*British Journal of Nutrition* (2024), 132, 1134–1142 doi:10.1017/S0007114524002381


# The relationship between the Mediterranean-DASH Intervention for Neurodegenerative Delay (MIND) diet and metabolic health status in adolescents with overweight and obesity: results from a cross-sectional study in Iran

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*(Submitted 19 June 2024 – Final revision received 8 September 2024 – Accepted 24 September 2024 – First published online 4 November 2024)*

## Abstract

Few studies investigated the association between Mediterranean-DASH Intervention for Neurodegenerative Delay (MIND) diet and metabolic health status, particularly among adolescents. The present study was designed to investigate the association of MIND diet with metabolic health status in Iranian adolescents with overweight/obesity. This cross-sectional study was done among 203 adolescents with overweight/obesity (12–18 years) in Isfahan, Iran. A validated FFQ was applied to collect dietary intakes. Anthropometric indices and blood pressure were also measured by standard procedures. Fasting blood samples were obtained to determine serum insulin, glucose and lipid profile. To categorise participants as being with metabolically healthy overweight/obesity (MHO) or metabolically unhealthy overweight/obesity (MUO), two methods including International Diabetes Federation (IDF) criteria and IDF plus Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) were applied. Participants had a mean age of 13·98 years and 50·2 % of them were girls. In fully adjusted models, participants with highest MIND diet adherence had lower odds of MUO status based on IDF (OR = 0·20; 95 % CI 0·08, 0·51) and IDF/HOMA-IR (OR = 0·22; 95 % CI 0·08, 0·59) criteria. Stratified analyses revealed that this association was stronger among girls and was only significant among individuals with overweight. An inverse association was also found between MIND diet score and odds of hyperglycaemia and insulin resistance (IR). Higher MIND diet adherence was associated with lower odds MUO in adolescents with overweight/obesity. Inverse associations were also found between MIND diet and odds of hyperglycaemia and IR. Future longitudinal prospective studies are necessary to confirm our results.

**Keywords:** **MIND diet: Metabolic health status: Overweight: Obesity: Adolescents**

Overweight and obesity, as a global epidemic and serious challenge in healthcare, have spread among children and adolescents[1]. The increasing rate of overweight/obesity has been observed in many parts of the world[2]. According to World Obesity Federation, over 206 million children and adolescents worldwide will develop obesity by 2025[3]. Among Iranian children and adolescents, the rate of being overweight has climbed by about 50 % in the last two decades[4]. The overall prevalence of overweight and obesity in the Iranian children and adolescents was estimated to be 35·09 %[5]. Excess weight is often associated with abnormalities in metabolic health, but some individuals with overweight/obesity have a healthy metabolic profile[6]. This condition is considered as metabolically healthy overweight/obesity (MHO)[6]. Individuals with MHO status display a desirable metabolic status, characterised by high insulin sensitivity, optimal lipid and glucose profiles[7]. However, MHO is an unstable and transient status, so that this condition may convert to metabolically unhealthy overweight/

**Abbreviations:** DASH, Dietary Approach to Stop Hypertension; HOMA-IR, Homeostasis Model Assessment of Insulin Resistance; IDF, International Diabetes Federation; MHO, metabolically healthy overweight/obesity; MIND, Mediterranean-DASH Intervention for Neurodegenerative Delay; MUO, metabolically unhealthy overweight/obesity.

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obesity (MUO) with high risk of developing cardiometabolic disorders[8].

Although genetics, age and sex affect the metabolically healthy status, modifiable factors may also play significant roles in the aetiology of this condition. Lifestyle factors such as energy intake, dietary macro- and micro-nutrient composition, physical activity, sedentary behaviour, sleep and smoking behaviours were found to be associated with cardiometabolic health in individuals with overweight or obesity[9,10]. Healthy dietary patterns are considered as preventive factors for transition from MHO to MUO phenotype[11]. In contrast, unhealthy dietary patterns resulted in increased inflammation and risk of chronic diseases[11]. Recently, the Mediterranean-DASH Intervention for Neurodegenerative Delay (MIND) diet, which has been constructed based on protecting brain health and avoiding unhealthy foods, has been suggested in relation to metabolic health[12].

A cross-sectional study showed that higher MIND diet score was associated with decreased odds of general obesity and hypo-HDL-cholesterolemia, but not with metabolic syndrome in adults[13]. However, another study in 2020 found no significant association between MIND diet with general and abdominal obesity in Iranian adults[14]. Another study on individuals with obesity evaluated MIND diet and cardiometabolic parameters and found only a significant association in relation to insulin sensitivity[15]. According to our knowledge, no investigation has been assessed MIND diet in relation to metabolic health status among children and adolescents, yet. Also, results of previous studies have been conflicted, and most of them were conducted in European and American countries. In addition, the increasing rate of overweight/obesity among adolescents creates this demand to identify MUO status and its related risk factors to optimise the delivery of health services. To address this gap, this study investigated the association of MIND diet with metabolic health status in Iranian adolescents with overweight/obesity.

