



Contents lists available at ScienceDirect

# European Journal of Obstetrics & Gynecology and Reproductive Biology

journal homepage: [www.elsevier.com/locate/ejogrb](http://www.elsevier.com/locate/ejogrb)

Full length article

## The association of trace elements with premenstrual syndrome, dysmenorrhea and irritable bowel syndrome in adolescents

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## ARTICLE INFO

## Article history:

Received 21 August 2018

Received in revised form 19 November 2018

Accepted 9 December 2018

## Keywords:

Zinc

Copper

Dietary intake

Nutrition

Premenstrual symptoms

## ABSTRACT

**Objective:** Premenstrual syndrome (PMS), primary dysmenorrhea (PD), and irritable bowel syndrome (IBS) are common complaints in women of reproductive age. Trace element status may be associated with the development of these disorders but the current data are unclear. The present study focused on the relationship between serum and dietary copper and zinc with some common physical and psychosomatic conditions among young females.

**Study design:** This cross-sectional study comprised 448 adolescent girls who were classified into four groups: individuals with PMS (n = 67), PD (n = 161), both PMS and PD (n = 146), and normal (n = 74). IBS was diagnosed according to the Rome III questionnaire. Flame atomic absorption (Varian AA240FS) was used to measure serum zinc and copper. Food intake of micronutrients was estimated using a three-day dietary record.

**Results:** There was a significant difference in the frequency of IBS across the four corresponding groups as the percentage of subjects. The prevalence of IBS was significantly higher in the PD group [PMS (13.6%), PD (19.9%), both PMS and PD (17.4%) and normal (8.1%); P value < 0.05]. There was no significant differences between the mean values for serum and dietary intake of zinc and copper among four groups (p value > 0.05). Although, the mean dietary zinc intake was significantly lower in subjects with IBS (6.7 ± 2.8 mg/day) versus those without IBS (7.9 ± 3.1 mg/day, p = 0.032).

**Conclusion:** Girls with IBS were found to have significantly higher rates of gynecological symptoms, including PD and PMS. The lower dietary intake of zinc in subjects with IBS indicate a need for greater attention towards dietary patterns in these individuals.

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## Introduction

A regular menstrual cycle is important for normal reproductive function, however the majority of women are affected by symptoms

related to menstrual dysfunction such as premenstrual syndrome (PMS) and dysmenorrhea [1,2]. PMS is a set of recurrent physical or psychological symptoms which occurred during the luteal phase of the menstrual cycle, that starts about a week prior to bleeding and

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stops 2–4 days afterwards [1]. More than 150 symptoms have been described for PMS which vary from woman to woman [1,3].

PMS causes impaired personal activities and social relationships, absence from work or school, and multiple health problems such as aggression, depression, and disturb quality of life. Several risk factors have been identified associated with PMS and intensity of its symptoms such as age, stress, body mass index, genetic vulnerability, civil status and sensitivity to hormonal instabilities [4,5].

Primary dysmenorrhea (PD) is another common gynecological complaint in adolescent girls. PD is defined as repetitive painful cramping sensation in midline of the lower abdomen during the first days of menstruation with spontaneously relief within two days after the termination of menstruation. PD is often accompanied by other symptom such as fatigue, sweating, tremulousness, mild fever, nausea, vomiting, diarrhea, nagging pain and dizziness [6]. It has been suggested that excessive production of endometrial prostaglandin (PG) and cyclooxygenase (COX) resulted to decrement uterine microcirculation, increment in contractility and ischemia of uterine muscles and eventually abdominal cramp [7].

Functional gastrointestinal (GI) diseases such as functional dyspepsia and irritable bowel syndrome (IBS) are highly prevalent in menstruating women due to the potential influence of fluctuations of female gonadal hormones (i.e. estrogen and progesterone) on GI function and visceral reactivity [8]. IBS is a common and troublesome disorder which comprises abdominal pain or inconvenience, bowel pattern alteration, bloating and viscerovisceral hyperalgesia [9].

The symptoms of IBS and the stool habit changes may differ during the phases of the menstrual cycle. Women suffer from more severe and frequent bowel symptoms of IBS through their bleeding time, and also more report other menstrual cycle-associated conditions, like PD compared to normal women [10–13].

