Original Article

Association between isocaloric substitution of macronutrient intake with sleep disorders and psychological health in male adults

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Background: Considering the insufficient data regarding the relationship between isocaloric substitution of macronutrients, sleep, and mental health in the Middle East, we sought to examine this association among Iranian adult men. **Materials and Methods:** This cross-sectional study was performed on 354 middle-aged Iranian men (mean age: 38.6 ± 5.34 years). Dietary data were collected using a validated food frequency questionnaire, and participants were divided into tertiles based on dietary macronutrient intake. Sleep quality was assessed using the Pittsburgh Sleep Quality Index, and sleep-related outcomes (daytime sleepiness and insomnia) and mental health (depression, anxiety, and stress) were evaluated using standard questionnaires. Multivariable logistic regression was applied to indicate the associations. **Results:** Participants in the highest tertile of protein intake showed significantly lower odds of poor sleep quality in both crude (odds ratio [OR]: 0.55; 95% confidence interval [CI]: 0.32, 0.95) and adjusted (OR: 0.53; 95% CI: 0.30, 0.93) models. Substituting carbohydrates with an equivalent amount of protein was associated with 26% lower odds of poor sleep quality (OR: 0.74; 95% CI: 0.55, 0.99). In addition, substituting animal protein with the same amount of plant protein was linked to 29% lower odds of poor sleep quality (OR: 0.71; 95% CI: 0.51, 0.99). No other significant associations were found in both pairwise and substitution models. **Conclusion:** Our findings indicate that isocaloric substitution of carbohydrates with protein, and animal protein with plant protein, is related to lower odds of poor sleep quality. We found no other significant associations between isocaloric substitution of macronutrients and sleep-related and mental health outcomes.

Key words: Cross-sectional studies, mental disorders, nutrients, sleep quality

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INTRODUCTION

The increasing prevalence of mental health disorders is a global concern, affecting approximately 25% of the world's population during their lifetime.[1] In addition, around 30% of the global population experiences sleep disturbances.[2] The prevalence of depression and anxiety among Iranian adults is reported to be 27.6% and 15.6%, respectively.[3] Studies have established a connection between sleep disturbances and mental health conditions, including depression, anxiety, and stress.[4] Individuals with sleep disorders have also significant deficits in their quality of life.[5] Therefore, developing effective preventive strategies is crucial to maintain both physical and mental health.

Lifestyle modification appears to be a key component in the prevention and treatment of sleep disorders, and it also plays a crucial role in promoting mental health disorders.[6] Consequently, dietary composition has gained significant attention as a crucial modifiable factor in the mitigation and prevention of mental health disorders.[6] Imbalances in macronutrient distributions can exacerbate mental health conditions and sleep disturbances, thus highlighting the significance of maintaining appropriate macronutrient proportions.[7]

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For instance, some cross-sectional studies have reported positive associations, such as a link between higher protein intake and reduced depressive symptoms in Japanese male adults[8] or lower carbohydrate/higher protein diets correlating with decreased symptoms of depression and anxiety.[9] However, a cohort study found no such association between carbohydrate intake and daytime sleepiness in adult males.[10] Similarly, findings on protein's impact on sleep quality are mixed, with one study showing that higher protein is associated with difficulties in maintaining sleep, and another study suggests that protein positively influences sleep by promoting its induction and reducing nocturnal awakenings.[11,12] In addition, we thought that using isocaloric substitution analysis results in more reasonable and precise associations, given that in an isoenergetic context, an increase in the intake of one macronutrient complied with a decrease in the intake of another to maintain a constant total energy intake. As far as we know, the current body of research lacks studies that explore the relationship between isocaloric substitution of macronutrients and sleep disorders, as well as mental health in Middle East countries, where carbohydrates are the primary energy source. The present study aimed to investigate the association between isocaloric substitution of macronutrients, sleep disorders, and mental health among Iranian male adults.

METHODS

This cross-sectional study, conducted in 2024, included Iranian male adults working at various healthcare centers associated with Baqiyatallah University of Medical Sciences. Rostami *et al*.'s study on Dietary Approaches to Stop Hypertension diet adherence and insomnia led us to compute a minimum sample size of 323, with an alpha value of 0.05 (two-sided) and a power of 80%.[13] We invited 400 participants to take possible dropout into account. Random cluster sampling was adopted 400 male adults from multiple healthcare centers. In this investigation, we excluded individuals with energy intake beyond the range of 800–4200 kcal/d (n = 46).[14] Finally, the present analysis comprised data from 354 participants who provided complete information. The study included male individuals aged ≥18 years without a history of chronic conditions such as cardiovascular disease, diabetes, colitis, cancer, renal failure, and hepatic diseases. Participants taking antidiabetic, anti-inflammatory, antidepressant, or antiobesity medications, as well as vitamin or mineral supplements such as Vitamin D, calcium, or iron within the last 6 months, were excluded. Each participant obtained written informed consent. The Medical Ethics Committeeof Baqiyatallah University of Medical Sciences granted ethical approval for this study IR.BMSU.REC.1403.005.

Dietary assessment

Participants' usual dietary intake was assessed using a validated 168-item semi-quantitative food frequency questionnaire in the Willett format. The reliability and validity of this questionnaire for the Iranian adult population have been previously tested.[15] Participants reported their daily intake frequency of each food item during an in-person interview with experienced nutritionists. Then, the reported frequencies and portion sizes of the consumed foods were converted to grams per day using household measurements. Finally, all food items were entered into the Nutritionist IV software (Version 7; N-squared computing, OR, USA) to determine the daily intake of all nutrients as well as total energy intake. Furthermore, animal protein was calculated from animal-based foods (meats, dairy products, and egg), while plant proteins were obtained from plant-based items (vegetables, fruits, grains, soy, nuts, and legumes). Mixed dishes were not considered due to insufficient data regarding their exact protein type amounts.

