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Menstrual irregularity and premenstrual syndrome in women with diabetes in the reproductive age group: a comparative study

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Author contributions

AKK, FTY and GD is responsible for data collection and processing, analysis and interpretation; AKK and FTY carried out conceptual design, supervision, documentation, literature review, manuscript writing, critical review and other work. All authors have read and agreed to the final manuscript.

Competing interests

The authors declare no conflicts of interest.

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Abbreviations

PMSS, premenstrual syndrome scale; PMS, premenstrual syndrome; BMI, body mass index.

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Abstract

Background: The study was conducted to determine the frequency of menstrual irregularity in women with diabetes in the reproductive period and to reveal the relationship between menstrual irregularity and premenstrual syndrome by comparing women with diabetes to women without diabetes. **Methods:** In this cross-sectional and comparative study included 98 women with diabetes and 98 women without diabetes, aged 15–49 years. The study was carried out in a university hospital in Turkey between 01 June-30 September 2021. The data were obtained by using the woman identification form, the menstrual irregularity evaluation form, and the premenstrual syndrome scale. Student t-test and chi-square test were used to evaluate the data. **Results:** It was determined that women with diabetes had a higher rate of menstrual irregularity than women without diabetes (54.1% vs. 39.8%). Oligomenorrhea and menorrhagia were found to be more common in women with diabetes than in women without diabetes ($P < 0.05$). It was determined that women with diabetes had a moderate premenstrual syndrome experience level, and nearly half (55.1%) of them experienced premenstrual syndrome. It was determined that there was no difference in terms of premenstrual syndrome symptoms between women with diabetes and women without diabetes ($P > 0.05$). **Conclusions:** One out of every two women with diabetes in the reproductive period experienced menstrual irregularity, and oligomenorrhea and menorrhagia were more common in these women than in women without diabetes. In order to improve women's health and improve the quality of life in women with diabetes, it is recommended to examine the menstrual irregularity status in addition to diabetes management.

Keywords: diabetes; menstrual cycle; menstruation; women

Background

Today, diabetes is at an alarming level and one of the major public health problems. There is a rapid increase in the number of individuals with diabetes in the world due to changes in lifestyle, especially in nutrition and activity habits. Turkey is expected to be among the top 10 countries in the world in 2045 due to the increasing prevalence of diabetes. The increasing prevalence of diabetes also increases the prevalence of diabetes in women. Indeed, nearly half of individuals with diabetes worldwide are women [1]. With this, it is predicted that the incidence of diabetes, which is among the first 10 causes of mortality in adults, is 9% in women, and it is stated that this rate will continue to increase in the years to come (Saeedi et al., 2019). Diabetes influences the menstrual cycle and causes reproductive disorders [2]. The fact that many women of reproductive age are diagnosed with diabetes has now increased interest in the effects of diabetes on reproductive health, especially on the menstrual cycle [3].

Menstruation, which starts with menarche and ends with menopause, is considered one of the most important indicators of femininity [4]. Abnormal menstrual cycle span or variability is defined as menstrual irregularity. Menstrual irregularity is considered to affect 10-38% of women of reproductive age [5]. Menstrual irregularity is an important indicator of existing and potential health problems in women [6]. Menstrual d irregularity is widely considered to be a condition that requires medical treatment and should be addressed in terms of women's health since it also adversely affects women's biopsychosocial quality of life [7].

The menstrual cycle can potentially be affected in women with endocrinological disorders such as diabetes [8]. In the literature, it is stated that menstrual cycle irregularities are common in adolescent and adult women with diabetes [4, 9, 10, 11]. It is thought that diabetes impairs normal hypothalamic-pituitary-gonadal function, and especially impaired disease management negatively affects the menstrual cycle [12]. Menstrual irregularity is common in women with diabetes due to reasons such as decreased gonadotropin levels and hyperinsulinemia [4]. Obesity and insulin resistance can cause ovarian dysfunction, especially in women with type 2 diabetes [2]. Moreover, the imbalance in glycemic control levels can also affect the menstrual cycle [13]. Studies show that the prevalence of menstrual irregularity, such as oligomenorrhea and amenorrhea, is higher in women with type 1 diabetes than in healthy women [10, 14]. It is stated in the literature that increased anovulation is also common in women with type 2 diabetes [3].

