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# *Adherence to Mediterranean-Like Dietary Pattern in Association with Gastroesophageal Reflux Disease in Adolescents*

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***ABSTRACT***

**Background:** Gastroesophageal reflux disease (GERD) is a common esophageal disorder affecting adolescents. Recent studies have indicated that the risk of GERD may be influenced by different dietary patterns. This study aimed to examine the relationship between an adherence to Mediterranean-like dietary pattern and GERD in a large group of adolescents from central Iran. **Methods**: This cross-sectional study involved 5141 adolescents aged 13-14 years. Dietary intake was assessed using a food frequency method which included in a reliable and valid Global Asthma Network (GAN) core questionnaire. GERD symptoms and the frequency of their occurrence over the last week were assessed using a validated GERD questionnaire. A binary logistic regression was used to evaluate the relationship between adherence to Mediterranean-like dietary pattern and GERD and its related symptoms. **Results**: The results showed that after controlling for potential confounding variables including age, sex, watching TV and computer, and BMI, the adolescents in the highest adherence to the Mediterranean style diet (MedDiet) score had lower odds of GERD [odds ratio (OR)=0.53; 95% CI 0.35-0.80, $P_{trend}$=0.005)], sense of reflux (OR=0.45; 95% CI 0.26-0.77, $P_{trend}$=0.01) and poor sleep (OR=0.54; 95% CI 0.31-0.96, $P_{trend}$=0.02) compared with those in the lowest adherence. No significant association found between MedDiet and other GERD symptoms. **Conclusion**s: This study found a negative relationship between following a MedDiet and having GERD among Iranian adolescents. Following the MedDiet may be a useful strategy to prevent GERD in adolescents.

## Introduction

Gastroesophageal reflux disease (GERD) is a condition that occurs when stomach contents flow back into the esophagus, causing symptoms such as heartburn and regurgitation (Hom and Vaezi, 2013, Hungin *et al.*, 2019, Silvia *et al.*, 2018). The prevalence of GERD in all age groups is

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increasing in the worldwide (Sherman *et al.*, 2009). GERD is one of the most common esophageal disorders (Herregods *et al.*, 2015). Studies have shown that adolescents experience more severe symptoms of GERD and this condition can affect negatively on their health and quality of life (Lightdale *et al.*, 2013, Wiklund, 2004). GERD is a multifactorial disorder (Çela *et al.*, 2013). Diet may have an important role in the development and management of GERD ((Jarosz and Taraszewska, 2014). Dietary modifications are recommended as the first step in treating GERD (Kubo *et al.*, 2014, Nandurkar *et al.*, 2004). Some dietary components, such as high-fat and high-carbohydrate foods, tomato products (Salehi *et al.*, 2019), chocolate (Roman and Kahrilas, 2013), alcohol (Pan *et al.*, 2019), coffee or tea (Cao *et al.*, 2019, Kim *et al.*, 2014) citrus fruits (Roman and Kahrilas, 2013), spicy foods (Jarosz and Taraszewska, 2014), acidic and fried foods (Roman and Kahrilas, 2013, Surdea-Blaga *et al.*, 2019) and mint (Choe *et al.*, 2017) have been reported to be potentially associated with GERD. However, previous studies have reported inconsistent results regarding the relationship between diet and GERD (Darvishmoghadam *et al.*, 2016, Martinucci *et al.*, 2018, Mone *et al.*, 2016). Keshteli *et al*. proposed adults who consume fruits and vegetables that are rich in fiber and antioxidant vitamins have lower odds of GERD (Keshteli *et al.*, 2017), which was consistent with other previous studies (El-Serag *et al.*, 2005, Nocon *et al.*, 2006). However, Zheng *et al*. found different results and suggested that other factors, such as genetics, body mass index (BMI), smoking, and physical activity, may affect the risk of GERD (Zheng *et al.*, 2007). Additionally, a study suggested that functional foods that contain biologically active components could potentially protect against the risk of GERD (Elmaliklis *et al.*, 2019). Current evidence shows that the assessment of dietary patterns may better elucidate the nutritional etiology of chronic diseases (Kant, 2004), this is because dietary patterns account possible interactions among all foods and nutrients, rather than a single food or nutrient (Tucker, 2010, Van Dam, 2005). The Mediterranean style diet (MedDiet) is high in plant food and vegetable oil, moderate in fish and dairy, and low in red meat and poultry (Mone *et al.*, 2016), which were associated with reduced risk of several diseases including cancer (Zavala-Gonzales *et al.*, 2014), cardiovascular disease (Owen *et al.*, 2000), metabolic syndrome (MetS), and type 2 diabetes (Sotos-Prieto *et al.*, 2021). Several studies have recommended that dietary modifications, such as increasing the intake of high-fiber diets and decreasing the intake of fat, may also have benefits in controlling GERD (Gong *et al.*, 2019). Only one cross-sectional study has investigated the association between MedDiet and GERD in adults, indicating that a greater adherence to a MedDiet is inversely associated with GERD (Mone *et al.*, 2016). However, to the best of our knowledge, there is no information on the adherence to MedDiet and its association with GERD in adolescents**.** Therefore, the aim of this study was to examine the relationship between adherence to Mediterranean-like dietary pattern and GERD in a large sample of adolescents from central Iran.