Demographic and anthropometric assessments

Using personal interviews and standardized questionnaires, basic demographic information, such as participants' ages, marital statuses (single/married), smoking statuses (yes/no), and levels of education (elementary/lower, high school, and college/university), were collected. Physical activity data were gathered using the International Physical Activity Questionnaire (IPAQ)-Short Form, presenting it as metabolic equivalent-min/day.[16] The validity and reliability of the IPAQ in Iran were previously examined.[16] Weight was measured in minimal clothing and without shoes with an accuracy of 0.5 kg. The height was measured to the nearest 0.1 cm using a wall-mounted tape meter. Body mass index (BMI) was calculated by dividing weight (kg) by height (m) squared.

Assessment of outcomes

Depression, anxiety, and stress were assessed using the Depression Anxiety and Stress Scale (DASS-21). DASS-21, a valid and reliable questionnaire, measures negative well-being in the general population.[17] The questionnaire has three subscales with 21 items. The seven items that make up each subscale all use a 4-point Likert scale ranging from 0 to 3 to assess the degree to which the individual is depressed, anxious, or stressed. Higher scores indicate severe, unfavorable feelings. Given that DASS-21 is a condensed version of DASS-42, we should double the total score for each subclass. Two categories were created for each of the three primary domains: no stress (score ≤ 14) or some level of stress (>14); no depression (score ≤ 9) or some level of depression (>9); and no anxiety (score ≤ 7) or some degree of anxiety (>7). The current study utilized the validated DASS-21 questionnaire in the Iranian population.[17]

The validated Persian version of the Pittsburgh Sleep Quality Index was utilized for evaluating sleep quality and quantity.[18] The questionnaire, comprising 19 items, assesses seven domains related to sleep: quality, duration, latency, disturbances, habitual efficiency, daytime dysfunction, and medication use. Each domain is scored on a 4-point scale (0–3), and the total score ranges from 0 to 21. A higher total score reflects poorer sleep quality, with scores above 5 indicating poor sleep and scores of 5 or less indicating normal sleep.

Daytime sleepiness was measured using the validated 8-item Epworth Sleepiness Scale (ESS).[19] Each question is scored from 0 to 3, resulting in a total score between 0 and 24. Higher scores indicate greater daytime sleepiness. Scores ≤10 were categorized as normal, while scores >10 were considered mild-to-moderate sleepiness. The validity and reliability of the ESS have been established in a previous study within the Iranian population.[19]

To assess insomnia, the Insomnia Severity Index (ISI) questionnaire was used. This questionnaire includes seven items; each scored from 0 (none) to 4 (extremely severe). The overall score runs from 0 to 28 points, and an ISI score over 7 is an indication of insomnia. The ISI questionnaire used in this study was validated for the Iranian population previously.[20]

Statistical analysis

Participants were categorized based on their energy-adjusted tertile of protein, carbohydrates, and fat. Given our moderate sample size, tertiles provide clear contrasts in intake levels and ensure adequate sample size in each group. Variables were tested for normality through the Kolmogorov–Smirnov test and Q–Q plot. Continuous variables are presented as means with standard deviations (SDs), and categorical variables as percentages (frequency), across these tertiles. For general characteristics, analysis of variance was used to compare continuous variables, and the Chi-square tests were performed for categorical variables to examine differences across tertiles of macronutrients. Analysis of covariance was applied to determine individuals' dietary intakes across the tertiles of protein, carbohydrate, and fat intake adjusted for age and energy intake. Binary logistic regression was performed to find the odds ratios (ORs) and 95% confidence intervals (CIs) for the association between macronutrients and outcomes of interest in both crude and adjusted models. In all the models, individuals in the first tertile of protein, carbohydrate, and fat intake were considered the reference category. The adjusted model controlled for age, energy intake, education level, marital status, smoking status, physical activity, dietary fiber intake, and BMI. Nonlinear curves for the association between macronutrients and outcomes were modeled using restricted cubic splines with three knots. The link between substituting 3% of the energy from different energy sources and study outcomes was assessed using the aforementioned multivariable model. We considered the nutrient density model and reporting values based on macronutrients' contribution to the energy intake, as this approach would provide a more understandable interpretation for using in clinical practice or policy making than reporting in grams/day. We implemented an energy partition model to estimate isocaloric substitution effects, where both macronutrients of interest are included simultaneously in the multivariable regression model. For instance, for substituting 3% of energy from carbohydrate with total protein, both macronutrients (carbohydrate and protein) as well as confounders (including energy intake, and age) were included in the model. The substitution effect is quantified as the difference between the β-coefficients of the two macronutrients, and its 95% CI is derived from their variance–covariance matrix.[21] The exponentiated substitution effect (95% CI) from the model is the OR for the observed association. Statistical analyses were performed using SPSS (version 26; IBM, Chicago, IL) and Stata (version 17; Stata Corp., College Station, TX), and $P < 0.05$ (two-sided) was regarded as statistically significant.

RESULTS

Participants had a mean age and BMI of 38.64 ± 5.34 years and 25.27 ± 3.20 kg/m^2, respectively [Supplemental Table 1]. The prevalence of study outcomes across tertiles of protein, carbohydrate, and fat intake is provided in Supplemental Table 2. Participants with the highest protein intake experienced a significantly lower prevalence of poor sleep quality (56.8%) compared to those with the lowest intake (70.3%), while no other significant difference was observed.

Table 1 outlines the general characteristics of participants across tertiles of macronutrients. No significant differences were observed across these intake groups regarding age, weight, BMI, physical activity, marital status, education level, and smoking status.