## Methods

### Participants

This cross-sectional study was carried out in 2020 on 203 Iranian adolescents with overweight or obesity, aged 12–18 years (102 girls and 101 boys). The sample size of this study was computed based on prior published articles that indicated about 60 % of adolescents with overweight/obesity in Iran have MUO[16,17]. Considering precision (d) of 7 %, power of 80 % and type I error of 0·05, a minimum of 188 people were anticipated to be required for the sample size. A multi-level cluster random sampling method was applied to select adolescents with wide range of social and economic backgrounds from sixteen schools in six regions of the city of Isfahan, Iran. Next, only adolescents with overweight/obesity were invited to participate in the current investigation, according to WHO criteria[18]. Exclusion criteria were having any specific weight-loss diet, taking vitamin/mineral supplements or any drugs that might affect their body weight and biochemical blood levels. Adolescents with any genetic or endocrine abnormalities (such as hypothyroidism, type 1 diabetes mellitus and Cushing syndrome) were also excluded. Finally, 203 adolescents with overweight/obesity participated in this study. All of the participants provided written informed consent. In addition, informed consent was obtained from their parents. The study protocol was approved by the local ethics committee at Isfahan University of Medical Sciences (no. 63158).

### Dietary intake assessment

A validated 147-item semi-quantitative FFQ was used for collecting dietary intake data of participants[19,20]. Several former validation studies showed that this FFQ could reliably evaluate the relationship between food consumption and a range of diseases among Iranian adolescents[21,22]. As a result, this questionnaire offers a respectable level of validity and reliability for assessing the dietary intakes of Iranian adolescents. Participants were asked to report the frequency (daily, weekly or monthly) and amount (standard common portion size) of ingested dietary items over the previous year. Next, using household measurements, the portion sizes of consumed items were converted to grams/d.[23]. We examined nutrient intake data by using Nutritionist IV software. The applied Nutritionist IV software was based on the USDA food composition database with a few adjustments for Iranian foods.

In the present study, as shown in online Supplemental Table 1, the MIND diet score was created by considering fourteen dietary parameters, including green leafy vegetables, other vegetables, berries, nuts, beans, olive oil, whole grains, fish and poultry, considering as healthy brain foods, and also fried/fast foods, red meat, butter and margarine sticks, cheese, pastries and candies that were considered as unhealthy brain foods[24]. Wine intake was not included in this score, due to religious limitations and lack of sufficient details. Although, this would not affect our findings as its consumption is not usual among adolescents. The scores for participants in the lowest, middle and highest tertiles of brain healthy food categories were 0, 0·5 and 1, correspondingly. On the other hand, those in the brain unhealthy food categories with the lowest, middle and highest tertiles received scores of 1, 0·5 and 0, respectively. Then, the total MIND diet score was calculated by summing up all dietary components; the total score ranged from 0 to 14.

### Assessment of anthropometric and cardiometabolic indices

Height and weight measurements were taken by a trained nutritionist. Adolescents were weighed by a digital scale (Seca Instruments) to the nearest 0·1 kg while wearing thin clothes without shoes. Also, a stadiometer was used to measure standing height to the nearest 0·1 cm when participants were standing with shoulders relaxed and without shoes. Height and weight were used to calculate BMI based on the Quetelet formula (weight (kg)/height$^2$ (m$^2$)). The waist circumference was measured by using an unstretched flexible tape (accurate to 0·1 cm), following a typical expiration and with no external pressure applied to the body. Systolic blood pressure and diastolic blood pressure were measured from right arm using a mercury sphygmomanometer in a sitting posture[25]. Two measurements were taken with 15 min apart, and then the average of two measurements was considered in this study.

Biochemical profiles of participants were assessed after 12 h of fasting. Serum levels of TAG, HDL-cholesterol, fasting blood glucose (FBG) and insulin were assessed. Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) was calculated using the following formula to measure insulin resistance (IR)[26]: ((fasting insulin (mU/l) × FBG (mmol/l))/22·5.