## Methods and Materials

This cross-sectional study used data from an international multi-center cross-sectional population-based study (GAN-2020) (Behniafard *et al.*, 2021, Ellwood *et al.*, 2020, Nafei *et al.*, 2021) conducted on Iranian adolescents aged 13–14 years from February 2020 to June 2020 in Yazd, Iran. The participants were recruited from 48 schools. The schools were selected from all public and private schools in Yazd city using cluster sampling and all students who met the inclusion criteria were recruited.

The questionnaire based on GAN was translated into Persian and its validity was assessed by experts. The reliability of the Persian version of the questionnaire was verified by a study on 100 students aged 13 to 14 years, using Cronbach's alpha coefficient. The internal consistency of the questionnaire for rhinitis and eczema symptoms was satisfactory, with an alpha coefficient of 0.74. Volunteer students completed electronic questionnaires on socio-demographic factors, dietary intake, and GERD symptoms, with the cooperation of school principals. All participants approved the



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informed consent through the electronic form before completing the questionnaires. Out of 7,214 adolescents who received the questionnaires, 5,141 people completed them (response rate of 71.3). Any unclear demographic information was re-checked by phone contact.

***Diagnosis of GERD and its symptoms***

Using the validated GERD questionnaire, participants' GERD symptoms and how often they occurred in the past week were reported (Jones *et al.*, 2009). The questionnaire consisted of six items: four positive predictors of GERD were measured based on a four-point Likert scale including frequency of heartburn, regurgitation, sleep disturbance, and the use of over-the-counter medications for these symptoms, and also two negative predictors were scored with a reversed Likert scale including stomach pain and nausea. Participants received a clear and simple explanation before completing the reflux questionnaire. The GERDQ score was calculated by adding the scores of each item, ranging from 0 to 8 (Jones *et al.*, 2009). The sum of the points for the aforementioned frequencies was considered as a participant's GERDQ score, and a diagnosis of GERD could be possible if the sum of all scores was ≥ 8 points (Jones *et al.*, 2009).

***Dietary intake assessment***

The dietary intake was assessed using a food questionnaire that listed 26 food items with standard serving sizes. The participants were asked how often they consumed each food item in the questionnaire during the past year, and the frequency of intake (never or very low/ one or two times per week/ often or every day) depending on the food type. A previous study confirmed the validity and reliability of this questionnaire (Nafei *et al.*, 2021). Participants were divided into tertiles according to their Med Diet scores.

***The calculation of MedDiet score***

Questions on food consumption were included based on frequencies of "never", "weekly" and "every day" as reported in the study of Garcia et al. (Garcia-Marcos *et al.*, 2007); however, the Med Diet score was developed based on the score used by Psaltopoulou (Psaltopoulou *et al.*, 2004) as follows: fruits, fish, vegetables, pulses, cereals, pasta, rice, and potatoes were considered as "pro-Mediterranean" food and scored 0, 1 or 2 from less frequent to more frequent intake, respectively. Meat, milk, and fast food were considered as "anti-Mediterranean" food scored 0, 1 or 2 from more frequent to less frequent intake, respectively.

