Dairy intake in association with asthma symptoms among a large sample of children and adolescents: a cross-sectional study

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Abstract

Background and Objective: Dairy products may be associated to an increased risk of asthma, although there is little scientific evidence to back this up. The goal of this study was to exploring the association between dairy consumption and asthma symptoms.

Materials and Methods: This cross-sectional study was conducted on children and adolescents aged 6-8 and 13-14 living in central Iran. Dietary food consumption was assessed using a multiple-choice questionnaire. Logistic regression was used to obtain odds ratios for the association between milk, other dairy products, and total dairy consumption with risk of asthma symptoms.

Results: In total, 7667 participants (3414 boys and 4253 girls) were included in the current study. Milk intake and total dairy consumption were not associated with the likelihood of wheezing, asthma confirmed by a doctor, current asthma, and asthma medication use. also, there was no association between other dairy products intake and odds of wheezing in the past 12 months in the crude model. But, after adjustment for several confounders those in the top category had lower odds of wheezing in the past 12 months than those in the bottom category (OR: 0.58; 95% CI: 0.40-0.85).

Conclusion: In conclusion, the consumption of dairy products other than milk, including cheese and yogurt, might reduce the likelihood of wheezing in children and adolescents.

Introduction

Asthma is the most common chronic condition in children and adolescents (1), affecting about 6.6 million children in the United States (2). Exacerbations of asthma are a leading cause of disease morbidity, higher health-care expenses, and, in some individuals, a faster loss of lung function (3). Wheezing, coughing, shortness of breath, and chest tightness are some of the symptoms that might occur (4). In 1980, the prevalence of asthma was accounted to be about 3.5% among children. However, the number has grown to 9.5% in about thirty years (5). Adolescents have asthma prevalence and morbidity rates in adolescents are comparable to, if not higher than, those of young children (6). In 2010, this disease in white Americans (7.8%) is less common than African Americans (11.9%) (5) and the highest prevalence rates are reported in developed countries like Australia (21%). 27 papers reported that the prevalence rate of “asthma ever” among Iranian children ranged from 0.5–11.0% (4).

The causes of asthma are not fully understood. However, several risk factors, including microbiome and viral infections, smoking (7), vitamin D status, chemical exposure, air pollution (8), pollen (9), stress, genetic factors (10), and dietary changes (11) are proposed to be associated with the development of the disease. The relation between nutrients, foods, food groups, dairy products, vitamin D3(12), antioxidants (13), soy isoflavones (14),and fish oil (15), with asthma has been explored by several studies (8, 16). Although dairy products are high in micronutrients, fatty acids, and probiotics, it is thought that they may raise the incidence of asthma and allergies in children (17). It is proposed that dairy products could flare-ups asthma symptoms,, although there is little scientific evidence to back up this theory (18). In this

regard, the results of epidemiological studies is inconsistent. Several studies have found a strong link between dairy consumption and asthma, wheezing, eczema, and rhinitis in children (19, 20), whereas a null association has been found in another studies of children and adults (21–27). For example, a study in Greece, showed that consumption of farm milk at age 5 is associated with a lower prevalence of atopy at age 11–19 (28). A case-control study published in 2015 found increased consumption of dairy products was significantly associated with more odds of asthma (29). In another study, whole milk and butter would be negatively, and the consumption of soy beverage, ricotta cheese, and low-fat cheese would be positively associated with asthma.(21). However, a double-blind, placebo controlled, cross-over study could not confirm that dairy products might induce bronchoconstriction or changes in asthma symptoms in adults (18). According to previous studies, more than half of people with asthma change their eating habits, with dairy products being the most typically avoided food (21).

To our knowledge data on dairy intake and asthma association are limited in Middle-Eastern countries. It is noteworthy that dietary habits have unique characteristics in this region. Therefore, the present study aimed to investigate the association between dietary milk and other dairy products consumption and asthma and its symptoms in a large sample of children and adolescents in Iran.