The mean (SD) of carbohydrate, protein, and fat intake was, respectively, 56.07 (7.75), 12.67 (2.35), and 33.85 (7.32) percentage of energy in the overall population. Dietary intakes of participants across macronutrient tertiles are reported in Table 2. A significant difference was observed across protein tertiles regarding fruits, dairy, meat, legumes, total energy, carbohydrate, fiber, saturated fatty acid, monounsaturated fatty acid, riboflavin, niacin, iron, and magnesium. Furthermore, dietary intakes of all major food groups, energy intake, protein, fat, fiber, thiamine, niacin, and iron were significantly different across tertiles of carbohydrate. In case of fat intake tertiles, significant difference was observed

Table 1: General characteristics of study participants across tertiles of total protein, carbohydrate, and fat intakea (n=354)

	Total protein			P^b	Carbohydrate			P^b	Fat			P^b
	T1 (n=118)	T2 (n=118)	T3 (n=118)		T1 (n=118)	T2 (n=118)	T3 (n=118)		T1 (n=118)	T2 (n=118)	T3 (n=118)	
Age (years)	38.26±5.01	38.83±5.72	38.83±5.26	0.64	38.96±5.05	38.33±5.51	38.62±5.45	0.67	38.30±5.26	38.65±5.24	38.97±5.53	0.63
Weight (kg)	79.38±9.30	79.42±10.31	76.96±8.24	0.07	78.04±9.20	78.74±9.19	78.97±9.75	0.73	78.36±9.55	79.08±9.43	78.32±9.17	0.78
BMI (kg/m^2)	25.46±3.13	25.47±3.45	24.85±2.97	0.23	25.32±3.22	25.14±3.27	25.33±3.11	0.88	25.05±3.23	25.44±3.07	25.29±3.30	0.65
Physical activity (MET min/day)	113.93±40.93	107.29±43.64	115.85±43.55	0.27	115.69±44.54	107.54±43.93	113.84±39.58	0.31	113.28±40.15	105.63±44.33	118.17±43.13	0.08
Marital status												
Single	25 (21.2)	20 (16.9)	20 (16.9)	0.62	15 (12.7)	24 (20.3)	26 (22.0)	0.14	26 (22.0)	23 (19.5)	16 (13.6)	0.23
Married	93 (78.8)	98 (83.1)	98 (83.1)		103 (87.3)	94 (79.7)	92 (78.0)		92 (78.0)	95 (80.5)	102 (86.4)	
Smoking status												
No	111 (94.1)	113 (95.8)	114 (96.6)	0.63	112 (94.9)	113 (95.8)	113 (95.8)	0.94	113 (95.8)	112 (94.9)	113 (95.8)	0.94
Yes	7 (5.9)	5 (4.2)	4 (3.4)		6 (5.1)	5 (4.2)	5 (4.2)		5 (4.2)	6 (5.1)	5 (4.2)	
Education												
≤Elementary	25 (21.2)	38 (32.2)	34 (28.8)	0.35	31 (26.3)	37 (31.4)	29 (24.6)	0.77	30 (25.4)	34 (28.8)	33 (28.0)	0.98
High school	69 (58.5)	55 (46.6)	59 (50.0)		62 (52.5)	56 (47.5)	65 (55.1)		63 (53.4)	60 (50.8)	60 (50.8)	
University graduate	24 (20.3)	25 (21.2)	25 (21.2)		25 (21.2)	25 (21.2)	24 (20.3)		25 (21.2)	24 (20.3)	25 (21.2)	

[a]Values are expressed as mean±SD for continuous and percentage (frequency) for categorical variables, [b]Obtained by ANOVA for continuous and Chi-square test for categorical variables. SD=Standard deviation; BMI=Body mass index; MET=Metabolic equivalent

for fruits, vegetables, grains, total energy, carbohydrate, fiber, thiamine, niacin, iron, and magnesium.

Table 3 provides crude and multivariable-adjusted ORs (95% CIs) for the association between total protein intake and study outcomes. Participants in the highest tertile of total protein intake, compared to those in the lowest, had significantly lower odds of poor sleep quality in crude (OR: 0.55; 95% CI: 0.32–0.95) and adjusted (OR: 0.53; 95% CI: 0.30–0.93) models. However, no significant relation was observed between protein intake and other outcomes, including insomnia, daytime sleepiness, depression, anxiety, and stress, in the crude and adjusted models. There was no evidence for a nonlinear association [Supplemental Figure 1].

Tables 4 and 5 present the crude and multivariable-adjusted ORs (95% CIs) for study outcomes across tertiles of carbohydrate and fat intake, respectively. Highest tertiles of carbohydrate and fat intake were not significantly related to study outcomes in both crude and adjusted models. There was no evidence for a nonlinear association [Supplemental Figures 2 and 3].

Substituting 3% of energy from carbohydrates with an equivalent amount of protein was linked to a 26% lower risk for poor sleep quality (OR = 0.74; 95% CI: 0.55–0.99). In addition, substitution of 3% of energy from animal protein with the same amount of plant protein was associated with a 29% lower risk for poor sleep quality (OR = 0.71; 95% CI: 0.51–0.99). No other significant relation was observed by the substitution models. More details are provided in Figure 1.

DISCUSSION

Sleep disturbances and mental disorders are highly prevalent among adults worldwide, and the global burden of them is remarkable.[2] Dietary interventions such as the substitution of foods could increase sleep quality and mental well-being.[22] According to the previous studies, isocaloric substitution of macronutrient intake could provide a more reliable estimate of associations between macronutrients and sleep quality and mental health.[23] To our knowledge, this study is the first cross-sectional analysis to determine the relation between isocaloric substitution of macronutrient intake and sleep disorders and mental health among Iranian adults. The study found that individuals in the highest tertile of dietary protein intake had lower odds of poor sleep quality, in both the crude and adjusted models. In addition, substituting 3% of energy from carbohydrates with protein reduced the odds of poor sleep quality. Furthermore, replacing 3% of energy from animal protein with plant protein was linked to lower odds of poor sleep quality.