***Assessment of other variables***

The participants' weight was measured to the nearest 100 g using digital scales with minimal clothes while no wearing shoes and their height was measured to the nearest 0.5 cm using a tape measure fixed on a wall, while they stood without shoes and in a normal position. BMI was calculated by dividing weight (kg) to the square of height ($m^2$). Data on race (Kord/Turk/fars/ Lor/Arab/Balooch) and watching television (TV) and computer use/ or internet (2-4 hours/ 5-8 hours/ 9-14 hours a day) were obtained through an electronic self-completed GAN questionnaire.

***Ethical considerations***

Written informed consent was obtained from all participants. Ethical approval was obtained from the Ethics Committee of Shahid Sadoughi University of Medical Sciences, IR.SSU.REC.1398.244). All procedures were performed in accordance with relevant guidelines.

***Data analyses***

General characteristics and dietary intakes across tertiles of MedDiet score are presented as means±SD for continuous variables and numbers (percentage) for categorical variables, respectively. One-way ANOVA and Chi-square test were used to compare continuous and categorical variables across tertiles of MedDiet score, respectively. Binary logistic regression was used to examine the association between adherence to MedDiet and GERD, as well as its symptoms, in the crude and multivariable adjusted models, age and sex in adjusted model I, and other variables like watching TV and using computer and/or internet in adjusted model II. In model III, BMI was also adjusted. All statistical analyses were performed using the statistical package for social sciences (SPSS, version 21, IBM Corporation and (USA). P-values



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less than 0.05 were considered statistically significant.

## Results

Out of 5141 adolescents who completed the data for the analysis, 153 participants had GERD. General characteristics of adolescents across tertiles of MedDiet score are provided in **Table 1**. Watching TV and using computer and/or internet were significant across tertiles of MedDiet score ($P$=0.026) and ($P$<0.001), respectively. GERD symptoms including sense of reflux and poor sleep significantly decreased in the highest tertile of MedDiet score compared to the lowest ($P$=0.005) and ($P$=0.008), respectively. No significant difference was observed in other GERD symptoms, age, BMI, sex, and race across tertiles of MedDiet score.

**Table 1.** Baseline characteristics of participants according to tertiles of MedDiet score.

| Variables | Total (N =5141 ) | 1st Tertile (N =1386 ) | 2nd Tertile (N =2095 ) | 3rd Tertile (N =1660 ) | P-value[c] |
|---|---|---|---|---|---|
| Age (y) | 13.32 ± 0.46[a] | 13.32 ± 0.46 | 13.33 ± 0.47 | 13.32 ± 0.46 | 0.73 |
| Body mass index (kg/m$^2$) | 20.68 ± 4.10 | 20.59 ± 4.05 | 20.67 ± 4.09 | 20.77 ± 4.17 | 0.49 |
| Sex | | | | | 0.076 |
| Girl | 2072(40.3)[b] | 594(42.9) | 823(39.3) | 655(39.5) | |
| Boy | 3069(59.7) | 792(57.1) | 1272(60.7) | 1005(60.5) | |
| Race | | | | | 0.17 |
| Kurd | 27(0.5) | 5(0.4) | 10(0.5) | 12(0.7) | |
| Turk | 40 (0.8) | 9(0.6) | 17(0.8) | 14(0.8) | |
| Fars | 4981(96.9) | 1342(96.8) | 2039(97.3) | 1600(96.4) | |
| Lor | 37(0.7) | 10(0.7) | 10(0.5) | 17(1) | |
| Arab | 38(0.7) | 10(0.7) | 15(0.7) | 13(0.8) | |
| Balouch | 18(0.4) | 10(0.7) | 4(0.2) | 4(0.2) | |
| Watching TV (h/day) | | | | | 0.026 |
| <1 | 649(12.6) | 192(13.9) | 258(12.3) | 199(12) | |
| 1-3 | 2622(51) | 663(47.8) | 1088(51.9) | 871(52.5) | |
| 3-5 | 1293(25.2) | 345(24.9) | 529(25.3) | 419(25.2) | |
| >5 | 577(11.2) | 186(13.4) | 220 (10.5) | 171(10.3) | |
| Computer and/or Internet use (h/day) | | | | | <0.001 |
| <1 | 1383(26.9) | 348(25.1) | 558(26.6) | 477(28.7) | |
| 1-3 | 2169(42.2) | 550(39.7) | 887(42.3) | 732(44.1) | |
| 3-5 | 962(18.7) | 272(19.6) | 420(20) | 270(16.3) | |
| >5 | 627(12.2) | 216(15.6) | 230(11) | 181(10.9) | |
| Nausea and vomiting | | | | | 0.29 |
| No | 5073(98.7) | 1362(98.3) | 2071(98.9) | 1640(98.8) | |
| Yes | 68(1.3) | 24(1.7) | 24(1.1) | 20(1.2) | |
| Epigastric pain | | | | | 0.056 |
| No | 4943(96.1) | 1318(95.1) | 2024(96.6) | 1601(96.4) | |
| Yes | 198(3.9) | 68(4.9) | 71(3.4) | 59(3.6) | |
| Sense of reflux | | | | | 0.005 |
| No | 5034(97.9) | 1345(97) | 2050(97.9) | 1639(98.7) | |
| Yes | 107(2.1) | 41(3) | 45(2.1) | 21(1.3) | |
| Heartburn | | | | | 0.11 |
| No | 5042(98.1) | 1351(97.5) | 2063(98.5) | 1628(98.1) | |
| Yes | 99(1.9) | 35(2.5) | 32(1.5) | 32(1.9) | |
| Drug use | | | | | 0.084 |
| No | 5077(98.8) | 1361(98.2) | 2072(98.9) | 1644(99) | |
| Yes | 64(1.2) | 25(1.8) | 23(1.1) | 16(1) | |
| Poor sleep | | | | | 0.008 |
| No | 5066(98.5) | 1354(97.7) | 2072(98.9) | 1640(98.8) | |
| Yes | 75(1.5) | 32(2.3) | 23(1.1) | 20(1.2) | |