Since PMS, PD and IBS are very common physical and psychosomatic diseases in the women [14], an in-depth investigation of the relationship between them is needed. In addition, it is unknown whether variations in the metabolism of some trace elements are involved in the development and progression of these disorders. Our previous studies have suggested a role of some micronutrients such as calcium and vitamin D in the development of PMS, PD [3] and IBS [15]. Zinc (Zn), copper (Cu) and other micronutrients may affect the development of these disorders but their role is currently unclear. Cu and Zn are essential nutrients that play a critical role in the oxidant/antioxidant balance and prevention of oxidative damage of cells/tissues. Zn potentially contributes to prolactin and ovarian hormone metabolism and function, binding to progesterone, and the phases of the menstrual cycle [16,17]. Das et al found that the highest Zn level occurred during menses when levels fall during the luteal phase and lowest level is observed during the ovulatory phase [18]. There is evidence suggesting decreased concentration of serum Zn in PMS, and that Zn supplementation can improve PD [19,20]. Zn deficiency is associated with low levels of Zn in the hippocampus, altered glucocorticoid synthesis, and progression to neuropathological and mood disorders such as unstable emotion, isolation, learning and behavioral deprivation, touchy and depression [21,22]. Zn also protects against gastrointestinal infections and diarrhea [23]. In the present study we aimed to explore the association between dietary intake and serum level of Cu and Zn with menstrual pattern, PMS, PD and IBS among adolescent females.

## Materials and methods

### Study design

This cross-sectional study was carried out among adolescent girls from the two cities of Khorasan province (Mashhad and

Sabzevar), Iran during January 2015, as described previously [2,24]. Subjects were selected through random sampling of girls between the ages of 12 to 18 years from different high schools in these areas. Participants had menarche at least one year before the onset of study. Informed consent was sign from the girls and their parents. Girls who had acute or chronic physical/psychological disease even without drug consumption were excluded from the study. Taking mineral supplementation during the six month prior to recruitment was an exclusion criterion. Finally, 448 met the inclusion criteria and entered the study. The study was approved by the Ethnic Committee of Mashhad University of Medical Sciences (MUMS).

### Anthropometric assessment

Anthropometric and demographic characteristics were assessed by a trained nurse. Height and weight of each case were measured by standard procedure and then body mass index was also calculated as (weight (kg)/height (m<sup>2</sup>)). A standard mercury sphygmomanometer was recruited to measure systolic and diastolic blood pressure after seating and resting. Measurements were made in duplicate over a 30-minute interval and the average of the measurements were recorded for systolic and diastolic blood pressure.

Weight and height of participants was related to the standard growth chart for age and sex and specific for children and adolescents, produced by Center for Disease Control and Prevention (CDC). BMI was categorized as follows: Underweight (BMI < 5<sup>th</sup> percentile), normal (BMI: 5<sup>th</sup>–85<sup>th</sup> percentile), overweight (BMI: 85<sup>th</sup>–95<sup>th</sup> percentile), and obesity (BMI ≥95<sup>th</sup> percentile). Furthermore, stature status was categorized as: short stature (height < 5<sup>th</sup> percentile), normal (height: 5<sup>th</sup>–95<sup>th</sup> percentile), and tall (height > 95<sup>th</sup> percentile).

### Laboratory measurements

After a 12-hour over-night fast, blood samples were collected from each participant in the early morning regardless of the menstrual cycle phase. Lipid profile including total cholesterol (TC), high-density-lipoprotein (HDL)-cholesterol, triglycerides (TG), and liver function tests including alanine transaminase (ALT), aspartate transaminase (AST), alkaline phosphatase levels (ALP) levels were assayed by using commercial kits (Pars Azmun, Iran) with BT-3000 auto-analyzer according to manufactures instruction (Biotechnica, Italy). Low-density-lipoprotein (LDL)-cholesterol was calculated based on the Friedewald formula.