One of the problems related to the menstrual cycle is premenstrual syndrome (PMS). PMS defines somatic, cognitive, emotional, and behavioral symptoms commonly seen in the reproductive age that occur in the luteal phase of the menstrual cycle in women and resolve with the onset of menstruation [7, 15]. Although PMS is not a life-threatening factor, it negatively affects women's quality of life and daily life activities. In the literature, it is stated that PMS affects women's family, work and friend relationships, and social activities negatively, alcohol and substance use, and tendency to crime [7]. When the literature was examined, no study was found that revealed the PMS status in women with diabetes.

Considering the increasing prevalence of diabetes today, it is possible that many women with diabetes may face menstrual irregularity, which may adversely affect women's health. It is envisaged that this study will guide counseling services in addressing the health problems that may develop related to the menstrual cycle in women with diabetes and make a scientific contribution to the literature.

This study aimed to determine the frequency of menstrual irregularity in women with diabetes in the reproductive period and to reveal the relationship between menstrual irregularity and PMS by comparing women with diabetes to women without diabetes.

Methods

Study design and population

The population of this cross-sectional and comparative study consisted of women who applied to the internal medicine, endocrinology, and metabolism outpatient clinics of a university hospital with complaints of diabetes between 01 June and 30 September 2021. The sample size in the study was calculated using power analysis. The values of p1 = 0.768 and p2 = 0.55 were taken as the basis for the menstrual irregularity variable in the reference study [16]. Accompanied by a sampling error of 0.05 to represent the population, the sample size was determined as the total number of people 162 at the significance level $\alpha = 0.05$, confidence interval of $1 - \alpha = 0.95$, risk of error of $\beta = 0.20$, at power of $1 - \beta = 0.80$ (group 1:81, group 2:81). In this context, 98 women with diabetes who were aged 15–49 years in the reproductive period, diagnosed with diabetes for at least six months, did not have any chronic diseases other than diabetes, were not pregnant, were not in the lactation or perimenopausal period, had no history of primary amenorrhea, polycystic ovarian syndrome, breast and ovarian carcinoma, do not use oral contraceptives, had no verbal communication barriers and agreed to participate in the study were included. For the control group, 98 healthy women without any chronic diseases and with similar characteristics who applied to the Family Health Center in the province where the study was conducted were included.

Data collection tools

The data were obtained by using the woman identification form, the menstrual irregularity, evaluation form, and the premenstrual syndrome scale (PMSS). The woman identification form was prepared by the researchers and includes the personal characteristics and disease information of women.

The menstrual irregularity evaluation form was created to determine the menstrual characteristics and irregularity of women. The presence of menorrhagia (more than 80 ml of blood loss in one cycle or menstruation lasting longer than 7 days), oligomenorrhoea (regular bleeding occurring at intervals longer than 35 days), polymenorrhea (regular bleeding occurring at intervals of less than 24 days), menorrhagia (bleeding at regular intervals and of normal duration, but requiring more than 21 pads during the menstrual period), hypomenorrhea (bleeding at regular intervals and of normal duration, but requiring less than 15 pads during the menstrual period), metrorrhagia (frequent bleeding at irregular intervals) and secondary amenorrhea (absence of bleeding for at least 3 normal cycle lengths) along with the menstrual cycle in the last three months was questioned to determine the menstrual disorder status. The participants who did not experience any of these were registered as having no menstrual irregularity while others were recorded as having menstrual irregularity [17].

The PMSS is a scale developed by Gencdogan to measure the severity of premenstrual symptoms [18]. In this scale, which is widely used in Turkey, there are 44 discourses marked by an individual considering "being in the term one week before the period". Five-point Likert-type PMSS consists of nine sub-dimensions (depressive affect, anxiety, fatigue, irritability, depressive thoughts, pain, appetite changes, sleep changes, bloating). Sub-dimension scores are obtained by summing the items in these dimensions, and the total score of PMSS is found by summing the sub-dimension scores. The lowest score that can be obtained from the scale is 44, while the highest score is 220. The higher the score, the more intense the PMS symptoms are. Moreover, those with a PMS total score greater than 50% are classified as PMS positive ($\leq$ 110 PMS negative; $\geq$ 111 PMS positive) [18]. In this study, the Cronbach's alpha value of the scale was found to be 0.82.