### Assessment of metabolic health status

To categorise individuals as being with MHO or MUO, two methods were applied. The first approach was based on the modified International Diabetes Federation (IDF) criteria[27]. According to this definition, participants who had two or more of the following risk factors were classified as being with MUO: increased TAG (≥150 mg/dl), decreased HDL-cholesterol (age of < 16 years: < 40 mg/dl; age of ≥ 16 years: < 50 mg/dl for girls/ < 40 mg/dl for boys), increased blood pressure (≥ 130/85 mmHg) and increased FBG (≥ 100 mg/dl). Otherwise, they were defined as individuals with MHO. In the second method, HOMA-IR was considered in addition to the IDF items. So that, individuals with HOMA-IR score ≥ 3·16 who had at least two other above-mentioned metabolic risk factors were classified as being with MUO; otherwise, they were considered as adolescents with MHO[28].

### Assessment of other variables

Physical activity of adolescents assessed through Physical Activity Questionnaire for Adolescents (PAQ-A)[29]. The validity and reliability of this questionnaire were assessed among Iranian children previously[30]. It was developed to assess the levels of physical activity for students with nine questions. The first eight items are about the typical activities of adolescents that scored from 1 to 5; a score of 1 indicated the least amount of physical activity, while a score of 5 indicated the most. The ninth question asks participants about unusual activity during the past 7 d. After summing up total scores, adolescents were divided into four categories[29]: sedentary (scoring < 2), low active (2 ≤ score < 3), active (3 ≤ score < 4) and very active (score ≥ 4). As few participants were classified as sedentary or very active, we merged the sedentary group with the less active group and the active group with the very active group, resulting in two final categories: low and high levels of physical activity. A questionnaire was applied to record the participants' age, sex, medical history, medications and supplements intake. In addition, a verified demographic questionnaire was used to gather data about socio-economic status of participants[31]. This questionnaire had several items including parental job, parental education level, family size, having cars in the family, taking trips in a year, having personal room and having computers/laptops. Each item had ≥ 2 response options and participants received the corresponding score for each chosen answer. The final socio-economic status score was considered as the sum of the scores of all items of the questionnaire.

### Statistical analysis

General characteristics of studied participants across tertiles of MIND diet score were expressed as mean and standard deviation for continuous and number (percentage) for categorical variables. In order to assess the participants' general characteristics, ANOVA and $\chi^2$ test were used for continuous and categorical variables. ANOVA was also applied to assess individuals' dietary intakes across tertiles of MIND diet score. To determine the relationship of the MIND diet score with odds of MUO, we used binary logistic regression. The OR and 95 % CI for MUO status were calculated in crude and multivariable-adjusted models. In the first model, adjustments were done for age, sex and total energy intake. In the second model, further adjustments were applied for socio-economic status (low/ moderate/high) and physical activity level (low/high). In the third model, BMI was added to previous adjustments. In all models, the first tertile of MIND diet score was considered as the reference category. We additionally estimated odds of MUO for each 1 tertile increase in MIND diet score as an independent variable. The Statistical Package for the Social Sciences (version 20; SPSS Inc.) was used for all statistical analyses.

## Results

The current study was performed on 203 adolescents with a mean (SD) age and weight of 13·98 (1·61) (years) and 73·48 (11·60) (kg), respectively. Overall, 50·2 % of study participants were girls. Based on IDF definition, seventy-nine participants were classified as being with MUO, while sixty-seven adolescents were MUO based on IDF/HOMA-IR criteria. General characteristics of study participants across tertiles of the MIND diet score are presented in Table 1. Adolescents with the highest adherence to the MIND diet, compared with the lowest one, had higher physical activity levels and were more likely to have better socio-economic status. About cardiometabolic factors, participants in the highest tertile of MIND diet score had lower FBG, insulin, HOMA-IR, TAG and higher HDL-cholesterol. No other significant differences were seen.

Dietary intakes of study participants among tertiles of the MIND diet score are indicated in Table 2. Individuals in the top tertile of MIND diet score, compared with the bottom tertile, had higher intakes of brain healthy and lower intakes of brain unhealthy foods. No significant difference was found in total energy intake across tertiles of the MIND diet score.

Figure 1 represents the prevalence of MUO across tertiles of the MIND diet score. According to both IDF and IDF/HOMA-IR definitions, adolescents in the top tertile of the MIND diet score (compared with the bottom one) had lower prevalence of MUO (IDF criteria: 15·9 *v.* 60·0 %; $P < 0·001$ and IDF/HOMA-IR criteria: 14·5 *v.* 54·3 %; $P < 0·001$).