Subjects And Methods

Participants

The current cross-sectional study was part of the Global Asthma Network (GAN), which took place in Yazd, central Iran, in early 2020. The GAN is a cross-sectional, multi-center, multi-country epidemiological study that builds on and enhances the ISAAC Phase three methodology (30). According to the GAN recommendation, at least 3,000 samples are required to estimate a good prevalence of asthma (31). In the present study, students from 48 and 36 high and elementary schools (state and private) were randomly selected from two educational districts using a cluster sampling design, respectively. Moreover, non-Iranian students were excluded from the study. All the subjects aged 13–14 and parents of 6–7 years were invited to fill out online electronic questionnaires on asthma and its symptoms and risk factors, which were designed and placed in the virtual education groups of schools. The information was collected using paper questionnaires for a group of participants aged 6–8 years. Due to the school closures during the COVID-19 pandemic, the rest of the 6-8year old students were provided with the electronic questionnaires. Out of 7214 and 3026 adolescents, and children, 5141 and 2526 completed the questionnaire, with response rates of 71.3% and 83.5%, respectively, and then demographic data that seemed unacceptable was reviewed by telephone and corrected if necessary. At the beginning of the study, due to schools' closure during the outbreak of COVID-19, an electronic questionnaire was designed and placed in the virtual education groups of schools.

The ethics committee of Shahid Sadoughi University (SSU) of Medical Sciences in Yazd, Iran, approved the GAN study on Iranian youngsters (IR.SSU.REC.1398.244). The ethics committee also gave its approval for the current study. The Yazd Education administration then granted permission to conduct

the study at elementary and guidance schools. Parents gave their informed consent as well. The consent form was included at the start of the internet questionnaires so that kids and their parents may feel entirely comfortable participating in the research.

Asthma and its symptoms confirmation

The GAN questionnaire, derived from the ISAAC questionnaire (29), includes questions about the symptoms of allergic diseases and related risk factors. In this study, we used some questions about asthma symptoms, "use of asthma medication" and "asthma confirmed by a doctor", as well as the amount of dairy consumed in the diet last year. According to the protocol of this study, current asthma was defined as a history of confirmed asthma by a doctor and having had wheezing and/or use of asthma medication in the past 12 months. Once the questionnaire was translated into Persian, the reliability of the translated version was confirmed by a study conducted on 100 selected subjects using Cronbach's alpha. The alpha coefficient for asthma symptoms was estimated to be 0.862, thus exhibiting appropriate internal consistency. Finally, the questionnaire was translated back into English and sent to the GAN principals in order to be approved.

Assessment of dietary intake

In this study, the dietary intake of children's food groups in the last 12 months was assessed using one of the multiple choice questions in the GAN questionnaire (32). The frequency response section had three options (never or occasionally/once or twice a week most or all days of the week). Milk, other dairy products, and total dairy consumption were assessed. The frequency of total dairy intake was assessed by summing dietary milk (including flavored milk), cheese, and yoghurt consumption.

Assessment of other variables: The data on participants' height, weight, ethnicity (Kord/Turk/Persian/Lor/Arab/Balooch), watching television and computer use (2–4 hours/5–8 hours/9–14 hours a day) were obtained using a self-reported online GAN questionnaire. The body mass index (BMI) was calculated by using the following formula: weight (kg) divided by height squared (m^2).

Statistical methods. We used STATA version 14 (State Crop., College Station, TX) for all analyses. To compare continuous and categorical variables between individuals with and without "asthma confirmed by a doctor" and "usage of asthma medication," independent samples of student t tests and chi-square testing was used, respectively. Multivariable logistic regression analysis was used in crude and multivariable controlled models to investigate the relationship between dairy intake and the odds of asthma confirmed by a doctor, current asthma, usage of asthma medication, and wheezing in the last 12 months. In the first model, adjustments were made for age and sex. Additional adjustments were made for watching TV and computer use in the second model. In the last model (third model), an additional adjustment for BMI was made. In all models, the lowest level of dairy intake (never or only occasionally) was considered as the reference category. P-value < 0.05 was considered as statistically significant.

Results

The current study included 7667 participants in total (3414 boys and 4253 girls). According to Table 1, frequency of asthma confirmed by a doctor and use of asthma medication were different among boys and girls and wheezing in the past 12 months ($p < 0.001$). also, frequency of use of asthma medication were different among ethnicity ($p < 0.01$). Subjects with asthma confirmed by a doctor (10.9 *vs*. 11.7, $p < 0.001$) and with use of asthma medication (10.9 *vs*. 11.3, $p = 0.05$) were older compared with those healthy subjects.