Serum Cu and Zn levels were determined using flame atomic absorption spectrometry (Varian AA240FS) which was described previously [25]. The activity of superoxide-dismutase (SOD) was measured as described previously [26]. In brief, a microassay was used based on the inhibitory activity of pyrogallol oxidation, which was adapted for Cu/Zn-SOD. Absorption was assessed through a plate reader at wave length of 405 nm.

A complete blood count (CBC) was made using the Sysmex K-800 analyzer, to determine hemoglobin as part of hematological parameters. A hemoglobin levels below 12 g/dL was used to define anemia regarding WHO gender-based definition in women [27].

### Menstrual pattern, PD and PMS assessment

The questionnaire administered to the girls was in 3 parts. The first part consisted of questions on menstrual pattern e.g., menarcheal age, the average days of menstruation, the mean interval time between menstruation, and quantity of blood loss per cycle regarding to the number of pad using for protection during

the bleeding time. Briefly, menstrual cycle patterns were classified as follows [28,29]:

- Early menarche (menarcheal age of 12 years or less); medium menarche (menarcheal age: 13–14 years); delayed menarche (menarcheal age over 14 years).
- Short bleeding periods (bleeding time of four days or less); long bleeding periods (bleeding time of 6 days or more)
- Use of four or more fully soaked pads/ day for protection (menorrhagia or heavy menstrual bleeding); use of one or less fully soaked pad or utilize of panty liner being suffice for protection (hypomenorrhea or light menstrual loss).
- Infrequent menses or menstrual cycles of 35–180 days (oligomenorrhea); cycle length time of 20 days or less (polymenorrhea)

The second part comprised a series of questions investigating whether the participant experienced PMS, and probable their signs, duration and severity. The teenage girls who had at least two signs, one physical and one psychological annoying manifestation in the 5 days before menses and relief within four days after of the onset were known as having PMS, while cases with only one or no features were considered as non-PMS [30].

The signs included in each of the 2 scales are as follows: physical and somatic symptoms (abdominal pain, foot pain, backache, nausea, diarrhea and vomiting,) and psychological symptoms (fatigue, palpitation, appetite changes, sleep pattern changes, irritability, lack of energy, tendency to cry easily, depression and sadness, decrease of interest, and loss of concentration).

In the final section of the questionnaire, the individuals were asked about the presence of PD which was characterized by episodic aching, cramping, or dull pain in the abdominal [31].

For further analysis, the study populations was categorized into four groups as follows: girls with PMS, girls with PD, those with both PMS and PD, and those without PMS or PD (normal).

#### Evaluation of IBS

IBS is a chronic GI disease with symptomatology that begins at least 6 months before diagnosis. Based on diagnostic criteria (Rome III) translated to Persian and validated [32], IBS is identified by abdominal pain or discomfort (at least 3 days/ month over the 12 weeks) accompanied with two or more of the following manifestation: i) Abdominal pain alleviated by defecation, and with the onset of pain closely related with ii) alterations in frequency of evacuations and iii) distortion in the appearance of stool.

#### Dietary assessment

Recent dietary intake of studied population was evaluated through record of content, type, the ready and time of food or drink consumed by subjects for 2 working days and 1 weekend. A three-day food record was obtained from each participant to analyze dietary micro- and macronutrient amount using the Nutritionist IV software (version 7.0; N-Squared Computing, Salem, OR, USA) which was adopted for Iranian food items [33].

#### Statistical method

All data analysis was performed using SPSS 16.0 software. The descriptive statistics was shown as mean  $\pm$  SD (standard deviation), frequencies and percentages. The inferential statistics consist of independent sample *t*-test, one-way ANOVA and chi-square test or Fischer's exact test. A *p* value below 0.05 indicated statistically significant.

## Results

The number of individuals with PMS, PD, both PMS and PD, and normal were 67(14.9%), 161(35.9%), 146 (32.7%) and 74(16.5%), respectively. The demographic, anthropometrics, and clinical characteristics of the participants are shown in Table 1. We did not find any significant differences in four groups (normal, PD, PMS, both PMS and PD) with respect to mean age, BMI and anthropometric measurements ( $p > 0.05$ ). Although, there is a statistical significant difference in the frequency of IBS across these four corresponding groups; the percentage of subjects with IBS was significantly higher in the PD group [PMS (13.6%), PD (19.9%), both PMS and PD (17.4%) and normal (8.1%);  $P < 0.05$ ]. Neither PMS, nor PD and both PMS and PD were significantly related with cardiovascular disease (CVD) risk factors such as blood pressure, lipid profile and the presence of anemia (Table 1).