Multivariable-adjusted OR for MUO status across tertiles of the MIND diet score are provided in Table 3. In the crude model, adolescents in the third tertile of the MIND diet score (compared with the first tertile) had 87 % lower odds for MUO status, based on IDF criteria (OR = 0·13; 95 % CI 0·06, 0·28). After adjustments for potential confounders, individuals in the top tertile of the MIND diet score had 80 % lower odds for MUO status (OR = 0·20; 95 % CI 0·08, 0·51). Also, in crude and fully -adjusted models, each tertile increase in MIND diet score was respectively associated with 63 % (OR = 0·37; 95 % CI 0·25, 0·54) and 56 %

https://doi.org/10.1017/S0007114524002381 Published online by Cambridge University Press

British Journal of Nutrition

**Table 1.** General characteristics of participants across tertiles of MIND diet score (*n* 203)†
(Mean values and standard deviations; numbers and percentages)

| | Tertiles of MIND diet score | | | | | | |
|---|---|---|---|---|---|---|---|
| | $T_1$ (*n* 70) score < 6 | | $T_2$ (*n* 64) score 6–8 | | $T_3$ (*n* 69) score > 8 | | |
| | Mean | SD | Mean | SD | Mean | SD | *P*‡ |
| Age (years) | 14·20 | 1·57 | 13·72 | 1·44 | 13·99 | 1·78 | 0·22 |
| Weight (kg) | 74·59 | 11·35 | 74·77 | 11·84 | 71·16 | 11·44 | 0·12 |
| BMI (kg/m$^2$) | 27·67 | 2·88 | 27·50 | 3·08 | 26·91 | 3·69 | 0·35 |
| | *n* | % | *n* | % | *n* | % | |
| Sex (*n*, (%)) | | | | | | | |
| Girl | 40 | 57·1 | 30 | 46·9 | 32 | 46·4 | 0·36 |
| Boy | 30 | 42·9 | 34 | 53·1 | 37 | 53·6 | |
| Physical activity levels (*n*, (%)) | | | | | | | |
| Low | 67 | 95·7 | 61 | 95·3 | 38 | 55·1 | < 0·001* |
| High | 3 | 4·3 | 3 | 4·7 | 31 | 44·9 | |
| Socio-economic status levels (*n*, (%)) | | | | | | | |
| Low | 30 | 42·9 | 16 | 25·0 | 13 | 18·8 | 0·02* |
| Moderate | 25 | 35·7 | 33 | 51·6 | 32 | 46·4 | |
| High | 15 | 21·4 | 15 | 23·4 | 24 | 34·8 | |
| | Mean | SD | Mean | SD | Mean | SD | |
| Systolic blood pressure (mmHg) | 115·27 | 16·03 | 111·70 | 22·55 | 111·03 | 16·06 | 0·35 |
| Diastolic blood pressure (mmHg) | 74·46 | 13·20 | 73·04 | 13·23 | 72·94 | 6·64 | 0·68 |
| Fasting blood glucose (mg/dl) | 101·20 | 9·47 | 99·30 | 7·11 | 93·94 | 6·97 | < 0·001* |
| Insulin (μUI/ml) | 24·53 | 15·19 | 20·23 | 7·88 | 16·44 | 12·29 | 0·01* |
| HOMA-IR index | 6·14 | 3·82 | 4·99 | 2·11 | 3·91 | 3·24 | < 0·001* |
| TAG (mg/dl) | 141·81 | 64·85 | 120·31 | 74·61 | 103·32 | 54·54 | 0·01* |
| HDL-cholesterol (mg/dl) | 42·41 | 8·01 | 44·55 | 7·02 | 47·52 | 7·90 | 0·01* |

MIND diet, Mediterranean-DASH Intervention for Neurodegenerative Delay diet; T, tertile; HOMA-IR, Homeostasis Model Assessment of Insulin Resistance.
* $P < 0·05$.
† All values are means and standard deviation, unless indicated.
‡ Obtained from ANOVA for continuous variables and $\chi^2$ test for categorical variables.

(OR = 0·44; 95 % CI 0·28, 0·70) lower odds of MUO profile. Similar findings were obtained when we defined MUO based on IDF/HOMA-IR criteria, such that, in fully adjusted model, adolescents in the third tertile of MIND diet score had 78 % reduced odds of MUO status (OR = 0·22; 95 % CI 0·08, 0·59) and also, each tertile increment in MIND diet score was related to 59 % reduced odds of MUO profile (OR = 0·41; 95 % CI 0·25, 0·68).

Multivariable-adjusted OR for MUO phenotype across tertiles of MIND diet score, stratified by BMI categories, are reported in online Supplemental Table 2. Based on IDF definition, adolescents with overweight were less likely to be MUO ($OR_{\text{fully adjusted}}$ = 0·06; 95 % CI 0·01, 0·36). However, in participants with obesity, no significant relationship was found ($OR_{\text{fully adjusted}}$ = 0·38; 95 % CI 0·11, 1·31). Considering IDF/HOMA-IR criteria, the same findings were obtained in participants with overweight ($OR_{\text{fully adjusted}}$ = 0·08; 95 % CI 0·01, 0·75) and obesity ($OR_{\text{fully adjusted}}$ = 0·39; 95 % CI 0·11, 1·35).