Table 2: Dietary intakes of study participants across tertiles of total protein, carbohydrate, and fat intakea (n=354)

	Total protein			P[b]	Carbohydrate			P[b]	Fat			P[b]
	T1 (n=118)	T2 (n=118)	T3 (n=118)		T1 (n=118)	T2 (n=118)	T3 (n=118)		T1 (n=118)	T2 (n=118)	T3 (n=118)	
Food groups												
Fruits (g/day)	431.89±24.76	323.23±25.45	281.07±24.72	<0.001	230.55±23.84	348.30±24.01	457.34±23.71	<0.001	434.20±24.13	360.96±24.40	241.03±24.24	<0.001
Vegetables (g/day)	193.90±12.93	179.93±13.29	179.99±12.91	0.68	163.84±12.70	172.24±12.79	217.74±12.63	0.006	211.79±12.64	188.04±12.78	153.99±12.69	0.01
Dairy (g/day)	117.20±9.81	143.10±10.08	188.26±9.80	<0.001	166.75±10.06	149.90±10.13	131.92±10.02	0.04	143.24±10.08	149.46±10.198	155.87±10.13	0.68
Meat (g/day)	31.22±2.56	43.41±3.35	76.39±3.25	<0.001	64.09±3.53	51.31±3.56	35.63±3.51	<0.001	43.71±3.65	54.05±3.69	53.27±3.67	0.09
Grain (g/day)	209.12±12.17	230.80. ±12.51	200.82±12.16	0.23	164.33±11.42	203.04±11.51	273.36±11.36	<0.001	284.55±11.09	196.32±11.22	159.86±11.15	<0.001
Legumes (g/day)	11.18±1.48	17.22±1.52	25.08±1.47	<0.001	19.60±1.54	19.60±1.55	14.21±1.54	0.02	16.15±1.55	19.62±1.57	17.63±1.56	0.29
Nutrients												
Total energy (kcal/day)	1972.60±62.65	1471.53±62.61	1964.92±62.61	<0.001	1941.68±64.89	1600.72±64.88	1866.65±64.85	0.01	1867.52±64.95	1604.31±64.90	1937.22±64.95	0.01
Carbohydrate (% of energy/day)	58.53±0.69	56.33±0.69	53.34±0.68	<0.001	48.00±0.36	55.82±0.36	64.39±0.36	<0.001	63.88±0.42	55.76±0.42	48.57±0.42	<0.001
Protein (% of energy/day)	10.39±0.13	12.64±0.13	14.99±0.13	<0.001	13.56±0.21	12.76±0.21	11.70±0.21	<0.001	12.51±0.22	12.91±0.21	12.60±0.22	0.39
Fat (% of energy/day)	34.19±0.68	33.47±0.67	33.89±0.67	0.75	40.95±0.41	33.99±0.41	26.62±0.41	<0.001	26.06±0.34	33.91±0.34	41.59±0.34	<0.001
Fiber (g/day)	16.73±0.47	16.23±0.48	15.12±0.46	0.04	13.74±0.43	16.03±0.44	18.31±0.43	<0.001	17.92±0.44	16.26±0.44	13.90±0.44	<0.001
SFA (g/day)	17.48±0.82	18.49±0.84	22.13±0.82	<0.001	20.18±0.83	18.36±0.84	19.56±0.83	0.31	20.82±0.83	18.08±0.84	19.20±0.83	0.07
MUFA (g/day)	20.08±0.93	20.98±0.96	24.33±0.93	<0.001	22.24±0.94	20.94±0.95	22.20±0.94	0.55	23.39±0.93	20.74±0.94	21.29±0.94	0.10
PUFA (g/day)	17.64±1.03	18.95±1.06	20.60±1.03	0.12	18.87±1.03	18.42±1.04	19.89±1.03	0.59	20.53±1.03	18.24±1.04	18.42±1.03	0.22
Thiamine (mg/day)	1.32±0.03	1.40±0.03	1.40±0.03	0.14	1.18±0.03	1.35±0.03	1.59±0.03	<0.001	1.61±0.03	1.35±0.03	1.15±0.03	<0.001
Riboflavin (mg/day)	1.32±0.04	1.56±0.04	1.90±0.04	<0.001	1.64±0.05	1.59±0.05	1.54±0.04	0.28	1.64±0.04	1.59±0.05	1.55±0.05	0.38
Niacin (mg/day)	16.60±0.33	18.59±0.34	20.13±0.33	<0.001	17.96±0.36	18.21±0.36	19.16±0.35	0.04	19.75±0.34	18.30±0.35	17.28±0.35	<0.001
Iron (mg/day)	11.84±0.18	12.68±0.19	13.08±0.18	<0.001	11.82±0.18	12.44±0.18	13.33±0.18	<0.001	13.61±0.17	12.46±0.17	11.52±0.17	<0.001
Magnesium (mg/day)	208.13±8.79	224.80±9.03	253.79±8.78	<0.001	224.78±8.90	221.84±8.96	240.10±8.85	0.30	250.36±8.76	224.47±8.56	211.89±8.80	0.01

[a]Values are expressed as mean±SE, [b]Obtained by ANCOVA. Energy intake and macronutrients are adjusted for age. All other variables are adjusted for age and energy intake. SE=Standard error; ANCOVA=Analysis of covariance; SFA=Saturated fatty acid; MUFA=Monounsaturated fatty acid; PUFA=Polyunsaturated fatty acids

Table 3: Multivariable odds ratio (95% confidence interval) for the association between total protein and study outcomes[a]

	Tertiles of energy-adjusted protein intake[b]			P_{trend}[c]
	T1 (*n*=118)	T2 (*n*=118)	T3 (*n*=118)	
Sleep quality				
Crude	1.00	0.66 (0.38–1.13)	0.55 (0.32–0.95)	0.03
Multivariable-adjusted[d]	1.00	0.59 (0.33–1.07)	0.53 (0.30–0.93)	0.03
ISI				
Crude	1.00	0.90 (0.54–1.51)	1.24 (0.73–2.08)	0.43
Multivariable-adjusted[d]	1.00	0.84 (0.48–1.46)	1.25 (0.73–2.13)	0.43
ESS				
Crude	1.00	1.07 (0.64–1.80)	0.93 (0.56–1.56)	0.79
Multivariable-adjusted[d]	1.00	1.05 (0.60–1.82)	0.99 (0.58–1.68)	0.96
Depression				
Crude	1.00	0.90 (0.53–1.52)	1.04 (0.61–1.78)	0.89
Multivariable-adjusted[d]	1.00	0.96 (0.53–1.71)	1.02 (0.58–1.80)	0.94
Anxiety				
Crude	1.00	0.96 (0.57–1.63)	1.07 (0.63–1.83)	0.78
Multivariable-adjusted[d]	1.00	0.93 (0.53–1.63)	1.02 (0.59–1.77)	0.93
Stress				
Crude	1.00	1.67 (0.98–2.84)	1.00 (0.60–1.67)	0.99
Multivariable-adjusted[d]	1.00	1.78 (1.00–3.15)	0.92 (0.54–1.58)	0.77