Table 1
General characteristics of the subjects according to asthma

Variables	Asthma confirmed by a doctor		p-value	Use of asthma medication		p-value
	Without (n = 7343)	With (n = 324)		Without (n = 7476)	With (n = 191)	
Sex						
Male	3226 (43.93)	188 (58.02)	< 0.001	3296 (44.09)	118 (61.7)	< 0.001
Female	4117 (56.07)	136 (41.98)		4180 (55.9)	73 (38.2)	
Age (years)	10.9 ± 3.37	11.7 ± 2.94	< 0.001	10.9 ± 3.36	11.3 ± 3.16	0.05
BMI (kg/m$^{2)}$	18.9 ± 10.4	19.1 ± 4.18	0.35	18.97 ± 10.3	18.73 ± 3.97	0.37
Ethnicity			0.13			0.003
Kord	38 (0.52)	5 (1.54)		38 (0.51)	5 (2.62)	
Turk	73 (0.99)	2 (0.62)		74 (0.99)	1 (0.52)	
Persian	7064 (96.2)	311 (95.9)		7192 (96.2)	183 (95.8)	
Lor	62 (0.84)	4 (1.2)		64 (0.86)	2 (1.05)	
Arab	55 (0.75)	1 (0.31)		56 (0.75)	0 (0.0)	
Balooch	51 (0.69)	1 (0.31)		52 (0.70)	0 (0.0)	
Watching television and computer use			0.38			0.29
2–4 hours	3945 (53.7)	163 (50.3)		4016 (53.7)	92 (48.1)	
5–8 hours	2463 (33.5)	103 (34.8)		2506 (33.5)	70 (36.6)	
9–14 hours	935 (12.7)	48 (14.8)		954 (12.7)	29 (15.1)	

Variables	Asthma confirmed by a doctor		p-value	Use of asthma medication		p-value
	Without (n = 7343)	With (n = 324)		Without (n = 7476)	With (n = 191)	
Wheezing (in the past 12 months)						
Yes	553 (7.5)	56 (17.2)	< 0.001	518 (6.9)	91 (47.6)	< 0.001
No	6790 (92.4)	268 (82.7)		6958 (93.0)	100 (52.3)	
Milk intake						
Never	1282 (17.4)	51 (15.7)	0.71	1300 (17.3)	33 (17.2)	0.21
Weekly	3854 (52.4)	175 (54.0)		3939 (52.6)	90 (47.1)	
Every day	2207 (7343)	98 (30.2)		2237 (29.9)	68 (35.6)	
Other dairy intake						
Never	286 (3.8)	10 (3.09)	0.15	287 (3.8)	9 (4.7)	0.16
Weekly	2273 (30.9)	86 (26.5)		2312 (30.9)	47 (24.6)	
Every day	4784 (65.1)	228 (70.3)		4877 (65.2)	135 (70.6)	
Total Dairy intake						
Never	178 (2.4)	7 (2.1)	0.21	178 (2.3)	7 (3.6)	0.19
Weekly	2061 (28.0)	77 (23.7)		2094 (28.0)	44 (23.0)	
Every day	5104 (69.5)	240 (74.0)		5204 (69.6)	140 (73.3)	

Values are mean (SD) or percentages

[a]χ^2 Test for ordinal qualitative variables and t-test for continuous variables

Table 2. The association between dairy intake and likelihood of asthma confirmed by a doctor

	Never or only occasionally	Once or twice per week	Most or all days	P_{trend}
	OR (95% CI)	OR (95% CI)	OR (95% CI)	
Milk				
No. with/without asthma	57/1276	168/3861	99/2206	
Crude	1.00	0.97 (0.71–1.32)	1.00 (0.72–1.40)	0.93
Model 1	1.00	0.95 (0.69–1.29)	0.98 (0.70–1.37)	0.99
Model 2	1.00	0.95 (0.70–1.29)	0.98 (0.70–1.37)	0.99
Model 3	1.00	0.95 (0.70–1.30)	0.99 (0.70–1.38)	0.98
Other dairy				
No. with/without asthma	8/288	99/2260	217/4795	
Crude	1.00	1.57 (0.75–3.27)	1.62 (0.79–3.33)	0.32
Model 1	1.00	1.51 (0.72–3.14)	1.45 (0.71–2.98)	0.70
Model 2	1.00	1.51 (0.72–3.14)	1.46 (0.71–2.99)	0.70
Model 3	1.00	1.51 (0.72–3.14)	1.46 (0.71–2.99)	0.69
Total dairy				
No. with/without asthma	6/179	87/2051	231/5113	