Multivariable-adjusted OR for MUO status across tertiles of MIND diet score, stratified by sex, are reported in online Supplemental Table 3. According to the IDF definition, we found reduced odds of MUO profile among girls and boys, in fully adjusted model (girls: OR = 0·12; 95 % CI 0·03, 0·53; boys: OR = 0·16; 95 % CI 0·04, 0·65). Based on IDF/HOMA-IR criteria, the same findings were seen in fully adjusted model (girls: OR = 0·14; 95 % CI 0·03, 0·82; boys: OR = 0·21; 95 % CI 0·05, 0·87).

Multivariable-adjusted OR for MUO components across tertiles of the MIND diet score are reported in Table 4. After adjustments of all potential confounders, participants with highest MIND diet adherence had reduced odds of hyperglycaemia (OR = 0·16; 95 % CI 0·06, 0·39) and IR (OR = 0·06; 95 % CI 0·02, 0·21). However, no significant associations were found in relation to high blood pressure, hypo-HDL-cholesterolemia and hypertriacylglycerolaemia.

## Discussion

Our findings revealed that more adherence to the MIND diet was related to lower odds of MUO, based on both IDF and IDF/HOMA-IR criteria, independent of confounders. This association was only meaningful among adolescents with overweight and was stronger among girls. In the context of MUO components, a significant relationship was revealed with hyperglycaemia and IR.

Childhood obesity is considered as a serious problem and is associated with an increased risk of health problems in adulthood[32]. It also reduces quality of life and frequently exerts an economic challenge on healthcare systems.[33]. Due to increased prevalence of overweight or obesity among adolescents, identification and modification of the factors related to metabolic health status could have a high priority. So, it is clinically notable to recommend adolescents to consume more healthy foods based on the MIND diet in order to have a lower risk of MUO status. Additionally, this could potentially lead to reduced risk of diseases and complication related to unfavourable metabolic status and might also offer significant social benefits in terms of both health and cost implications.

**Table 2.** Dietary intakes of selected food groups of participants across tertiles of MIND diet score ($n$ 203)†
(Mean values and standard deviations)

| | Tertiles of MIND diet score | | | | | | |
|---|---|---|---|---|---|---|---|
| | $T_1$ ($n$ 70) score < 6 | | $T_2$ ($n$ 64) score 6–8 | | $T_3$ ($n$ 69) score > 8 | | |
| | Mean | SD | Mean | SD | Mean | SD | $P$‡ |
| Energy (kcal/d) | 2866·52 | 444·03 | 2967·47 | 476·79 | 2821·44 | 866·16 | 0·34 |
| Brain healthy foods: | | | | | | | |
| Green leafy vegetable (g/d) | 28·70 | 15·37 | 48·50 | 30·54 | 89·56 | 43·06 | < 0·001* |
| Other vegetables (g/d) | 151·20 | 122·22 | 229·04 | 182·11 | 302·09 | 154·22 | < 0·001* |
| Berries (g/d) | 4·09 | 4·44 | 7·13 | 5·89 | 8·82 | 15·53 | 0·02* |
| Nuts (g/d) | 7·06 | 5·97 | 11·70 | 11·40 | 17·82 | 12·57 | < 0·001* |
| Whole grains (g/d) | 45·25 | 65·56 | 71·78 | 93·77 | 147·46 | 116·63 | < 0·001* |
| Fish (g/d) | 2·16 | 2·61 | 5·11 | 5·06 | 8·34 | 6·87 | < 0·001* |
| Beans (g/d) | 23·80 | 14·05 | 41·60 | 22·56 | 53·99 | 28·26 | < 0·001* |
| Poultry (g/d) | 32·31 | 25·00 | 48·02 | 34·03 | 42·95 | 31·37 | 0·01* |
| Olive oil (g/d) | 0·55 | 1·69 | 4·00 | 6·51 | 8·13 | 9·94 | < 0·001* |
| Brain unhealthy foods: | | | | | | | |
| Butter and margarine (g/d) | 7·97 | 11·30 | 6·59 | 8·04 | 3·54 | 7·13 | 0·01* |
| Cheese (g/d) | 32·85 | 19·07 | 33·64 | 19·36 | 42·00 | 20·79 | 0·02* |
| Red meat products (g/d) | 32·00 | 17·83 | 30·21 | 21·15 | 21·32 | 16·30 | 0·002* |
| Fast fried foods (g/d) | 58·00 | 32·25 | 50·34 | 27·81 | 32·67 | 28·44 | < 0·001* |
| Pastries and sweets (g/d) | 151·72 | 75·16 | 122·38 | 61·85 | 57·10 | 48·80 | < 0·001* |

MIND diet, Mediterranean-DASH Intervention for Neurodegenerative Delay diet; T, tertile.
* $P < 0·05$.
† All values are means and standard deviation.
‡ Obtained from ANOVA.