Application

The data were collected by the researchers through face-to-face interviews in a room where they could meet comfortably. The HbA1c value of women with diabetes was obtained from the laboratory result paper. The height and weight of the women were measured by the researchers with the measuring instruments in the institution where

the study was conducted. In line with the obtained values, body mass index (BMI) was calculated according to kg/m^2 calculation and, body structure was categorized as underweight (< 18.5 kg/m^2), normal weight (18.5–24.9 kg/m^2), overweight (25–29.9 kg/m^2) and obese (>30 kg/m^2). In the study, the presence of menstrual irregularity of in all participants was questioned in detail. It took approximately 20–25 minutes for the researchers to fill out the data forms and make the measurements.

In order to reduce the risk of bias in the study, data were collected through a scale with Turkish validity and reliability, and the literature review and article review processes were carried out independently by the researchers. The researchers controlled for extraneous variables by reviewing previous studies on the same subject.

Statistical analysis

The Statistical Package for the Social Sciences (SSPS) 22.0 program was used to evaluate the data obtained from the study. The distribution of the participants' sociodemographic, disease, and menstrual cycle characteristics was evaluated with the percentage and mean test. In the comparison of menstruation irregularity and PMS experience status in women with diabetes and women without diabetes, the student's t-test was used for quantitative data, the chi-square test was used for qualitative data, and the Fisher's Exact Test was used when any of the frequencies in the eyes was less than 5. Data were tested with 95% confidence levels. Statistical significance was evaluated at the 0.05 significance level in the evaluation of the data.

Ethical approval

Before collecting the data, written permission was obtained from the Sivas Cumhuriyet University Non-Invasive Clinical Research Ethics Committee (decision no: 2021-05/17) and the institution where the study would be conducted. Moreover, every woman in the study was informed about the content of the study and the voluntary participation, and their verbal and written consents were obtained.

Results

The average o age of women with diabetes was 36.63 ± 8.77 years, 87.7% were married, 34.7% were primary school graduates, 76.5% were unemployed, and 21.4% still smoked. It was determined that 21.4% of women with diabetes were overweight, and 31.6% were obese. The average o age of women without diabetes was 36.96 ± 7.10, 54.9% were married, 38.7% were primary school graduates, 19.4% still smoked, 19.8% were overweight, and 28.6% were obese. There is no statistically significant difference between age, education status, and body structure of women with diabetes and women without diabetes ($P < 0.05$).

The mean disease duration of women with diabetes was 6.15 ± 4.57 years, and 52% had type 2 diabetes. The mean HbA1c value of women with diabetes was found to be 6.76% ± 1.37%. Of the women, 44.9% received oral antidiabetic therapy, and 37.8% received insulin therapy. Of the women with diabetes, 88.8% stated that they used their medications regularly, and 64.3% received training from health professionals about their disease.

In Table 1, the menstruation-related characteristics of women are given. It was determined that there was a difference between women with diabetes and women without diabetes in terms of menstrual cycle pattern and menstrual irregularity ($P < 0.05$), and the rate of women with diabetes with irregular menstrual cycles and menstrual irregularities was higher. In the study, it was determined that oligomenorrhea and menorrhagia were observed more frequently in women with diabetes than in women without diabetes ($P < 0.05$).

In the study, it was determined that the PMS experience level of women with diabetes was moderate (112.17 ± 30.22), and nearly half (55.1%) of them experienced PMS. It was determined that women with diabetes did not differ in the level of depressive affect, anxiety, fatigue, irritability, depressive thoughts, pain, appetite changes, sleep changes, and bloating compared to women without diabetes ($P > 0.05$) (Table 2).

In the study, it was found that the duration of the disease, HbA1c value, body structure, smoking status, and the presence of other chronic diseases other than diabetes were not associated with the presence of menstrual irregularity in women with diabetes ($P > 0.05$). On the other hand, it was determined that the average age of women with diabetes who had menstrual irregularities was higher, and the rate of incidence of menstrual irregularity was more common in women with type 2 diabetes and using oral antidiabetic drugs ($P < 0.05$).