We did not find a significant difference between the mean values of biochemical variables including liver function tests, serum trace elements and serum SOD activity as well as dietary intake of total energy, protein, carbohydrate, fat, fiber, Zn and Cu among the different four groups ( $p > 0.05$ )(Table 2).

The relationship between IBS, menstrual pattern and associated symptoms to serum and dietary intake of Zn and Cu was shown in Table 3. The mean dietary Zn intake was significantly lower in subjects with IBS ( $6.7 \pm 2.8$  mg/day) versus those without IBS ( $7.9 \pm 3.1$  mg/ day,  $p = 0.032$ ) as well as among those with hypomenorrhea ( $6.9 \pm 2.9$  mg/day) when compared to normal bleeding ( $8.0 \pm 3.3$  mg/day) and menorrhagia ( $8.8 \pm 1.9$  mg/day,  $p = 0.017$ ). Girls with an early menarche or delayed menarche had lower dietary Cu intake compared to medium menarcheal age ( $p = 0.044$ ).

## Discussion

The present study focused on the most common physical and psychosomatic symptoms among young females, and also relating these with serum concentrations and dietary intake of two important trace elements, Zn and Cu. Individuals with PMS and PD are often referred to gynecology clinics. PMS affects between 20–48% of reproductive age female and has a variety of physical and psychological symptoms [34]. It is estimated 50–80% of women have recurrent and/or severe visceral pain during menstrual bleeding. Progesterone withdrawal in the late luteal phase of menstrual cycle leads to raised levels of PG-F2 $\alpha$ , leukotrienes, vasopressin and reduced prostacyclin concentrations which play an important role in the pathophysiology of PD through myometrial stimulation, myometrial hyperactivity and vasoconstriction [35].

Our results show that the frequency of IBS among four groups as the percentage of subjects with IBS was significantly higher in the PD group. It appears that girls with IBS have a significantly higher rate of distressing gynecological symptoms such as PD and PMS. A growing body of evidence shows an overlap between IBS and PD. It has been found women with PD experience significantly more GI symptoms former to or simultaneous with uterine cramping pain during menstruation than those free of PD [36]. Also, female IBS patients are more probable to receive a diagnosis of PD in comparison with those free of IBS [37–39].

The prevalence of IBS is between 10–20% in adolescents and adults globally [40].

It has been reported about 8–50% of woman with IBS concurrently suffer from PD or PMS [41,42]. In IBS patients, there are changes in bowel habit, sensitivity of visceral and rectum as well as abdominal pain severity has been occurred within menses [43]. Hormonal fluctuations, higher PG release, increased ovarian hormone level and effect of menstrual cycle on the sympatric nervous system are other possible reasons [10]. Similar hypersensitivity of the sigmoid colon

**Table 1**

The association between clinical and demographic characteristics with PMS and dysmenorrhea among participants.