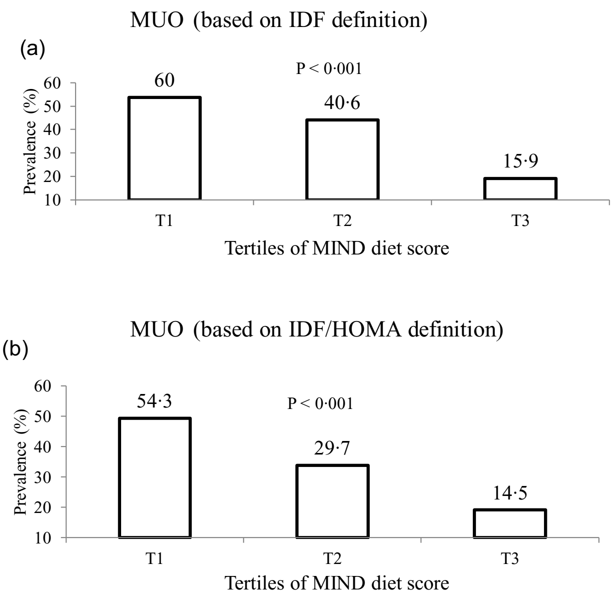


**Fig. 1.** Prevalence of MUO based on IDF/IDF-HOMA-IR: (a) MUO (based on IDF definition) across tertiles of MIND diet score and (b) MUO (based on IDF/HOMA definition) across tertiles of MIND diet score. MUO, metabolically unhealthy overweight/obesity; IDF, International Diabetes Federation; HOMA-IR, Homeostasis Model Assessment of Insulin Resistance; MIND diet, Mediterranean-DASH Intervention for Neurodegenerative Delay diet.

Our results revealed reduced likelihood of metabolic unhealthy among adolescents with overweight/obesity. As far as we know, limited studies have reported association between MIND diet, as a combination of the Mediterranean and Dietary Approach to Stop Hypertension (DASH) diets, and MUO, especially among children and adolescents. A cohort study on 1299 adults (with a healthy metabolic profile at baseline), after 5·91 years of follow-up, reported that the highest adherence to the DASH, Mediterranean and MIND dietary patterns was associated with a lower odds of MUO phenotype[34]. Contrary to what we discovered, a cohort study on 229 Iranian women with overweight and obesity did not indicate a significant association between MIND diet score and metabolically healthy/unhealthy phenotypes[35]. A study involving 5801 older men and women at high cardiovascular risk in the PREDIMED trial, with a 5-year follow-up period, revealed a correlation between a high adherence to a traditional Mediterranean diet and transition from metabolically unhealthy phenotype to healthier conditions[36]. Also, a cross-sectional study conducted on 341 children and adolescents with overweight has documented that adherence to the DASH diet was inversely associated with MUO based on the HOMA-IR definition[37]. However, they found no significant differences between DASH diet and each cardiometabolic risk factors[37].

Several studies have examined the association of the MIND diet with cardiometabolic risk factors. In a cross-sectional study involving 163 adults, researchers investigated the relationship between adherence to the MIND, Mediterranean and DASH diets with metabolic syndrome characteristics and visceral obesity. Their findings indicated that while all of these diets were inversely associated with metabolic syndrome, only higher adherence to the MIND diet was linked to reduced visceral adiposity and metabolic syndrome components in adults[38]. In an Iranian cohort study with 10·6 years follow-up and encompassing 2863 participants, it was revealed that greater adherence to the MIND diet was associated with a decreased likelihood of CVD[39]. Furthermore, in a cross-sectional study involving 339 adults with obesity, elevated adherence to the

https://doi.org/10.1017/S0007114524002381 Published online by Cambridge University Press

**Table 3.** Multivariable-adjusted OR for MUO (based on IDF and IDF/HOMA-IR criteria) across tertiles of MIND diet score (*n* 203)†
(Odds ratios and 95 % confidence intervals)