Crude	1.00	1.26 (0.54–2.93)	1.34 (0.59–3.07)	0.44
Model 1	1.00	1.19 (0.51–2.76)	1.18 (0.52–2.71)	0.84
Model 2	1.00	1.18 (0.51–2.76)	1.18 (0.51–2.71)	0.85
Model 3	1.00	1.18 (0.50–2.75)	1.18 (0.51–2.70)	0.84

Model 1: adjusted for age and sex

Model 2: further adjusted for watch TV & computer use

Model 3: additionally adjustment for BMI

Tables 2, 3, and 4 show the multivariable-adjusted odds ratios and 95% confidence intervals for asthma confirmed by a doctor, current asthma, and use of asthma medication in the past 12 months across categories of dietary milk, other dairy, and total dairy consumption are presented in Tables 2,3 and 4. According to the findings, there is no association between dairy consumption and doctor-diagnosed asthma, current asthma, or asthma medication use.

Table 3
The association between dairy intake and likelihood of current asthma

	Never or only occasionally	Once or twice per week	Most or all days	P trend
	OR (95% CI)	OR (95% CI)	OR (95% CI)	
Milk				
No. with/without current asthma	10/1172	28/3578	18/2040	
Crude	1.00	0.91(0.44–1.89)	1.03(0.47–2.24)	0.86
Model 1	1.00	0.93(0.45–1.93)	0.98(0.45–2.15)	0.98
Model 2	1.00	0.93(0.45–1.93)	0.98(0.45–2.15)	0.98
Model 3	1.00	0.93(0.45–1.93)	0.99(0.45–2.15)	0.98
Other dairy				
No. with/without asthma	3/257	20/2096	33/4437	
Crude	1.00	0.81(0.24–2.76)	0.63(0.19–2.09)	0.28
Model 1	1.00	0.81(0.24–2.77)	0.70(0.21–2.32)	0.47
Model 2	1.00	0.81(0.24–2.77)	0.70(0.21–2.32)	0.47
Model 3	1.00	0.81(0.24–2.77)	0.70(0.21–2.32)	0.47
Total dairy				
No. with/without asthma	3/163	16/1895	37/4732	
Crude	1.00	0.45(0.13–1.59)	0.42(0.12–1.39)	0.34
Model 1	1.00	0.47(0.13–1.65)	0.47(0.14–1.57)	0.52
Model 2	1.00	0.47(0.13–1.65)	0.47(0.14–1.57)	0.52

	Never or only occasionally	Once or twice per week	Most or all days	P_{trend}
Model 3	1.00	0.47(0.13–1.65)	0.47(0.14–1.57)	0.52

Model 1: adjusted for age and sex

Model 2: further adjusted for watch TV & computer use

Model 3: additionally adjustment for BMI

Table 4
The association between dairy intake and use of asthma medication

	Never or only occasionally	Once or twice per week	Most or all days	P trend
	OR (95% CI)	OR (95% CI)	OR (95% CI)	
Milk				
No. with/without use of asthma medication	33/1300	90/3939	68/2237	
Crude	1.00	0.90 (0.60–1.34)	1.19 (0.78–1.82)	0.24
Model 1	1.00	0.87 (0.58–1.30)	1.12 (0.73–1.71)	0.38
Model 2	1.00	0.87 (0.58–1.30)	1.12 (0.73–1.71)	0.38
Model 3	1.00	0.87 (0.58–1.31)	1.12 (0.73–1.72)	0.37
Other dairy products				
No. with/without use of asthma medication	9/287	47/2312	135/4877	
Crude	1.00	0.64 (0.31–1.33)	0.88 (0.44–1.75)	0.26
Model 1	1.00	0.60 (0.29–1.25)	0.78 (0.39–1.56)	0.46
Model 2	1.00	0.61 (0.29–1.26)	0.79 (0.39–1.57)	0.47
Model 3	1.00	0.60 (0.29–1.25)	0.78 (0.39–1.56)	0.49
Total dairy				
No. with/without use of asthma medication	7/178	44/2094	140/520	