P value	PMS + PD n = 146(32.7%)	PD n = 161(35.9 %)	PMS n = 67(14.9%)	Normal n = 74(16.5%)	Variables
0.15	33(22.5)	45(28.0)	17(26.1)	23(31.3)	<12
	70(47.8)	64(39.7)	32(47.8)	24(33.0)	12-14
	43(29.7)	52(32.3)	18(26.1)	27(35.7)	>14
0.25	1(0.4)	1(3.1)	2(3.0)	1(0.7)	Underweight (<5%)
	114(77.8)	126(78.7)	54(80.4)	61(83.2)	Normal (5-85%)
	18(12.6)	22(13.7)	8(12.2)	7 (9.4)	Overweight (85-95%)
	13(9.2)	12(7.5)	3(4.4)	5(6.7)	Obese (≥95%)
0.39	8(5.7)	4(2.5)	2(2.4)	4(5.2)	< 149 (<5%)
	133(90.8)	150(93.2)	65(97.6)	69(93.5)	149 –168 (5-95%)
	5(3.5)	7(4.3)	0(0)	1(1.3)	>168 (>95%)
<b>0.05</b>	25(17.4)	32(19.9)	9(13.6)	6(8.1)	Yes
	121(82.6)	129(80.1)	58(86.4)	68(91.9)	No
0.78	19(13.0)	25(15.5)	11(16.2)	8(10.7)	Yes
	127(87.0)	136(84.5)	56(83.8)	66(89.3)	No
0.99	143(97.8)	158(98.1)	65(97.7)	73(98.6)	< 130
	3(2.1)	3(1.9)	2(2.3)	1(1.4)	≥ 130
0.83	143(97.8)	155(96.0)	65(97.7)	72(97.1)	< 85
	3(2.1)	6(4.0)	2(2.3)	2(2.8)	≥85
0.95	140(96.0)	156(96.6)	65(97.7)	71 (95.7)	< 1.7
	6(4.0)	5(3.4)	2(2.3)	3(4.1)	≥ 1.7
0.93	135(92.4)	149(92.7)	62(92.2)	70(95.0)	< 5.2
	11(7.6)	12(7.4)	5(6.8)	4(4.7)	≥ 5.2
0.54	137(93.5)	143(89.1)	62(92.6)	70(93.9)	< 3.4
	9(6.5)	18(10.9)	5(7.4)	4(6.1)	≥ 3.4
0.47	42(28.7)	57(35.4)	18(26.2)	27(36.4)	≥1.3
	104(71.3)	104(64.7)	49(73.8)	47(63.6)	< 1.3

PMS: premenstrual syndrome; PD; primary dysmenorrhea; BMI: body mass index; Hb: hemoglobin; IBS: Irritable bowel syndrome; SBP: systolic blood pressure; DBP: diastolic blood pressure; TC: total cholesterol; LDL: low density lipoprotein; HDL: high-density lipoprotein.

Data presented as number (%). By using chi-square test or Fischer's exact test. Significance of bold values are P < 0.05.

and rectum to painful stimulant during menstruation have been reported in women with PD [44].

The pathobiology of IBS is complicated and involves peripheral and central frameworks [45,46]. It has been suggested that food and diet could contribute in IBS through several mechanisms such as gut microbiota, intestinal mobility and penetrance, bile metabolism, visceral sensibility and psychosomatic aspects [45]. There are limited and inconsistent results regarding to the association of Zn and Cu with IBS. Our findings show that the mean value of dietary Zn intake was significantly lower in subjects with IBS versus those without IBS. Recently, a large 36,448 adult's French population, showed that IBS subjects had a lower intake of micronutrients such as Zn, which is consistent with other studies

[47–49]. But in one report, IBS patients and normal control did not differ regarding dietary Zn intake [48]. Zn is an antioxidant, and protects sulfhydryl groups belonging to proteins and enzymes from free radical invasion/oxidative stress and regulated multiple biological processes. Zn deficiency result to slow growth, anemia, delayed wounds healing, sliming, weak immune system, and elevated susceptibility to infection [50]. Hence, patients with IBS, aware of these effects, may have managed their consumption of food to avoid the symptoms of IBS. Although, this conclusion should be interpreted with caution since no document of a dose–response correlation was found.

We did not find any association between intake of total energy, protein, carbohydrate, fat among the PMS, PD, both PMS and PD

**Table 2**

Biochemical characteristic and dietary intakes of study population.