*[a]: Means±SD; [b]: n (%); [c]: Obtained from one-way ANOVA for continuous variables and Chi-square test for categorical variables.*



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**Table 2.** Adolescents' intake of food groups according to tertiles of MedDiet score .

| Variables | Total | 1st Tertile | 2nd Tertile | 3rd Tertile | P-value[b] |
|---|---|---|---|---|---|
| Meat | | | | | <0.001 |
| Never | 2452(47.7)[a] | 697(50.3) | 1037(49.5) | 718(43.3) | |
| Weekly | 2385(46.4) | 589(42.5) | 950(45.3) | 846(51.0) | |
| Every day | 304(5.9) | 100(7.2) | 108(5.2) | 96(5.8) | |
| Total fast food | | | | | <0.001 |
| Never | 190(3.7) | 81(5.8) | 62(3.0) | 47(2.8) | |
| Weekly | 2163(42.1) | 648(46.8) | 917(43.8) | 598(36.0) | |
| Every day | 2788(54.2) | 657(47.4) | 1116(53.3) | 1015(61.1) | |
| Total dairy | | | | | <0.001 |
| Never | 3779(73.5) | 989(71.4) | 1537(73.4) | 1253(75.5) | |
| Weekly | 1270(24.7) | 354(25.5) | 530(25.3) | 386(23.3) | |
| Every day | 92(1.8) | 43(3.1) | 28(1.3) | 21(1.3) | |
| Fish | | | | | <0.001 |
| Never | 3014(58.6) | 1106(79.8) | 1256(60) | 652(39.3) | |
| Weekly | 2054(40.0) | 277(20) | 829(39.6) | 948(57.1) | |
| Every day | 73(1.4) | 3(0.2) | 10(0.5) | 60(3.6) | |
| Fruits | | | | | <0.001 |
| Never | 145(2.8) | 120(8.7) | 24(1.1) | 1(0.1) | |
| Weekly | 890(17.3) | 447(32.3) | 341(16.3) | 102(6.1) | |
| Every day | 4106(79.9) | 819(59.1) | 1730(82.6) | 1557(93.8) | |
| Legumes | | | | | <0.001 |
| Never | 124(2.4) | 99(7.1) | 23(1.1) | 2(0.1) | |
| Weekly | 2849(55.4) | 1092(78.8) | 1281(61.1) | 476(28.7) | |
| Every day | 2168(42.2) | 195(14.1) | 791(37.8) | 1182(71.2) | |
| Macaroni | | | | | <0.001 |
| Never | 1365(26.6) | 652(47) | 522(24.9) | 191(11.5) | |
| Weekly | 3603(70.1) | 717(51.7) | 1536(73.3) | 1350(81.3) | |
| Every day | 173(3.4) | 17(1.2) | 37(1.8) | 119(7.2) | |
| Rice | | | | | <0.001 |
| Never | 32(0.6) | 28(2.0) | 4(2.0) | 0 (0.0) | |
| Weekly | 556(10.8) | 261(18.8) | 204(9.7) | 91(5.5) | |
| Every day | 4553(88.6) | 1097(79.1) | 1887(90.1) | 1569(94.5) | |
| Total vegetables | | | | | <0.001 |
| Never | 1283(25.0) | 760(54.8) | 426(20.3) | 97(5.8) | |
| Weekly | 2762(53.7) | 577(41.6) | 1381(65.9) | 804(48.4) | |
| Every day | 1096(21.3) | 49(3.5) | 288(13.7) | 759(45.7) | |
| Wheat, barley, Popcorn | | | | | <0.001 |
| Never | 1702(33.1) | 939(67.7) | 611(29.2) | 152(9.2) | |
| Weekly | 2688(52.3) | 412(29.7) | 1302(62.1) | 974(58.7) | |
| Every day | 751(14.6) | 35(2.5) | 182(8.7) | 534(32.2) | |
| Potatoes | | | | | <0.001 |
| Never | 275(5.3) | 178(12.8) | 80(3.8) | 17(1.0) | |
| Weekly | 3357(65.3) | 1053(76) | 1512(72.2) | 792(47.7) | |
| Every day | 1509(29.4) | 155(11.2) | 503(24.0) | 851(51.3) | |