	Never or only occasionally	Once or twice per week	Most or all days	P trend
Crude	1.00	0.53 (0.23–1.20)	0.68 (0.31–1.48)	0.52
Model 1	1.00	0.49 (0.22–1.12)	0.60 (0.27–1.31)	0.83
Model 2	1.00	0.49 (0.21–1.12)	0.59 (0.27–1.30)	0.85
Model 3	1.00	0.50 (0.22–1.13)	0.59 (0.27–1.30)	0.87

Model 1: adjusted for age and sex

Model 2: further adjusted for watch TV & computer use

Model 3: additionally adjustment for BMI

Table 5 shows the multivariable-adjusted odds ratios and 95% confidence intervals for wheezing in the previous 12 months by dairy consumption category. there was no association between milk or total dairy intake with odds of wheezing in the past 12 months. Also, there was no association between other dairy products intake and odds of wheezing in the past 12 months in the crude model. But, after adjustment for several confounders those in the top category had lower odds of wheezing in the past 12 months than those in the bottom category (OR: 0.58; 95% CI: 0.40–0.85).

Table 5
The association between dairy intake and likelihood of wheezing in the past 12 months

	Never or only occasionally	Once or twice per week	Most or all days	P trend
	0R (95% CI)	0R (95% CI)	0R (95% CI)	
Milk				
No. with/without wheezing	114/1219	311/3718	184/2121	
Crude	1.00	0.89 (0.71–1.11)	0.92 (0.72–1.18)	0.65
Model 1	1.00	0.87 (0.69–1.09)	0.90 (0.70–1.15)	0.54
Model 2	1.00	0.88 (0.70–1.10)	0.91 (0.71–1.17)	0.60
Model 3	1.00	0.88 (0.70–1.10)	0.91 (0.71–1.17)	0.61
Other dairy products				
No. with/without wheezing	34/262	184/2175	391/4621	
Crude	1.00	0.65 (0.44–0.96)	0.65 (0.44–0.94)	0.18
Model 1	1.00	0.62 (0.42–0.91)	0.58 (0.39–0.84)	**0.03**
Model 2	1.00	0.63 (0.42–0.93)	0.58 (0.40–0.85)	**0.02**
Model 3	1.00	0.63 (0.42–0.93)	0.58 (0.40–0.85)	**0.02**
Total dairy				
No. with/without wheezing	19/166	172/1966	418/4926	
Crude	1.00	0.76 (0.46–1.25)	0.74 (0.45–1.20)	0.37
Model 1	1.00	0.71 (0.43–1.18)	0.65 (0.40–106)	0.09
Model 2	1.00	0.70 (0.42–1.16)	0.63 (0.38–1.03)	0.07

	Never or only occasionally	Once or twice per week	Most or all days	P trend
Model 3	1.00	0.70 (0.42–1.16)	0.63 (0.38–1.03)	0.07

Model 1: adjusted for age and sex

Model 2: further adjusted for watch TV & computer use

Model 3: additionally adjustment for BMI

Discussion

According to this study, higher consumption of other dairy products (such as cheese or yogurt), was related to a lower risk of wheezing in the previous 12 months. To our knowledge, this study is among the first studies that reports the association between dairy intake and odds of asthma symptoms in a Middle Eastern country.

We found a significant inverse association between other dairy products and risk of wheezing in the previous 12 months. Similarly to our results a cross-sectional study of 1601 participants in Melbourne, showed a negative relationship between dairy product consumption and risk of asthma (21). Hijazi et al. in a cross-sectional study, found that decreased milk consumption is associated to a higher prevalence of asthma symptoms and allergy symptoms (19). PIAMA birth cohort research, between 2978 children, found that frequent use of milk fat-containing items was associated to a lower risk of asthma symptoms (8). It is noteworthy that, eating dairy products (even a few times a week) had an inversely significant influence on asthma compared to never eating them (33). according to data from the national health and examination survey I (NHANES I), Low levels of vitamin A and milk consumption were related to an increased risk of airway blockage among heavy smokers, in the United States (34). In contrast, Malaeb et al. found that consuming less milk on a regular basis was reduced the current asthma risk (35). Another cross-sectional study between 1014 students (5–14 years old) illustrated that respiratory symptoms being stronger among those consumed less fresh milk and milk fat and more margarine (20). A cohort study in Japan showed higher maternal intake of total dairy products, cheese, yogurt, and calcium during pregnancy may reduce the risk of infantile eczema in the previous 12 months, physician-diagnosed asthma, physician-diagnosed atopic eczema, and physician-diagnosed atopic eczema (36). However,Tabak et al. found no apparent relation between dairy products and asthma (25). Milk and dairy products are high in saturated fat, which has been related to a lower incidence of allergy disorders and asthma (35). Butter and whole milk consumption may be beneficial for asthma and allergy symptoms. However, margarine consumption was found to be detrimental to asthma and allergy symptoms (37). The beneficial effect of milk and butter may be stem from the fatty acid of milk (37) and the fact that digestion of lactose is different from other carbohydrates, and it may act as a conditional prebiotic (38). Prebiotic activity of dairy products is probably resulted from stimulation of the growth of beneficial bacteria in the intestines, which may modulate immune responses and thus protect humans from asthma