[a]All values are ORs and 95% CIs, [b]Intakes are adjusted for energy intake based on residual method, [c]Obtained by considering tertiles of protein intake as an ordinal variable, [d]Adjusted for age (continuous), energy intake (continuous), education level (≤elementary/high-school/university graduate), marital status (single/married), smoking status (yes/no), physical activity (continuous), dietary fiber intake (continuous), and BMI (continuous). CIs=Confidence intervals; ORs=Odds ratios; ISI=Insomnia Severity Index; BMI=Body mass index; ESS=Epworth Sleepiness Scale

Table 4: Multivariable odds ratio (95% confidence interval) for the association between carbohydrate intake and study outcomes[a]

	Tertiles of energy-adjusted carbohydrate intake[b]			P_{trend}[c]
	T1 (*n*=118)	T2 (*n*=118)	T3 (*n*=118)	
Sleep quality				
Crude	1.00	1.04 (0.61–1.75)	1.34 (0.79–2.28)	0.28
Multivariable-adjusted[d]	1.00	1.00 (058–1.76)	1.47 (0.81–2.65)	0.20
ISI				
Crude	1.00	1.20 (0.71–2.02)	0.75 (0.45–1.27)	0.29
Multivariable-adjusted[d]	1.00	1.10 (0.63–1.92)	0.67 (0.38–1.18)	0.16
ESS				
Crude	1.00	1.07 (0.64–1.81)	0.76 (0.45–1.27)	0.29
Multivariable-adjusted[d]	1.00	0.90 (0.52–1.57)	0.57 (0.32–1.02)	0.06
Depression				
Crude	1.00	1.35 (0.79–2.31)	1.07 (0.63–1.82)	0.78
Multivariable-adjusted[d]	1.00	1.33 (0.74–2.39)	0.92 (0.51–1.68)	0.77
Anxiety				
Crude	1.00	1.20 (0.70–2.06)	0.87 (0.51–1.46)	0.59
Multivariable-adjusted[d]	1.00	1.24 (0.70–2.20)	0.91 (0.51–1.63)	0.75
Stress				
Crude	1.00	0.87 (0.52–1.46)	1.24 (0.73–2.11)	0.42
Multivariable-adjusted[d]	1.00	0.96 (0.55–1.67)	1.46 (0.81–2.64)	0.21

[a]All values are ORs and 95% CIs, [b]Intakes are adjusted for energy intake based on residual method, [c]Obtained by considering tertiles of protein intake as an ordinal variable, [c]Adjusted for age (continuous), energy intake (continuous), education level (≤elementary/high-school/university graduate), marital status (single/married), smoking status (yes/no), physical activity (continuous), dietary fiber intake (continuous), and BMI (continuous). CI=Confidence intervals; ORs=Odds ratios; ISI=Insomnia Severity Index; BMI=Body mass index; ESS=Epworth Sleepiness Scale

As opposed to our findings, previous studies suggest an inverse relationship between fat and carbohydrates with protein substitution and the occurrence of excessive daytime sleepiness. Furthermore, replacing saturated fat with protein was also found to reduce the odds of excessive daytime sleepiness.[24] Moreover, in opposition to our conclusion, a cross-sectional study involving Iranian adults demonstrated that a diet high in plant protein was significantly associated with a reduced risk of mental disorders.[25] However, a prospective cohort study indicates

Table 5: Multivariable odds ratio (95% confidence interval) for the association between fat intake and study outcomes[a]

	Tertiles of energy-adjusted fat intake[b]			P_{trend}[c]
	T1 (*n*=118)	T2 (*n*=118)	T3 (*n*=118)	
Sleep quality				
Crude	1.00	0.70 (0.41–1.18)	0.93 (0.54–1.59)	0.79
Multivariable-adjusted[d]	1.00	0.64 (0.37–1.11)	0.88 (0.49–1.59)	0.65
ISI				
Crude	1.00	1.32 (0.79–2.22)	1.15 (0.69–1.92)	0.60
Multivariable-adjusted[d]	1.00	1.38 (0.81–2.37)	1.31 (0.75–2.31)	0.33
ESS				
Crude	1.00	1.23 (0.73–2.07)	1.11 (0.66–1.85)	0.69
Multivariable-adjusted[d]	1.00	1.31 (0.76–2.25)	1.36 (0.77–2.40)	0.28
Depression				
Crude	1.00	0.89 (0.52–1.53)	0.93 (0.54–1.59)	0.78
Multivariable-adjusted[d]	1.00	1.00 (0.57–1.77)	1.13 (0.62–2.05)	0.68
Anxiety				
Crude	1.00	1.39 (0.82–2.38)	1.04 (0.61–1.75)	0.89
Multivariable-adjusted[d]	1.00	1.38 (0.79–2.40)	1.00 (0.56–1.77)	0.97
Stress				
Crude	1.00	1.00 (0.59–1.69)	0.87 (0.51–1.46)	0.59
Multivariable-adjusted[d]	1.00	1.00 (0.58–1.74)	0.78 (0.44–1.39)	0.41

[a]All values are OR and 95%sCIs, [b]Intakes are adjusted for energy intake based on residual method, [c]Obtained by considering tertiles of fat intake as an ordinal variable, [d]Adjusted for age (continuous), energy intake (continuous), education level (≤elementary/high-school/university graduate), marital status (single/married), smoking status (yes/no), physical activity (continuous), dietary fiber intake (continuous), and BMI (continuous). OR=Odds ratios; CIs=Confidence intervals; BMI=Body mass index; ISI=Insomnia Severity Index; ESS=Epworth Sleepiness Scale

that plant protein may be link with better sleep quality than animal protein.[26] Plant proteins provide anti-inflammatory bioactive compounds that reduce oxidative stress and promote beneficial gut bacteria producing sleep-promoting metabolites like gamma Aminobutyric acid (GABA).[26]