*[a]: n (%); [b]: Obtained from Chi-square test.*

Frequency of dietary intakes across tertiles of MedDiet score is presented in **Table 2**. Frequency of meat, fast food, dairy, fish, meat, fruits, vegetables, legumes, macaroni, rice, potatoes, wheat, barley and popcorn intake differed significantly between tertiles of MedDiet (*P*=<0.001).

Multivariable-adjusted ORs (95% CI) for GERD and its symptoms based on tertiles of MedDiet score are presented in Table 3. Adolescents in the third tertile of MedDiet score had lower odds of GERD (OR=0.53; 95% CI 0.35-0.80 $P_{trend}$=0.005), sense of reflux (QR=0.45; 95% CI 0.26-0.77, $P_{trend}$=0.01), and poor sleep



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(OR=0.54; 95% CI 0.31-0.96, $P_{trend}$=0.02). This association was significant even after adjusting for confounding factors such as age, sex, watching TV and computer, and BMI. No significant association was found between adherence to MedDiet and other symptoms of GERD (*P*>0.05).

**Table 3.** Logistic regression analysis for GERD and its related symptoms among adolescents, according tertiles of MedDiet score.

| Variables | 1st tertile (N=1386) | 2nd tertile (N=2095) | 3rd tertile (N=1660) | $P_{trend}$ |
|---|---|---|---|---|
| GERD | | | | |
| Crude | 1 | 0.58 ( 0.40-0.84) | 0.49(0.32-0.75) | 0.001 |
| Model [1] | 1 | 0.58(0.40-0.84) | 0.49(0.32-0.74) | 0.001 |
| Model [2] | 1 | 0.62(0.42- 0.90) | 0.53(0.35-0.81) | 0.005 |
| Model [3] | 1 | 0.62(0.42-0.90) | 0.53(0.35-0.80) | 0.005 |
| Nausea and vomiting | | | | |
| Crude | 1 | 0.65(0.37-1.16) | 0.69(0.38-1.25) | 0.29 |
| Model [1] | 1 | 0.63(0.36-1.12) | 0.67(0.37-1.22) | 0.24 |
| Model [2] | 1 | 0.68(0.38-1.21) | 0.73(0.40-1.34) | 0.39 |
| Model [3] | 1 | 0.68(0.38-1.21) | 0.73(0.40-1.34) | 0.39 |
| Sense of reflux | | | | |
| Crude | 1 | 0.72(0.46-1.1) | 0.42(0.24-0.71) | 0.006 |
| Model [1] | 1 | 0.71(0.46-1.09) | 0.41(0.24-0.70) | 0.005 |
| Model [2] | 1 | 0.77(0.50-1.18) | 0.45(0.26-0.77) | 0.01 |
| Model [3] | 1 | 0.77(0.49-1.18) | 0.45(0.26-0.77) | 0.01 |
| Heartburn | | | | |
| Crude | 1 | 0.59(0.36-0.97) | 0.75(0.46-1.23) | 0.11 |
| Model [1] | 1 | 0.59(0.36-0.96) | 0.75(0.46-1.22) | 0.10 |
| Model [2] | 1 | 0.64(0.39-1.05) | 0.82(0.50-1.35) | 0.21 |
| Model [3] | 1 | 0.64(0.39-1.05) | 0.82(0.50-1.34) | 0.21 |
| Epigastric pain | | | | |
| Crude | 1 | 0.68(0.48-0.95) | 0.71(0.50-1.02) | 0.05 |
| Model [1] | 1 | 0.65(0.46-0.92) | 0.69(0.48-0.99) | 0.03 |
| Model [2] | 1 | 0.69(0.49-0.98) | 0.75(0.52-1.07) | 0.10 |
| Model [3] | 1 | 0.69(0.49-0.98) | 0.75(0.52-1.07) | 0.10 |
| Drug use | | | | |
| Crude | 1 | 0.6 (0.34-1.06) | 0.53(0.28-0.99) | 0.08 |
| Model [1] | 1 | 0.58(0.33-1.03) | 0.51(0.27-0.96) | 0.06 |
| Model [2] | 1 | 0.61(0.34-1.09) | 0.55(0.29-1.04) | 0.11 |