P value	PMS + PD n = 146(32.7%)	PD n = 161(35.9 %)	PMS n = 67(14.9%)	Normal n = 74(16.5%)	Variables
<i>Biochemical parameters</i>					
0.08	19.9 ± 6.3	20.2 ± 7.4	18.1 ± 4.6	20.6 ± 8.8	AST(IU/L)
0.11	12.0 ± 7.1	11.4 ± 6.0	10.6 ± 5.3	13.1 ± 10.9	ALT(IU/L)
0.28	360.6 ± 192.8	336.1 ± 174.1	318.3 ± 174.0	344.6 ± 161.2	ALP(IU/L)
0.87	14.5 ± 3.4	14.6 ± 3.2	14.3 ± 3.1	14.3 ± 14.3	Serum zinc (μmol/l)
0.78	18.9 ± 8.5	18.2 ± 7.8	9.2 ± 7.6	18.4 ± 9.0	Serum copper (μmol/l)
0.30	0.9 ± 0.5	1.0 ± 0.5	0.8 ± 0.4	1.0 ± 7.0	Zinc copper Ratio
0.98	0.05 ± 0.01	0.05 ± 0.02	0.05 ± 0.02	0.05 ± 0.02	SOD (U/ml)
<i>Dietary intakes</i>					
0.39	2036.7 ± 694.1	1860.0 ± 644.7	1891.5 ± 648.7	1925.3 ± 676.5	Energy (kcal)
0.15	61.7 ± 22.7	60.2 ± 22.1	58.7 ± 24.8	53.2 ± 20.6	Protein(g)
0.37	227.1 ± 77.1	60.2 ± 22.1	223.6 ± 80.2	203.9 ± 75.0	Carbohydrate(g)
0.13	16.7 ± 8.7	15.4 ± 7.2	14.3 ± 7.0	14.1 ± 7.1	Fiber(g)
0.18	99.1 ± 38.3	101.5 ± 45.7	87.2 ± 36.9	93.1 ± 44.7	Total Fat(g)
0.70	7.6 ± 3.3	7.4 ± 3.1	7.6 ± 2.6	8.0 ± 3.0	Zinc (mg/day)
0.37	1.6 ± 0.9	1.6 ± 1.0	1.3 ± 0.6	1.5 ± 0.9	Copper (mg/day)

PMS: premenstrual syndrome; PD; primary dysmenorrhea; ALT: alanine transaminase; AST: aspartate transaminase; ALP: alkaline phosphatase; SOD: superoxide dismutase. Values expressed as mean ± SD. Between-group comparisons were assessed by One-way ANOVA.

**Table 3**  
Relation of irritable bowel syndrome, menstrual pattern and associated symptoms to serum and dietary intake of trace elements.

Zinc Copper Ratio	Dietary copper intake (mg/day)	Serum copper (μmol/l)	Dietary zinc intake (mg/day)	Serum zinc (μmol/l)	
<b>Irritable bowel syndrome</b>					
0.97 ± 0.5	1.4 ± 1.1	17.9 ± 8.1	6.7 ± 2.8	14.3 ± 3.0	Yes (n = 72)
1.0 ± 0.5	1.6 ± 0.9	18.0 ± 7.9	7.9 ± 3.1	14.8 ± 3.9	No (n = 376)
0.88	0.32	0.88	<b>0.032</b>	0.35	<b>P-value</b>
<b>Menstrual pattern</b>					
1.0 ± 0.6	1.4 ± 0.8	18.2 ± 7.6	7.6 ± 3.2	14.7 ± 3.6	Early menarche (n = 211)
0.94 ± 0.5	1.6 ± 0.9	18.4 ± 7.4	7.7 ± 3.1	14.4 ± 3.3	Medium menarche (n = 143)
0.90 ± 0.5	1.2 ± 0.5	19.6 ± 9.3	8.2 ± 4.1	13.8 ± 2.3	Delayed menarche (n = 94)
0.54	<b>0.046</b>	0.70	0.86	0.34	<b>P</b>
1.1 ± 0.7	1.5 ± 0.8	17.0 ± 6.9	8.5 ± 5.0	14.9 ± 5.7	Short bleeding periods(n = 22)
0.9 ± 0.4	1.5 ± 0.9	18.4 ± 8.0	7.7 ± 3.2	14.1 ± 3.4	Normal periods(n = 363)
1.0 ± 0.6	1.5 ± 0.9	17.2 ± 7.5	7.2 ± 2.6	14.1 ± 2.9	Long bleeding periods (n = 63)
<b>0.044</b>	0.99	0.26	0.29	0.41	<b>P</b>
0.9 ± 0.4	1.5 ± 0.9	18.2 ± 7.8	6.9 ± 2.9	14.4 ± 3.2	Hypomenorrhea (n = 102)
0.9 ± 0.05	1.5 ± 0.8	17.9 ± 7.8	8.0 ± 3.3	14.1 ± 3.9	Normal bleeding (n = 337)
0.8 ± 0.3	0.9 ± 0.3	20.2 ± 8.0	8.8 ± 1.9	13.8 ± 3.5	Menorrhagia (n = 9)
0.49	0.24	0.57	<b>0.017</b>	0.68	<b>P</b>
1.0 ± 0.5	1.6 ± 1.1	17.9 ± 7.6	7.4 ± 2.7	14.5 ± 3.7	Oligomenorrhea (n = 20)
0.9 ± 0.5	1.5 ± 0.8	18.0 ± 7.7	7.7 ± 3.3	14.1 ± 3.8	Regular menses (n = 331)
0.9 ± 0.4	1.7 ± 1.2	20.1 ± 8.5	7.7 ± 4.5	14.4 ± 2.9	Polymenorrhea (n = 97)
0.69	0.41	0.40	0.67	0.62	<b>P</b>