According to our results, the greatest adherence to carbohydrate intake was not significantly linked to lower odds of poor sleep quality, insomnia, daytime sleepiness, depression, anxiety, and stress in both the crude and adjusted models. However, a recent cross-sectional study by Song *et al*.[27] demonstrated that daily substitution of low-quality carbohydrates with high-quality carbohydrates is associated with 15% reduction in the risk of depression. Furthermore, consumption of high-quality carbohydrates at breakfast and dinner has been shown to negatively associate with the incidence of depression.[27] It is also important that this study was performed on US adults, and variations in the nationalities of the study population may lead to inconsistencies. In addition, a cross-sectional study by Melaku *et al*.[24] revealed that substituting 5% of energy intake from protein with an equal amount of carbohydrate increased excessive daytime sleepiness. The authors concluded that replacing protein with carbohydrate was positively associated with daytime sleepiness.[24] Carbohydrate-to-protein substitution enhances sleep quality by increasing amino acid precursors (tryptophan and tyrosine) essential for synthesizing sleep-regulating neurotransmitters such as serotonin and melatonin[28] while improving glycemic stability and preventing nocturnal hypoglycemic episodes that disrupt sleep continuity. Different sample sizes of studies and various health statuses and age ranges of the study population would be considered sources of disparity between results.

We found no significant association between higher fat intake and the aforementioned study outcomes in either the crude or fully adjusted models. Furthermore, the substitution of 3% of energy from carbohydrates with fat did not change the odds of having poor sleep quality, anxiety, depression, insomnia, and stress. In agreement with our results, a study of Brazilian adults revealed that there was no link between dietary fatty acid intake and depression.[29] In opposition to our findings, a population-based cross-sectional study revealed that replacing 5% of energy intake from protein with an identical amount of fat increased excessive daytime sleepiness.[24] Totally, the authors recommended that the substitution of protein with fat was positively associated with daytime sleepiness.[24] It should be mentioned that considering various residual confounding factors that could cause different forms of bias may lead to the contradictoriness between findings. Regarding fat and carbohydrates, a low-fat and high-carbohydrate diet can increase plasma insulin, leading to reduced alertness. Furthermore, high-fat and low-carbohydrate meals caused an increase in cholecystokinin as a satiety hormone. Increased cholecystokinin could be responsible for the immediate effect of increasing daytime sleepiness and reducing alertness.[30] In addition, isocaloric substitution of fat with carbohydrate has caused a remarkable reduction in postprandial alertness and concentration.[31] On the

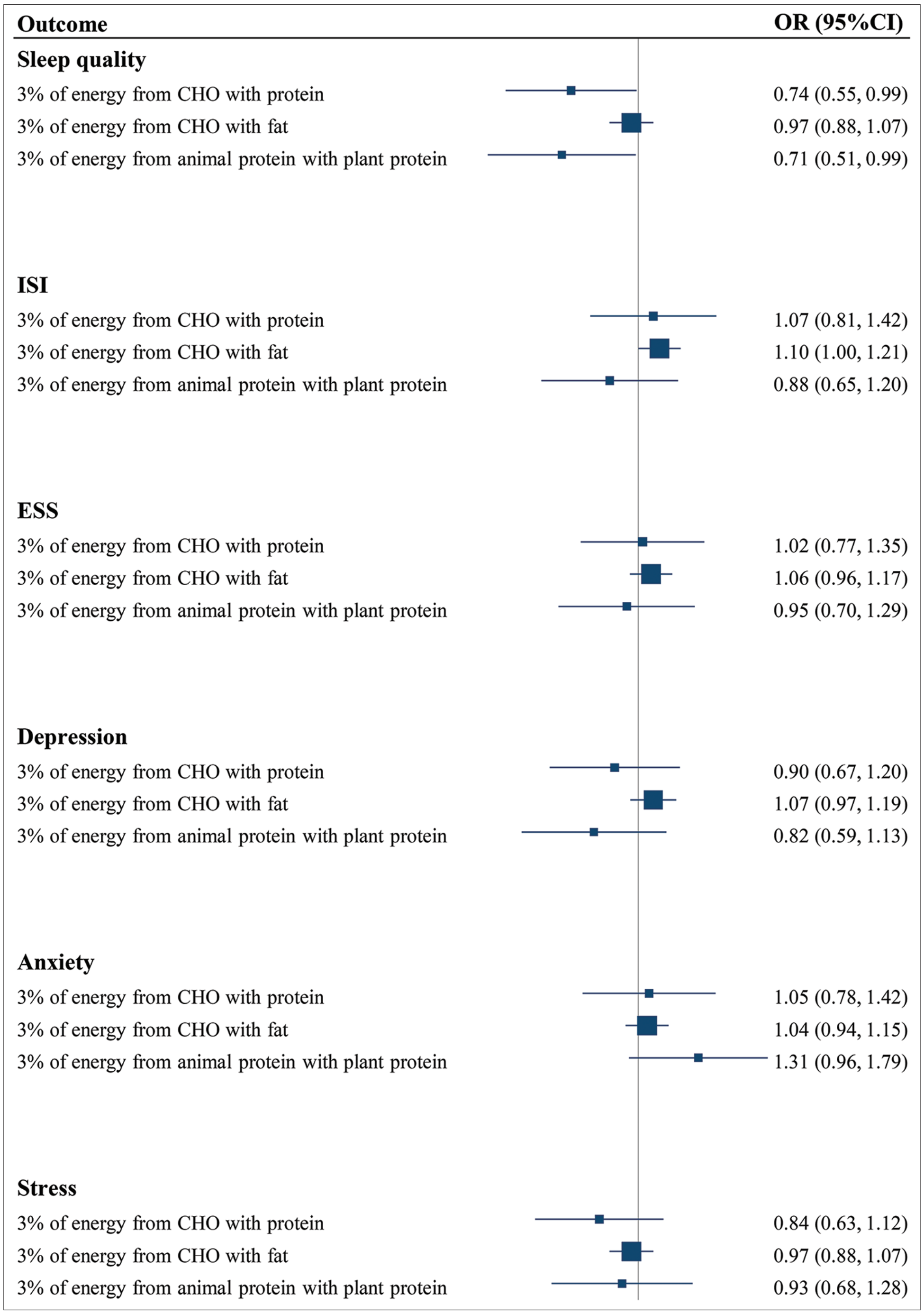

Figure 1: Substitution of macronutrient intake on sleep quality, Insomnia Severity Index, Epworth Sleepiness Scale, depression, anxiety, and stress. ISI = Insomnia Severity Index; ESS = Epworth Sleepiness Scale; CI = Confidence interval; CHO = Carbohydrate

whole, the acute effect of high-fat and carbohydrate intake contributes to sedation by decreasing serum levels of ghrelin and increasing serum levels of glucose, insulin, enterostatin, leptin, peptide YY, and cholecystokinin, which modulates wake neuron signaling, orexin, serotonin, and norepinephrine.[32]