| | Tertiles of MIND diet score | | | | | | Per 1 tertile increase | |
|---|---|---|---|---|---|---|---|---|
| | | T2 (*n* 64) score 6–8 | | T3 (*n* 69) score > 8 | | | | |
| | T1 (*n* 70) score < 6 | OR | 95 % CI | OR | 95 % CI | $P_{trend}$ | OR | 95 % CI |
| MUO phenotype based on IDF criteria | | | | | | | | |
| Cases (*n*) | 42 | 26 | | 11 | | | | |
| Crude | 1·00 | 0·46 | 0·23, 0·91 | 0·13 | 0·06, 0·28 | < 0·001* | 0·37 | 0·25, 0·54 |
| Model 1 | 1·00 | 0·43 | 0·21, 0·88 | 0·14 | 0·06, 0·32 | < 0·001* | 0·38 | 0·25, 0·57 |
| Model 2 | 1·00 | 0·41 | 0·19, 0·85 | 0·22 | 0·09, 0·54 | 0·01* | 0·46 | 0·29, 0·71 |
| Model 3 | 1·00 | 0·41 | 0·19, 0·86 | 0·20 | 0·08, 0·51 | < 0·001* | 0·44 | 0·28, 0·70 |
| MUO phenotype based on IDF/HOMA-IR criteria | | | | | | | | |
| Cases (*n*) | 38 | 19 | | 10 | | | | |
| Crude | 1·00 | 0·36 | 0·17, 0·73 | 0·14 | 0·06, 0·32 | < 0·001* | 0·38 | 0·25, 0·56 |
| Model 1 | 1·00 | 0·29 | 0·13, 0·62 | 0·15 | 0·06, 0·36 | < 0·001* | 0·37 | 0·24, 0·57 |
| Model 2 | 1·00 | 0·27 | 0·12, 0·59 | 0·25 | 0·09, 0·65 | 0·01* | 0·44 | 0·27, 0·71 |
| Model 3 | 1·00 | 0·27 | 0·12, 0·59 | 0·22 | 0·08, 0·59 | 0·01* | 0·41 | 0·25, 0·68 |

IDF, International Diabetes Federation; HOMA-IR, Homeostasis Model Assessment of Insulin Resistance; MIND diet, Mediterranean-DASH Intervention for Neurodegenerative Delay diet; T, tertile; MUO, metabolically unhealthy overweight/obesity.
* $P < 0·05$.
† All values are OR and 95 % CI. Model 1: Adjusted for age, sex, energy intake. Model 2: More adjustments for physical activity levels, socio-economic status. Model 3: Further adjustments for BMI.

**Table 4.** Multivariable-adjusted OR for MUO components across tertiles of MIND diet score (*n* 203)†
(Odds ratios and 95 % confidence intervals)

| | Tertiles of MIND diet score | | | | | |
|---|---|---|---|---|---|---|
| | | T2 (*n* 64) score 6–8 | | T3 (*n* 69) score > 8 | | |
| | T1 (*n* 70) score < 6 | OR | 95 % CI | OR | 95 % CI | $P_{trend}$ |
| High blood pressure | | | | | | |
| Crude | 1·00 | 1·24 | 0·50, 3·04 | 0·51 | 0·18, 1·47 | 0·24 |
| Fully adjusted model‡ | 1·00 | 1·41 | 0·53, 3·76 | 0·60 | 0·16, 2·21 | 0·60 |
| Hyperglycaemia | | | | | | |
| Crude | 1·00 | 0·85 | 0·43, 1·68 | 0·13 | 0·06, 0·29 | < 0·001* |
| Fully adjusted model‡ | 1·00 | 0·75 | 0·36, 1·55 | 0·16 | 0·06, 0·39 | < 0·001* |
| Low HDL-cholesterolemia | | | | | | |
| Crude | 1·00 | 0·50 | 0·25, 1·00 | 0·27 | 0·13, 0·56 | < 0·001* |
| Fully adjusted model‡ | 1·00 | 0·55 | 0·26, 1·15 | 0·50 | 0·21, 1·19 | 0·08 |
| Hypertriacylglycerolaemia | | | | | | |
| Crude | 1·00 | 0·45 | 0·21, 0·96 | 0·30 | 0·14, 0·68 | 0·01* |
| Fully adjusted model‡ | 1·00 | 0·37 | 0·16, 0·86 | 0·43 | 0·16, 1·11 | 0·04* |
| Insulin resistance | | | | | | |
| Crude | 1·00 | 0·42 | 0·13, 1·29 | 0·05 | 0·02, 0·14 | < 0·001* |
| Fully adjusted model‡ | 1·00 | 0·24 | 0·06, 0·89 | 0·06 | 0·02, 0·21 | < 0·001* |

MUO, metabolically unhealthy overweight/obesity; MIND diet, Mediterranean-DASH Intervention for Neurodegenerative Delay diet; T, tertile.
* $P < 0·05$.
† All values are OR and 95 % CI.
‡ Fully adjusted model: adjusted for age, sex, energy intake, physical activity levels, socio-economic status and BMI.