Table 1 Menstruation-related characteristics of women with diabetes and women without diabetes

Characteristic	Women with diabetes (n = 98)		Women without diabetes (n = 98)		Test	*P*
	n	%	n	%		
Age of menarche (year) (M ± SD)	13.53 ± 1.34		13.30 ± 1.05		t = 1.298	0.197
Menstrual cycle pattern						
Regular	72	73.5	85	86.7	χ^2 = 5.410	0.020*
Irregular	26	26.5	13	13.3		
Menstrual irregularity						
Yes	53	54.1	39	39.8	χ^2 = 4.015	0.045*
No	45	45.9	59	60.2		
Type of menstrual irregularity[a]						
Menorrhagia	18	18.4	20	20.4	χ^2 = 0.131	0.718
Oligomenorrhea	20	20.4	9	9.2	χ^2 = 4.897	0.027*
Polymenorrhea	14	14.3	11	11.2	χ^2 = 0.413	0.521
Menorrhagia	24	34.7	11	11.2	χ^2 = 5.878	0.015*
Hypomenorrhea	5	5.1	1	1.0	χ^2 = 2.751[b]	0.097
Metrorrhagia	14	14.3	1	1.0	χ^2 = 1.048[b]	0.306
Secondary amenorrhea	2	2.0	2	2.0	χ^2 = 0.000[b]	1.000

[a]The number n has increased; [b]Fisher Exact Test; *$P < 0.05$

Table 2 Premenstrual syndrome experience levels of women with diabetes and women without diabetes

The premenstrual syndrome scale	Women with diabetes	Women without diabetes	Test, *P*
Depressive affect	18.25 ± 5.85	19.27 ± 6.25	t = −1.178; 0.240
Anxiety	15.17 ± 5.68	14.85 ± 5.49	t = 0.396; 0.692
Fatigue	14.46 ± 5.31	17.42 ± 547	t = −1.245; 0.215
Irritability	13.27 ± 5.51	14.26 ± 5.34	t = −1.276; 0.204
Depressive thoughts	14.14 ± 5.52	15.86 ± 6.09	t = −0.872; 0.385
Pain	8.32 ± 3.00	7.98 ± 3.32	t = 0.744; 0.458
Appetite changes	9.15 ± 3.47	8.94 ± 3.45	t = 0.413; 0.680
Sleep changes	7.69 ± 3.28	7.97 ± 2.97	t = −0.866; 0.388
Bloating	8.78 ± 3.59	9.21 ± 3.79	t = −0.811; 0.418
General	112.17 ± 30.22	115.82 ± 31.25	t = −0.832; 0.407
PMS negative, n (%)	44 (44.9)	41 (41.8)	χ^2 = 0.187; 0.665
PMS positive, n (%)	54 (55.1)	57 (58.2)	

In the study, in the comparison between diabetic women with and without PMS, it was determined that the HbA1c value of diabetic women with PMS was higher than those without it, and the type of diabetes treatment was associated with PMS experience ($P < 0.05$) (Table 3).

Discussion

Menstrual irregularities can cause problems related to fertility and sexual life and can complicate the management of chronic diseases [5, 19]. On the other hand, menstrual irregularity are generally perceived as minor health problems and are ignored by women until they face with life-threatening situations [20]. Women with diabetes experience more menstrual irregularities and irregularity than women without diabetes, and this is ignored. In the study, it was determined that approximately half of the women with diabetes (54.1%) experienced menstrual irregularity, and this situation was higher than that of women without diabetes (39.8%). Another study found that women with type 1 diabetes had more menstrual irregularity (oligomenorrhoea, prolonged menstrual bleeding, and heavy menstrual bleeding) up to age 30 than their sisters and women without diabetes. In the same study, it was shown that type 1 diabetes was an independent risk factor for menstrual irregularity [16]. In a study conducted with Saudi young women with type 1 diabetes, it was determined that approximately one-fourth of the participants (26.5%) experienced menstrual irregularity [21]. In another study, it was found that 20.5% of young women with type 2 diabetes had menstrual irregularity [11]. In addition to these studies, a study of young women with type 1 diabetes found that irregular menstruation was quite common; It was determined that there was no difference (47.8% vs 40.3%) when compared with healthy women [14]. On the other hand, a cohort study found that women with irregular menstrual cycles had a 17% higher risk of diabetes compared to women with regular menstrual cycles [22]. Our study finding is similar to the literature. This study show that menstrual irregularity are common in women with diabetes in Turkey. Both the hormonal effect of diabetes and the emotional changes brought about by the disease can cause menstrual irregularities in women. This situation reveals the necessity of addressing women with diabetes in terms of improving their quality of life.