and allergies (39). Milk proteins, including-lactalbumin,-lactoglobulin, and immunoglobulins, whey proteins such as serum albumin, lactoferrin, and lactoperoxidase, as well as various enzymes and cytokines found in dairy products, are thought to be responsible for this protective effect (40).

Many researchers have looked at the medicinal and preventative effects of yogurt and the lactic acid bacteria that are widely utilized in yogurt production (41). The relation between cytokine imbalance and asthma symptoms have attracted attention. A shift away from a TH1 interferon gamma (IFN-γ) pattern toward a TH2 (IL-4, IL-5, and IL-13) profile is seen in Atopic illness immunological responses. Interferon gamma is a lymphokine that activates macrophages. Incomplete IFN-γ production, according to these findings, predisposes to the development of allergy disorders and asthma (42). human studies showed long-term consumption of substantial amounts of yogurt (450 g/d) resulted in to boosting the production of IFN-γ by lymphocytes, separated T cells. Oral ingestion of Lactobacillus casei and other probiotic strains (43), has been shown to reduce immunoglobulin E (IgE) production. These findings suggest eating yogurt could help to reduce IgE-mediated diseases, including asthma (41). Conjugated linoleic acid (CLA) is one of the other probable pathways discussed in the papers. These compounds have a wide range of biological features that could help asthma sufferers, including impacts on energy management, lipid metabolism, inflammation, and immunological function. CLA's metabolic benefits, which include fat loss and adipokine regulation, may be beneficial for respiratory mechanics and systemic inflammation, which may apply to asthmatic airway inflammation (44).

The present study has considerable strengths. This was the first study exploring the relation between dairy intake and risk of asthma in Middle-Eastern region. A high sample size that reduce the risk of selection bias and, because the study was conducted on a general population, it included different ethnicity. The current study includes various flaws that should be taken into account when evaluating the results. The current study relied solely on self-reported data, with questions about milk and other dairy products included in the questionnaire. Furthermore, although the associations were adjusted for several possible confounding variables, we had no data on some other variables, including energy intake, physical activity, and other variables. Therefore, residual confounding might be a limitation of the current study. As each dairy product intake was not asked in the questionnaire, we were unable to check the association for each dairy product. In cross-sectional studies, the dependent and independent variables were gathered at the same time; therefore, no causal association can be inferred from their results. Therefore, future prospective studies are highly recommended.

Conclusion

In conclusion, the current investigation shown that children and adolescents in the highest category of dairy products other than milk, such as cheese and yogurt were 12% times less likely to have wheezing in the past 12 months than those in the lowest category. These findings will need to be confirmed in prospective cohort studies.

Declarations

Ethical Approval and Consent to participate

This Research involving human participants, human material, or human data, was performed in accordance with the Declaration of Helsinki and was approved by Shahid Sadoughi University (SSU) of Medical Sciences ethics committee (IR.SSU.REC.1398.244). written informed consent was obtained from a parent or guardian for participants under 16 years old.

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Authors' contribution

Mona Jamalvandi and Bahareh Sasanfar participated in the analysis and drafted the initial version of the manuscript. Marjan Jafari helped with data collection. Nasrin Behniafard and Zahra Nafei contributed to the conception and design. All authors reviewed the final version of the manuscript. Nasrin Behniafard, Zahra Nafei and Amin Salehi-Abargouei supervised the study.

Conflict of interest

There is no conflict of interest in this study to declare.

Consent for Publication

There is no personal information regarding any patients in our article.

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Availability of Supporting Data

The datasets used and/or analyzed during the current study available from the corresponding author on reasonable request.

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