| Model [3] | 1 | 0.61(0.34-1.09) | 0.55(0.29-1.04) | 0.11 |
| Poor sleep | | | | |
| Crude | 1 | 0.47(0.27-0.80) | 0.51(0.29-0.90) | 0.01 |
| Model [1] | 1 | 0.45(0.26-0.77) | 0.49(0.28-0.87) | 0.006 |
| Model [2] | 1 | 0.48(0.28-0.84) | 0.54(0.31-0.96) | 0.02 |
| Model [3] | 1 | 0.48(0.28-0.84) | 0.54(0.31-.096) | 0.02 |

***GERD**: Gastroesophageal reflux disease; **Model** 1: Age and sex adjusted; **Model** 2: Age, sex, watching TV, using computer and/or internet additionally adjusted; **Model** 3: Age, sex, watching TV, using computer and/or internet and body mass index was also adjusted..*

## Discussion

The present study found that adolescents who followed more MedDiet had lower chances of GERD, sense of reflux, and poor sleep. The prevalence of GERD is increasing in Iran. According to a recent study, 43.07% of the Iranian population suffers from GERD symptoms (Azami *et al.*, 2021). Behavioral changes such as quitting smoking, limiting alcohol intake, exercising regularly, and eating a healthy diet may help prevent GERD (Taraszewska, 2021). Thus, studying the association of these modifiable factors



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with GERD may be useful for public health organizations and patients. As far as we know, this is the first cross-sectional study that examined the relationship between the MedDiet and GERD among Iranian adolescents.

Diet is a factor that can be changed to prevent or reduce GERD (Darvishmoghadam *et al.*, 2016). The present study revealed that higher adherence to MedDiet was linked to a 47% lower chance of having GERD. A cross-sectional study also reported that adults who scored higher on MedDiet had a lower risk of GERD (Mone *et al.*, 2016). The MedDiet was characterized by high intake of food that may protect against GERD and low intake of food that may increase the risk of this condition (Mone *et al.*, 2016). Only a few studies have examined how eating components such as fruits and vegetable (Keshteli *et al.*, 2017), legumes (Martinucci *et al.*, 2018) which are part of MedDiet associated with GERD. In a cross-sectional study, Keshteli et al. (Keshteli *et al.*, 2017) found that people who ate more fruits had a 25% lower risk of GERD than those who ate less fruits. However, they did not find any association between vegetable intake and GERD, after adjusting for other factors (Gong *et al.*, 2019). Mary-Joe et al. conducted a cross-sectional study and suggested that some food types in the Lebanese version of MedDiet may prevent GERD (Youssef *et al.*, 2021). Another study found a positive correlation between meat consumption and GERD in Han Chinese people (Niu *et al.*, 2012). Kim et al. found that eating more sweets, fatty food, and caffeinated drinks significantly increased the risk of GERD (Kim *et al.*, 2019).