Despite improved treatment of diabetes in recent years, delayed menarche and menstrual irregularity are high in adolescent women with diabetes [23]. In the study, there was no difference in terms of age at menarche between women with diabetes and women without diabetes. There are many studies that investigated whether the age of menarche in diabetic women is different from the normal population. Findings in the literature contain contradictory data on this subject. For example, in the study by Morariu et al., it was determined that there was no difference between women with and without type 1 diabetes in terms of the age of menarche [13]. A study which was conducted with women with type 2 diabetes also found that age at menarche did not differ when compared to women without diabetes. Despite this, some studies found that women with type 1 diabetes had delayed menarches compared to women without diabetes [16, 19, 24]. In the study by Braham et al., it was determined that the age of menarche was delayed by 0.64 years in women diagnosed with diabetes after menarche when compared to women with type 1 diabetes diagnosed with diabetes before menarche [21]. Our study finding is not compatible with the literature. The fact that the age of menarche did not differ between diabetic and women without diabetes in this study may be due to the inclusion of women with both type 1 and type 2 diabetes in the study.

PMS is an important issue that should be addressed in women with diabetes in order to improve the quality of life, as it causes emotional problems and deterioration in daily life functions in women [18]. In the study, it was determined that nearly half (55.1%) of women with diabetes experienced PMS. However, in the study, it was determined that there was no difference between women with diabetes and women without diabetes in terms of PMS symptoms. In the study by Codner, Merino, and Tena-Sempere, it was emphasized that PMS was not a common complaint in women with type 1 diabetes, but glucose disorders were more common in women with PMS than in women without it [12]. Women with diabetes often report that they have difficulty in maintaining normal blood glucose control during their menstrual periods [25]. In women with PMS, especially emotional symptoms may further disrupt the regulation of blood glucose. This study is the first to evaluate the presence of PMS in women with diabetes.

In the literature, it is stated that physical and psychological factors such as age, age of menarche, BMI, physical activity, smoking, nutritional status, presence of chronic diseases are associated with menstrual irregularities [5, 6, 8, 20]. In the study, it was determined that the average age of women with diabetes who had menstrual irregularity was higher, and the rate of incidence of menstrual irregularity was higher in women with type 2 diabetes and using oral antidiabetic drugs. In the study by Kelsey et al., with women with type 2 diabetes, it was found that, when the regular and non-regular menstrual cycles were compared, there was no significant relationship between age, diabetes duration, smoking status, treatment method and HbA1c values [11]. In another study, it was stated that type 1

Table 3 Menstrual irregularity experience status of women with diabetes by individual and disease characteristics

Characteristics	Menstrual Irregularity				Test, *P*	PMS				Test, *P*
	Yes (n = 53)		No (n = 45)			Positive (n = 54)		Negative (n = 44)		
	n	%	n	%		n	%	n	%	
Age (year)	38.22 ± 8.01		34.75 ± 9.33		t = 2.181; 0.047*	35.98 ± 8.99		37.43 ± 8.53		t = 0.813; 0.419
Duration of the disease (year)	6.37 ± 4.67		5.88 ± 4.49		t = 0.525; 0.601	6.85 ± 4.87		5.29 ± 4.06		t = −1.691; 0.094
HbA1c (%)	6.69 ± 0.85		6.85 ± 1.81		t = −0.577; 0.565	7.02 ± 1.60		6.45 ± 0.93		t = −2.092; 0.039*
Body structure					χ^2 = 1.715; 0.424					χ^2 = 0.225; 0.893
Underweight/normal weight	25	47.2	21	46.6		26	48.1	20	45.5	
Overweight	9	17.0	12	26.7		12	22.2	9	20.5	
Obese	19	35.8	12	26.7		16	29.6	15	34.1	
Smoking status					χ^2 = 0.042; 0.979					χ^2 = 0.056; 0.972
Smoker	11	20.8	10	22.2		12	22.2	9	20.5	
Never	34	64.1	28	62.2		34	63.0	28	63.6	
Left	8	15.1	7	15.6		8	14.8	7	15.9	
Type of diabetes										
Type 1 diabetes	20	37.7	27	60.0	χ^2 = 4.833; 0.028*	24	44.4	23	52.3	χ^2 = 0.595; 0.440
Type 2 diabetes	33	62.3	18	40.0		30	55.6	21	47.7	
Type of treatment										
Oral antidiabetic drugs	27	51.0	17	37.8		21	38.9	23	52.3	
Insulin	13	24.5	24	53.3	χ^2 = 9.719; 0.008*	19	35.2	18	40.9	χ^2 = 6.281; 0.043*
Both of them	13	24.5	4	8.9		14	25.9	3	6.8	
Presence of other chronic diseases										
Yes	17	32.1	12	26.7	χ^2 = 0.342; 0.559	17	31.5	12	27.3	
No	36	67.9	33	73.3		37	68.5	32	72.7	χ^2 = 0.206; 0.650