Study strengths and weaknesses

The strengths of this study include its examination of the relationship between isocaloric macronutrient substitution and sleep disorders and mental health in Iranian adults, as well as its consideration of several confounding factors such as age, BMI, marital status, education levels, smoking status, physical activity, and dietary fiber intake to examine the associations. Furthermore, we used the validated questionnaires to assess dietary intake, sociodemographic variables, psychological disorders, and sleep health status of participants. However, some methodological limitations would be addressed for the interpretation of the obtained conclusions. Due to the cross-sectional nature of the present study, we are unable to determine causality. Sample size was calculated based on sleep quality, and therefore, the lack of significant associations with mental disorders could be explained, at least in part, by insufficient power to detect smaller effects. As food frequency questionnaires have drawbacks in measuring dietary intakes, recall bias could affect the obtained conclusion. Furthermore, there would be a measurement bias because of using a self-reported standardized instrument to evaluate study outcomes, which could lead to misclassification of the study participants. Finally, based on the study hypothesis, we categorized participants into two groups based on study outcomes scores. Although this approach would enhance the results more understandable, it would limit statistical power. Our findings are specific to the Iranian male healthcare workers and should be generalized to other population including females or those with other occupations cautiously. Further well-designed studies among different nations and study groups are required.

CONCLUSION

Our findings revealed that higher protein intake might be linked to lower odds of poor sleep quality. Conversely, no substantial relation was observed between higher fat and carbohydrate intake and the odds of poor sleep quality, insomnia, daytime sleepiness, depression, anxiety, and stress. These findings are related mostly to healthcare male workers and may not represent females or those with other occupations. Further studies with greater sample sizes are recommended.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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Supplemental Table 1: Demographic characteristics of participants in total and across sleep quality categories[a]

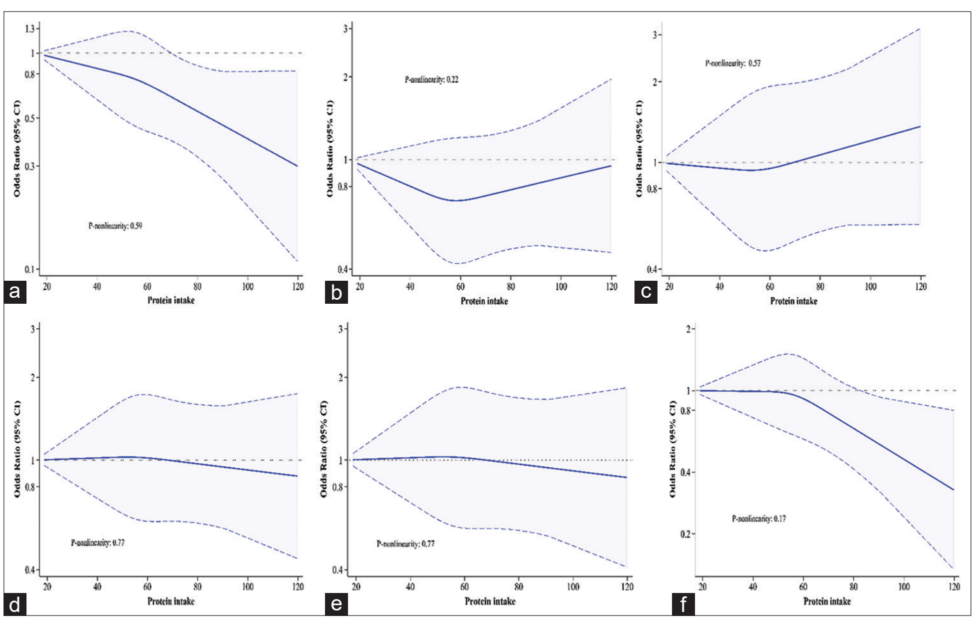
Variable	Total population	Poor sleep quality	Good sleep quality	P^b
Age (years)	38.64±5.34	38.58±5.50	38.75±5.06	0.77
Weight (kg)	78.59±9.37	79.07±8.82	77.77±10.21	0.23
BMI (kg/m^2)	25.27±3.20	25.39±3.13	25.05±3.31	0.34
Physical activity (MET min/day)	112.34±42.77	112.82±41.02	111.58±45.70	0.79
Marital status				
Single	65 (18.4)	49 (22.1)	16 (12.1)	0.02
Married	289 (81.6)	173 (77.9)	116 (87.9)	
Smoking status				
No	338 (95.5)	211 (95.0)	127 (96.2)	0.79
Yes	16 (4.5)	11 (5.0)	5 (3.8)	
Education				
≤Elementary	97 (27.4)	63 (28.4)	34 (25.8)	0.82
High school	183 (51.7)	112 (50.5)	71 (53.8)	
University graduate	74 (20.9)	47 (21.2)	27 (20.5)	

[a]Values are expressed as mean±SD for continuous and percentage (frequency) for categorical variables, [b]Obtained by independent sample *t*-test for continuous and Chi-square test for categorical variables. SD=Standard deviation; BMI=Body mass index; MET=Metabolic equivalent

