also with an increased risk of insulin resistance.[33] Gavela-Pérez et al. stated in their study that the pattern of secretion of adipokines, particularly leptin, appears to be more sensitive to weight gain at the age of 6–8 compared to youth. Therefore, an increase in leptin secretion during this growth phase can make individuals more susceptible to weight gain and early puberty.[34] Early menstruation and prolonged exposure to steroid hormones, both increase the likelihood of maintaining obesity.[11] The loss of sensitivity of body cells to insulin and the resistance of fat tissue to insulin result in a person becoming susceptible to diabetes.[35] Although, Fredriks et al. showed in their study the direct effect of early onset of puberty and hormonal factors on the risk of diabetes. and BMI has a limited effect on this relationship,[36] in some studies, the risk of increasing diabetes in people with a body mass index equal to or greater than 25 kg/m^2 was reported without relation to early menarche age.[18,27] It should be noted that most of the studies that have investigated the relationship between age at menstruation and

TABLE 3 Odds ratio (OR) of diabetes in participants according to demographic variables.

Variable		Without diabetes	With diabetes	OR (95% CI)
Age (year)	35–44	1889 (90.2)	204 (9.8)	1
	45–54	1599 (76)	503 (24)	2.89*** (2.42–3.44)
	55–65	1078 (65.5)	567 (34.5)	4.86*** (4.07–5.80)
	65	136 (53.5)	118 (46.5)	8.08*** (6.06–10.74)
Marriage status	Married	3882 (77.7)	1112 (22.3)	1
	Single	133 (88.6)	17 (11.4)	0.45** (0.27–0.75)
	Widow	677 (71.2)	271 (28.8)	1.41*** (1.20–1.65)
BMI	<18.5	145 (94.1)	9 (5.9)	1
	18.5–24.9	1229 (86.7)	243 (13.3)	3.15** (1.58–6.28)
	25–29.9	1768 (76.3)	549 (23.7)	4.98*** (2.52–9.83)
	30	1552 (72.1)	599 (27.9)	6.15*** (3.11–12.15)
Education	Unable to read and write	1201 (67)	578 (33)	1
	Elementary and high school level 1	2181 (79)	577 (21)	0.54*** (0.47–0.62)
	High school level 2 and diploma	918 (83.9)	180 (16.1)	0.39*** (0.32–0.48)
	Undergraduate/ postgraduate	395 (68.8)	68 (31.2)	0.36*** (0.27–0.48)
Physical activity	Inactive	3743 (75.6)	1205 (24.4)	1
	Active	952 (83)	194 (17)	0.64*** (0.54–0.75)
Cigarette smoking	No	4566 (76.8)	1377 (23.2)	1
	Yes	108 (72)	42 (28)	1.02 (0.50–1.83)
Family history of diabetes	No	1984 (77.9)	561 (22.1)	1
	Yes	2210 (62.2)	1339 (37.8)	2.57*** (2.27–2.90)
Child number	0–1	276 (87.8)	38 (12.2)	1
	2–3	891 (81)	209 (19)	0.92 (0.63–1.34)
	4–5	1320 (77.9)	373 (22.1)	1.45* (1.01–2.09)
	5	1771 (62.1)	1079 (37.9)	2.53*** (1.77–3.62)
Age of first pregnancy	<15	528 (58.9)	367 (41.1)	1
	15–19	1537 (69.8)	662 (30.2)	0.75* (0.60–0.94)
	20–24	1452 (77.8)	412 (22.2)	0.63*** (0.49–0.79)
	25	703 (84)	135 (16)	0.47*** (0.35–0.63)
History of gestational diabetes	No	4523 (78.2)	1257 (21.8)	1
	Yes	182 (57.9)	132 (42.1)	4.18*** (3.26–5.36)
Menopause	No	2910 (84.8)	522 (15.2)	1
	Yes	1780 (67.2)	882 (32.8)	2.71*** (2.40–3.07)
Taking oral contraceptive pill	No	2051 (77.5)	593 (22.5)	1
	Yes	2641 (76.5)	809 (23.5)	1.02 (0.89–1.16)

Abbreviations: CI, confidence interval; OR, odds ratio.