MIND diet was associated with improved insulin sensitivity after accounting for certain confounding factors(40). A cross-sectional study of 1912 schoolchildren pointed out that more adherence to dietary patterns that are relatively similar to MIND diet score which decreased consumption of sweets, margarine and savoury snacks was significantly associated with improved IR; breakfast consumption had also an inverse association with HOMA-IR(41). The inconsistencies in findings might come from variations in study design, composition of study populations, methods used to calculate the MIND diet score and diverse range of controlled confounders.

Our findings indicated that adherence to the MIND diet has a stronger association with MUO among girls than boys. Protective actions of endogenous oestrogens, mainly through oestrogen $\alpha$ receptor in various tissues, could justify sex differences in metabolic status(42). Besides sex hormones, other factors like the fetal/neonatal programming, sex chromosomes and epigenetic changes have been suggested to have an important role in this field(43). We also observed that the association was significant in adolescents with overweight, but not obesity. It is obvious that regional-specific distribution of body fat is more important than overall amount of body fat(44). Furthermore, lean body mass is more metabolically active than fat mass and accounts for a significant proportion of basal metabolism of individuals[45]. So, despite having lower weight in adolescents with overweight than those with obesity, they could be more susceptible to various metabolic dysfunctions and consequently might take more benefits from this pattern to overcome metabolic disorders. We should interpret these results cautiously as our study sample size might not be enough for examining such stratified analyses by sex or BMI, resulting in insufficient power. However, these findings may broaden researchers' insights for future studies. Further studies with larger sample sizes are warranted to extract the probable mechanisms behind these findings.

In terms of its underlying mechanism, the MIND diet embodies an overall healthy dietary pattern, with reduced energy intake, animal and high-saturated fatty foods, and conversely increased natural plant-based foods intake[24]. A diet with high intake of fruits and vegetables has been correlated with reduced IR, as a main factor of MUO, due to its anti-oxidative and anti-inflammatory features[46]. Among all fruits and vegetables, the MIND diet emphasises the consumption of green leafy vegetables and berries. These vegetables are related to reduced odds of diabetes due to their high amounts of fibre, low glycaemic index and Mg[47,48]. Green leafy vegetables are also rich in potassium that is inversely related to hypertension[49]. Among fruits, berries are wealthy in phytochemicals, especially anthocyanin that could decrease the blood glucose levels by deactivating $\alpha$-glucosidase and $\alpha$-amylase enzymes[50]. Also, berries could alleviate hypertension and dyslipidemia by modifying nitric oxide synthesis[51].

As far as we are aware, this is the first research that examined the relationship between the MIND diet and MUO profile in adolescents. We have considered both boys and girls to be included in this study. Additionally, effects of several confounding factors were taken into account during the analyses. We also used two distinct descriptions of metabolic health status, one of which had included IR that is of the important factors of metabolic health status. However, we are well aware of some limitations while interpreting our results. The study design was cross-sectional that makes it impossible to provide evidence about causality. Additional prospective studies are required to validate the causality. Moreover, participants were only overweight and obese adolescents, so our results may not be generalisable to all BMI categories, particularly those with normal weight who suffer from metabolic disorders. Even after adjustments for probable confounders, some other confounding factors such as pubertal growth stage, lack of sleep, dietary preferences and overweight/obesity in their parents might remain and influence our results. Despite using FFQ for assessing dietary intakes, misclassification of participants may not be completely ruled out. Finally, the distribution of body fat and body composition, which are significant confounders in predicting metabolic health status, were not assessed.

## Conclusions

To summarise, this cross-sectional study indicated that higher adherence to the MIND diet was associated with lower odds of MUO status in Iranian adolescents with overweight/obesity. We also found an inverse relationship between higher adherence to the MIND diet and odds of hyperglycaemia and IR. Given the relation between MUO and risk of developing chronic diseases later in life, our findings underscore that higher compliance to MIND diet could be a viable strategy for early prevention of metabolic disorders. As a take-home message, adopting the MIND diet may significantly reduce the possibility of metabolically unhealthy obesity and related metabolic disorders in adolescents with overweight/obesity. Future research with prospective study designs in other populations with different food cultures and genetic backgrounds as well as clinical trials are needed to validate our findings.

## Acknowledgements

None.

The financial support for this study comes from Nutrition and Food Security Research Center, Isfahan University of Medical Sciences, Isfahan, Iran (no. 63158).

M. K. H., D. P., S. M., A. A., M. A. and P. S. contributed to conception, design, data collection, data analyses and manuscript drafting and agreed for all aspects of the work.

There are no conflicts of interest to declare.

The study procedure was performed according to declaration of Helsinki and STROBE checklist. All participants provided informed written consent. The study protocol was approved by the local Ethics Committee of Isfahan University of Medical Sciences.

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Consent for publication: Not applicable.

## Supplementary material

For supplementary material/s referred to in this article, please visit https://doi.org/10.1017/S0007114524002381

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