*$P < 0.05$

diabetes increased the risk of any menstrual problems approximately twice before the age of 30, and long menstrual cycles and long menstrual bleeding were seen intensely in women aged 20–29 years and younger [16]. The finding of the study differs from the literature information and indicates that more studies are needed on this subject.

Hyperglycemia can cause menstrual irregularity in women with diabetes, both directly and because it affects the ovaries by inducing insulin resistance [12]. In this study, it was determined that the HbA1c level did not differ in women with diabetes and with and without menstrual irregularity. However, the HbA1c value was higher in women with diabetes and PMS than in women without it. Contrary to our study, in a study conducted, it was found that HbA1c value differed between women with and without menstrual irregularity, that as HbA1C values increased, the rate of women with menstrual irregularity increased [26]. In a study conducted with adolescents with type 1 diabetes, it was stated that increased cycle time, menstrual cycle variability, and oligomenorrhea were common in women with HbA1c levels between 7.6% and 8.9% compared to healthy adolescents. In the same study, it was stated that a unit increase in HbA1c increased the menstrual cycle by 5.1 days and the risk of oligomenorrhea by 4.8 times more [10]. In another study, it was emphasized that the rate of oligomenorrhea was higher when the HbA1c value increased or hypoglycemia was more frequent [24]. In another study, it was stated that women who reported having difficulty in glycemic control had a higher rate of irregular menstruation than women without diabetes [13].

Obesity is one of the factors affecting the menstrual cycle [27]. In this study, there was no difference between body structures according to BMI value in women with diabetes with and without menstrual irregularity. Contrary to this study finding, in the study by Kelsey et al., with women with type 2 diabetes, it was found that BMI value was higher in those with irregular menstrual cycles [11]. In another study, it was found that the frequency of oligomenorrhea differed by 18.9% in obese women with diabetes, 13.9% in non-obese women with diabetes, and 8.5% in women without diabetes [28]. In this study, the fact that the incidence of menstrual irregularity did not differ according to body structure in women with diabetes may be due to the small sample size.

This study has some limitations. The most important limitation of the study is the inability to generalize the results since no probabilistic sample was chosen, and it was conducted in a single center. Moreover, since the study was conducted in a certain time period, cross-sectional data are presented. Therefore, causal relationships could not be determined. Furthermore, data on menstrual irregularity and PMS from the study are based on self-reports of women with diabetes. Despite these limitations, our study is an important study that reveals the frequency of menstrual irregularity and PMS in women with diabetes compared to women without diabetes. In this study, we determined the prevalence of menstrual irregularity in women with diabetes.

Conclusion

In this study, it was determined that menstrual irregularity and irregularity, especially oligomenorrhea and menorrhagia, were more common in women with diabetes compared to healthy women in the same age group. In the study, it was determined that nearly half of the women experienced PMS symptoms, but this situation was similar to that of women without diabetes. It is important to examine the menstrual irregularity status in addition to diabetes management in order to improve women's health and improve the quality of life in women with diabetes. Nurses who care for women with diabetes should be actively involved in the diagnosis, prevention, and management of menstrual disorders and PMS symptoms. Nurses who care for women with diabetes should be actively involved in the diagnosis, prevention and management of menstrual irregularity, and PMS symptoms. In this context, it is important to increase the awareness of nurses, too. Nurses should evaluate women with diabetes for menstrual irregularity. Moreover, nurses should provide health education and counseling services to women with diabetes who have menstrual irregularity and PMS to protect their physical and psychological health. Furthermore, it is recommended to conduct prospective studies with a large sample group to determine the causes of menstrual irregularity and PMS.

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