The possible mechanism of how the MedDiet prevents GERD may be related to fiber intake (Elmaliklis *et al.*, 2019, Keshteli *et al.*, 2017). Some components of MedDiet that are rich in fiber are fruits, vegetables, and legumes (Trichopoulou *et al.*, 2014). Dietary fiber acts as a nitrite scavenger in the stomach, reducing the formation of carcinogenic compounds (Møller *et al.*, 1988). Dietary nitrate converts to nitric oxide in stomach (McKnight *et al.*, 1997), which increases the action of non-adrenergic non-cholinergic inhibitory nerves and reduces the lower esophageal sphincter pressure. Nitric oxide can be a risk factor for reflux esophagitis (Tomita *et al.*, 2003). Nitrate is also used as a food additive in meat products, where it serves as a colorant, an antimicrobial agent, and a flavor enhancer (Dahle, 1979). Low processed food intake is recommended in MedDiet (Hoffman and Gerber, 2015). Vegetables and fruits, which are rich in antioxidants, may lower the risk of GERD (Lukić *et al.*, 2012). GERD may be caused by the excessive production of reactive oxygen species (ROS) and the impairment of the natural antioxidant defense system in the body (Nelkine *et al.*, 2020). Antioxidants are substances that neutralize free radicals and may protect the esophageal mucosa from damage by eliminating these harmful molecules (Lee *et al.*, 2001). This study found that higher adherence to MedDiet was associated with less GERD poor sleep and sense of reflux. Some components of MedDiet such as olive oil, nuts, legumes, fruits, and vegetables (Widmer *et al.*, 2015), are rich in antioxidants, magnesium, and monounsaturated fatty acids (MUFA) (Wahrburg *et al.*, 2002). Magnesium may improve sleep quality by increasing the levels of cortisol and melatonin which are hormones that regulate the sleep-wake cycle (Abbasi *et al.*, 2012). Higher adherence to the MedDiet was related to increased total antioxidant capacity (TAC) (Pitsavos *et al.*, 2005). TAC was directly associated with the intake of fruits, vegetables, and olive oil, but it was inversely correlated with the intake of red meat (Pitsavos *et al.*, 2005). Evidence has reported a negative association between dietary TAC (DTAC) and poor sleep (Daneshzad *et al.*, 2020). Moreover, MedDiet includes food such as olives and grapes that are rich in melatonin that regulates the circadian rhythm (Iriti and Varoni, 2015). Melatonin is used in the management of sleep disorders (Ferracioli-Oda *et al.*, 2013). A diet enriched with MUFA can affect rapid eye movement sleep (REM). Moreover, dietary intake of MUFA can improve insulin function in the brain, which in turn affects the cortical activity and sleep quality (Sartorius *et al.*, 2012).

To the best of our knowledge, the present study



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is the first study investigated the association of adherence to MedDiet and odds of GERD in adolescents. It was conducted on large sample size of Iranian adolescents. The current study has also several limitations. Due to the nature of cross-sectional studies, they could not explore causal association (Van Der Stede, 2014). This study is prone to recall bias and measurement error should be considered, since questionnaires assessed both exposure and outcome variables; these errors can cause misclassification of the study subjects.

## Conclusion

The present study revealed an inverse association between adherences to MedDiet and GERD among adolescents. Adherence to MedDiet may be a useful strategy to prevent and manage GERD in clinical settings. Future studies are required to confirm these findings.

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## Author's contributions

A AhmadiVasmehjani, Z Darabi, and S Beigrezaei participated in writing the first draft of the manuscript. S Beigrezaei and A Salehi-Abargouei conducted the statistical analyses. M Aflatoonian helped in data collection. N Behniafard and Z Nafei contributed to the conception and design. M Aflatoonian, Z Nafei and A Salehi-Abargouei supervised the study. All authors reviewed the final version of the manuscript.

## Conflict of interests

The authors declare that they have no competing interests.

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