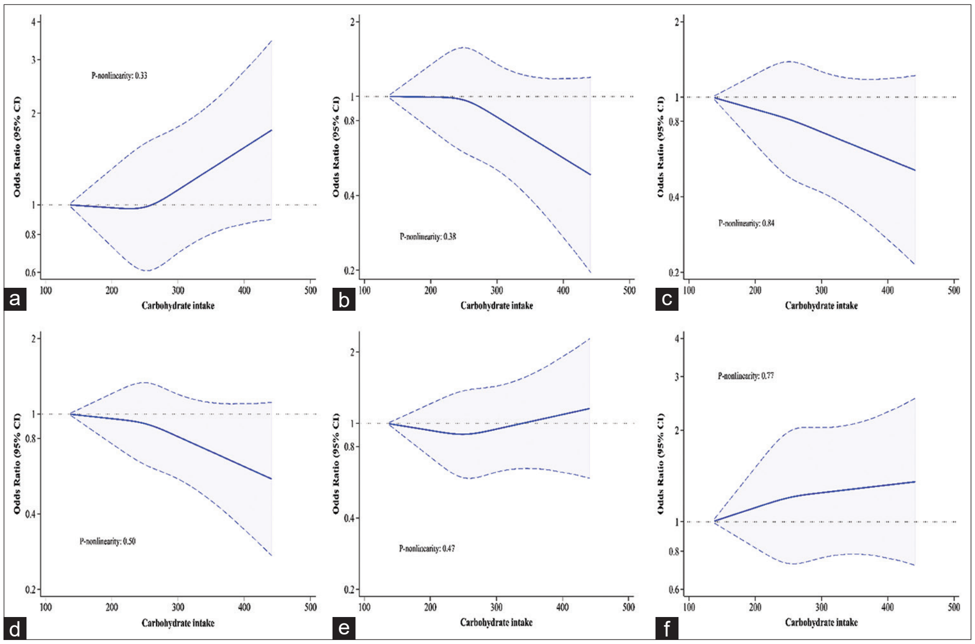
Supplemental Table 2: Prevalence of study outcomes across tertiles of total protein, carbohydrate, and fat intake[a] (*n*=354)

	Total protein			P^b	Carbohydrate			P^b	Fat			P^b
	T1 (*n*=118)	T2 (*n*=118)	T3 (*n*=118)		T1 (*n*=118)	T2 (*n*=118)	T3 (*n*=118)		T1 (*n*=118)	T2 (*n*=118)	T3 (*n*=118)	
SQ	83 (70.3)	72 (61.0)	67 (56.8)	0.04	71 (60.2)	72 (61.0)	79 (66.9)	0.50	78 (66.1)	68 (57.6)	76 (64.4)	0.36
ISI	68 (57.6)	65 (55.1)	74 (62.7)	0.48	70 (59.3)	75 (63.6)	62 (52.5)	0.22	65 (55.1)	73 (61.9)	69 (58.5)	0.57
ESS	68 (57.6)	70 (59.3)	66 (55.9)	0.87	70 (59.3)	72 (61.0)	62 (52.5)	0.38	65 (55.1)	71 (60.2)	68 (57.6)	0.73
Depression	77 (65.3)	74 (62.7)	78 (66.1)	0.85	73 (61.9)	81 (68.6)	75 (63.6)	0.53	78 (66.1)	75 (63.6)	76 (64.4)	0.92
Anxiety	74 (62.7)	73 (61.9)	76 (64.4)	0.92	74 (62.7)	79 (66.9)	70 (59.3)	0.48	71 (60.2)	80 (67.8)	72 (61.0)	0.41
Stress	67 (56.8)	81 (68.6)	67 (56.8)	0.09	71 (60.2)	67 (56.8)	77 (65.3)	0.41	73 (61.9)	73 (61.9	69 (58.5)	0.83

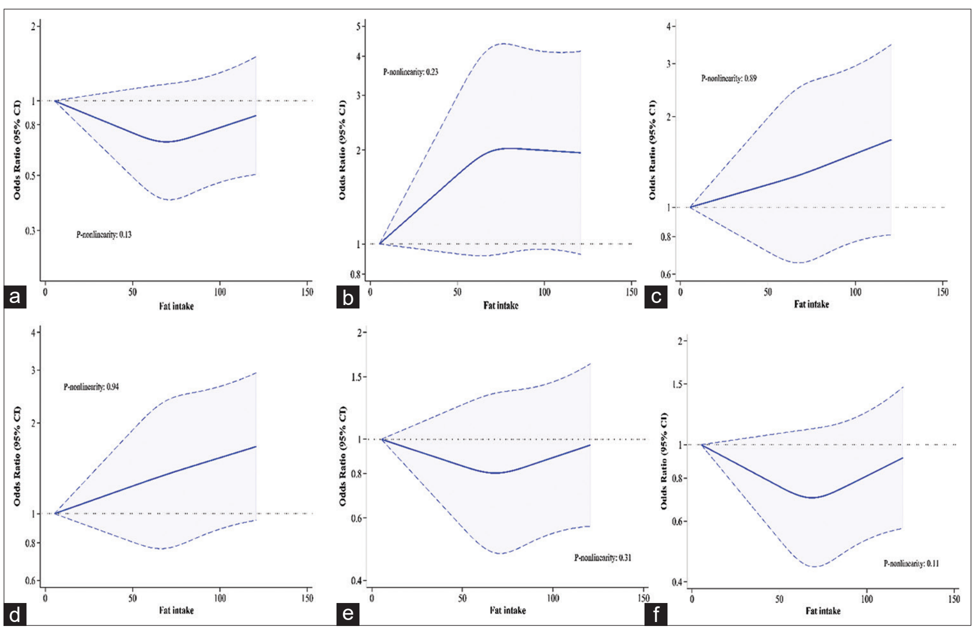
[a]Values are presented as percentage (frequency), [b]Obtained by Chi-square test. SQ=Sleep quality; ESS=Epworth Sleepiness Scale; ISI=Insomnia Severity Index



Supplemental Figure 1: Nonlinear curves for the association between total protein intake (g/d) and sleep quality (a), ISI (b), ESS (c), depression (d), anxiety (e), and stress (f)



Supplemental Figure 2: Nonlinear curves for the association between carbohydrate intake (g/d) and sleep quality (a), ISI (b), ESS (c), depression (d), anxiety (e), and stress (f)



Supplemental Figure 3: Nonlinear curves for the association between total fat intake (g/d) and sleep quality (a), ISI (b), ESS (c), depression (d), anxiety (e), and stress (f)