Values expressed as mean ± SD.  
Using One-way ANOVA or independent sample t-test.

and normal groups. Serum and nutrient intake of Zn and Cu have also did not differ between four groups. Prior research of the association between specific dietary intake and PMS or PD has been limited to attention to the prevalence and/or symptoms intensity. In the Nurses’ Health Study II, that included 1257 women with PMS and 2463 matched controls, intakes of total energy, total fat, total carbohydrate and total Zn were not associated with PMS [51,52]. In Japanese women dietary fat had no impact on the intensity of PD [53]. Furthermore, in one study performed in Iran no significant relationship was found between intake of energy, carbohydrate, protein and fat with PMS and PD(P>0.05) [54]. Shamberger and colleagues have reported that serum Zn and sodium levels were significantly increased in the blood of PMS patients [55], but a review of the literature showed that serum Zn may be related with a reduced risk of PMS, since lower serum Zn concentrations in PMS patients compared with healthy groups [1,56–58]. Zekavat et al reported both pain duration and intensity of PD were reduced by Zn sulphate supplementation in adolescent females [20]. In another intervention study, Zn sulfate was reported to improve PMS symptoms [59]. Concerning to these controversial results, large prospective studies have evaluated food intake of patients with different gynecological disorders is needed.

However, this study has several limitation is necessary to mention. The diagnosis of IBS was made using the Rome III criteria alone, and the diagnostic of PMS and PD by self-administrated questionnaire instead of face-to-face interviews by clinicians. The difficulty of subjects in recalling the symptoms and in remembering the phase of the menstrual cycle may be another limitation of our work.

In conclusions, it appears that girls with IBS have significantly higher rates of distressing gynecological symptoms such as PD and PMS. Further investigation into the interaction of female menstrual disorders with gastrointestinal function and extensive pain syndromes is warranted. The lower dietary intake of Zn in subjects with IBS suggest that greater attention toward food and intake of these girls is necessary. We did not find any evidence for association between dietary intake and prevalence of PMS or PD. As this is the first study of the association between dietary intakes with common complaints between female (PMS, PD, and IBS), the fact that these findings possibly acquired by chance as a result of multiple testing, additional prospective studies is required for support these results.

**Grant**

This study was supported by grants [grant nu# 93118 (Majid Ghayour-Mobarhan)] from Mashhad University of Medical Sciences, Mashhad, Iran.

**Disclosure statement**

All authors state that they have no conflicts of interest.

**Ethical approval**

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

**Informed consent**

Informed consent was obtained from all individual participants included in the study.

**Authors contribution**

A.B. performed all analyses and drafted the manuscript. A.B., K. G., S.D. and S.K. coordinated the fieldwork of the study. M.T., N.J., G. A.F, S.E. and H.B. provided methodological feedback. A.B, M.Gh. and K.F. supervised the overall research project and helped to draft the manuscript. All of the authors have read and confirmed the final manuscript.

All authors state that they have no conflicts of interest.

**Acknowledgments**

We are thankful to all study participants and their parents.

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