*$p < 0.05$; **$p < 0.01$; ***$p < 0.001$.

the risk of developing diabetes in the later stages of life considered adult BMI as a criterion. They argue that overweight and obesity tend to follow the same pattern throughout life.[18,19]

Another finding of the present study showed that after entering education into the model, the effect of menarche age on the occurrence of diabetes decreased slightly. So the risk of diabetes decreased in people with higher education. Studies that investigated the impact of socioeconomic factors and their relationship with diabetes showed that the risk of diabetes is lower in people with higher education.[34,35] Another finding of the present study showed that after entering education into the model, the effect of menarche age on the occurrence of diabetes decreased slightly. So the risk of diabetes decreased in people with higher education. Studies that investigated the impact of socioeconomic factors and their relationship with diabetes showed that the risk of diabetes is lower in people with higher education.[37,38] It seems that people with higher levels of education may have better access to health information and are more concerned about their health, which leads to a healthier diet and lifestyle and less obesity. However, some findings such as population disproportion with high education compared to other groups, the type of screening or undiagnosed cases of diabetes require further research. According to the findings of the present study, the presence of factors such as a history of gestational diabetes or diabetes in the family along with premature menarche can increase the risk of diabetes by 23%. Other studies in different populations also reported similar results.[39,40] Type 2 diabetes is a hereditary factor from first-degree family members and is associated with gene mutations that can be passed on to an individual.[41]

On the other hand, the age of onset of menarche also has a high degree of heredity, which is estimated between 57% and 82%, so the relationship between the age of menarche independent of other factors may be biologically through exposure to hormones and changes in glucose metabolism increase the incidence of diabetes in women with premature menarche.[40] In the present study, after adjusting for fertility factors (number of children, first pregnancy, and use of birth control pills), no correlation was found between early menarche and diabetes. However, the number of children factor was independently related to the probability of diabetes so women with more children were 25% more at risk than women with fewer children. In line with the results of the present study, a cohort study also reported an increase in the risk of diabetes with an increase of 6% per live birth.[39] Researchers stated the cumulative exposure of repeated periods of increased insulin resistance and proliferation of pancreatic beta cells following pregnancy and the subsequent dysfunction of beta cells as the possible reason for increasing the risk of diabetes,[42] but other studies of the relationship between the number of pregnancies and other factors They did not report fertility with an increased risk of diabetes.[18,43] The maximum number of children, the sample size, and the age of the research population can influence the contradiction of the results.

One of the strengths of the current study was the investigation of the relationship between the age of menstruation and diabetes in a large sample of women, based on the first cohort study of the Sistani and Baloch peoples in southeastern Iran. Therefore, these results can be generalized to women in the age group of 35 years and above but should be interpreted with caution in other age groups.

This study also had limitations, which include not performing a glucose tolerance test or performing a hemoglobin A1C (HbA1C) laboratory test, as well as bias related to recalling the age of menarche can affect the results. Another limitation of the study is that we could not control for many demographic characteristics. We did not know about BMI during childhood or menstruation onset nor about the lifestyle of that period. Also, this study was a self-reported record. To control this limitation, clinical interviewers and physicians performed a detailed clinical evaluation and reviewed available documentation. Therefore, it is recommended to conduct further studies controlling for demographic characteristics, more accurate diagnostic tests, and other ethnicities.

5 | CONCLUSION

The results of the present study, based on a large population-based group, showed that the age of menarche has a role in the risk of diabetes in women, so it should be considered as a risk factor in diabetes screening, to identify people at risk. The risk and implementation of prevention programs reduced the adverse outcomes of diabetes. Therefore, it is recommended to implement strategies to prevent premature menstruation along with other risk factors such as overweight and obesity.

AUTHOR CONTRIBUTIONS

Somayyeh Khazaeian: Conceptualization; data curation; formal analysis; project administration; writing—original draft; writing—review and editing. **Fariba Shahraki-Sanavi**: Conceptualization; data curation; investigation; project administration; resources; supervision; visualization; writing—original draft; writing—review and editing. **Alireza Ansarimoghaddam**: Conceptualization; data curation; investigation; project administration; supervision; writing—original draft; writing—review and editing.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

All authors have read and approved the final version of the manuscript. F.S. had full access to all of the data in this study and takes complete responsibility for the integrity of the data and the accuracy of the data analysis.

ETHICS STATEMENT

The study was approved by the ethics committee of the Zahedan University of Medical Sciences (ethics committee approval code IR. ZAUMS. REC.1402.112.). As we used routinely collected anonymized electronic data, patient consent was not required. In this study, informed consent was not necessary because of the use of an online database.

TRANSPARENCY STATEMENT

The lead author Fariba Shahraki-Sanavi affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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