

The association between deficiency of nutrient intake on resting metabolic rate (RMR) in overweight and obese women: a cross-sectional study

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Research

Keywords: Resting metabolic rate, fat-free mass, obesity, overweight, double burden of malnutrition, Nutrient Adequacy Ratio

Posted Date: November 17th, 2020

DOI: <https://doi.org/10.21203/rs.3.rs-103676/v1>

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Abstract

Background: The double burden of malnutrition is an emerging public health concern nowadays which a correlation with Obesity. The aim of this study was to examine the relationship between resting metabolic rate (RMR) and dietary intake of zinc, vitamin C, and riboflavin based on Nutrient Adequacy Ratios (NAR) in overweight and obese women.

Methods: We enrolled 293 overweight and obese women in this cross-sectional study. BMI, body fat mass, fat-free mass, insulin level were assessed. RMR was measured using indirect calorimetry. NAR was measured by calculating the ratio of daily individual intakes to the standard recommended amounts.

Results: the RMR/FFM showed a significant association with riboflavin ($\beta=1.59$; 95% CI: 1.04-23.26, $P=0.04$) and zinc ($\beta=0.78$; 95% CI: 1.04-4.61, $P=0.03$) in the crude model. Moreover, differences in vitamin C and RMR/FFM was marginal significant ($\beta=0.75$; 95% CI: 0.95-4.77, $P=0.06$). After adjust for confounders the riboflavin association change to marginal significance ($\beta=1.52$; 95% CI: 0.91-23.04, $P=0.06$). After controlling for potential confounders, the associations change between zinc and RMR/FFM ($\beta=0.66$; 95% CI: 0.78-4.86, $P=0.15$) and between RMR/FFM and vitamin C ($\beta=0.48$; 95% CI: 0.66-3.96, $P=0.28$).

Conclusion: Our study showed a significant association between dietary intake of zinc, riboflavin, and vitamin C and change in RMR/FFM in overweight and obese women.

Background

Obesity rates are growing globally (1), which is defined as excessive or abnormal fat accumulation that may impair health (2). More than 26% of the Iranian adult community is currently obese (3) Females were much more affected than males (4, 5). Obesity and its associated metabolic disorders develop when energy intake is more than energy expenditure; this can be caused by diminished physical activity, the disability of the central nervous system to down-regulate the ingestion of high-calorie foods, or appetite (6). Although various factors contribute to the etiology of obesity, sedentary lifestyles and unhealthy eating habits are among the principal contributors to the world obesity epidemic (7). 60-75% of total energy expenditure is correlated with resting metabolic rate (RMR), which is an important part of daily energy consumption (8). weight gaining and obesity may be associated with low RMR(9).

Diet quality can be evaluated to better understand overall eating patterns (10). Poor diet quality is a significant factor in compromised health status and leads to the development of many chronic diseases, including obesity (11). Investigations revealed, however, intake of vegetables and fruit is associated with a lower risk of obesity (12), inappropriate food behavior contributes to obesity and contributes to vitamin deficiency. Studies revealed that most vitamins are inadequate in obese individuals, particularly fat-soluble vitamins, vitamin B₁₂, folic acid, and vitamin C (13). Lower than normal levels of some antioxidants may be connected with enhanced fat deposition in the body (12). The double burden of malnutrition (DBM) is an emerging public health concern nowadays that happens as an inevitable consequence of nutritional transition (14). The coexistence of overnutrition and undernutrition is often referred to as the DBM (15). Nutrient Adequacy Ratio (NAR) and mean adequacy ratio (MAR), known as healthier diet quality indices. Higher scores in diet quality inversely connected with body mass index (BMI), overweight, and obesity (16). Similarly, zinc and vitamin C are closely related to the adiposity(17, 18). In particular, some diet with a high score of diet quality like the mediterranean dietary pattern has been reported to be inversely connected with BMI, waist-to-height ratio, and waist circumference (19).

To the best of our knowledge, this is the first study to investigate the relationship between deficiency of nutrient intake such as zinc, vitamin C, and riboflavin and RMR in the adult women population. Accordingly, this study was performed to examine the NAR with RMR/FFM among a group of Iranian adult women.

Materials And Methods

Study population

This cross-sectional research performed in 2018, 293 adult women aged between 18 and 56 years old who were selected by a random sampling method that had been referred to health centers in Tehran recruited. Participants were enrolled in the study according to inclusion and exclusion criteria. Individuals were included if they met following eligibility criteria: good general health, overweight and obese women with BMI in the range of 25-40 kg/m². The exclusion criteria were as follows: regular use of medicine (including oral contraceptive pill), history of hypertension, cardiovascular diseases, diabetes mellitus, impaired renal and liver function, alcohol use, smoking, pregnancy, lactation period, and menopause. Furthermore, participants were excluded from chronic diseases affecting their diet, as well as those who had been following an arbitrary special dietary regimen, and also those with any significant body weight fluctuations over the past 1 year. Participants whose reported daily energy intakes lower than 800 kcal/d or higher than 4200 kcal/d were also excluded. The final analysis has been conducted on 293 participants. Each participant was fully informed about the study protocol and provided a written and informed consent form prior to taking part in the study.

Energy Expenditure Measurements

RMR was measured by indirect calorimetry (spirometer METALYZERR 3B-R3, Cortex Biophysik GmbH, Leipzig, Germany). According to the manufacturer's instructions, gas ventilation and exchange is calibrated before each test. RMR is evaluated by measuring the amount of O₂ consumed and CO₂ produced. The RMR was assessed in the morning, after a comfortable night's sleep, and following a 10-12 hour fast. Participants were asked to avoid caffeine or alcohol consumption and severe exercise for a day before RMR measurements. After reclining in a steady-state and a supine position in a quiet room, the

RMR was measured for 30 minutes. The respiratory exchange ratio and oxygen uptake (VO_2) were analyzed within the middle 20 min of the resting period. Predictive RMR was determined using the Harris-Benedict equation, which considers the weight, height, and age of participants.

Body Composition Measurement

Body composition, including weight, BMI, fat mass, and fat-free mass (FFM) were acquired using a multi-frequency bioelectrical impedance analyzer InBody 770 scanner (Inbody Co., Seoul, Korea). This electrical impedance analyzer calculates the resistance of body tissues to the flow of an electrical signal sent through both hands and feet. According to the manufacturer's instructions, participants removed their shoes, coats, and sweaters, and stood on the balance scale in bare feet and grasped the handles of the machine. The measurements took place in approximately 20 seconds, and the output was printed.

Biochemical Assessment and Hormonal Assay

Metabolic health was assessed using the metabolic parameters that measured following standard chemical procedures. A 12-hour fasting venous blood sample was used to measure all biochemical markers. Serum glucose was evaluated by a colorimetric method based on the GOD-PAP method. Serum insulin concentrations were analyzed by enzyme-linked immunosorbent assay (ELISA) method (Human insulin ELISA kit, Monobind Inc., Lake Forest, USA). All measurements were taken at the Nutrition and Biochemistry Laboratory of the School of Nutritional Sciences and Dietetics.

HOMA and QUICKI Calculations

Insulin resistance was estimated by homeostasis model assessment (HOMA). The HOMA was calculated according to the following equation: $HOMA = [Fasting Plasma Glucose (mmol/L) \times Fasting Plasma Insulin (mIU/L)]/22.5$ (20). Insulin sensitivity quantitative insulin sensitivity check index (ISQUICKI) was assessed by: $ISQUICKI = 1/[\log (fasting insulin) + \log (fasting glucose)]$ (21).

Dietary intake assessment

Dietary intake data of the past year were obtained using a validated semi-quantitative food-frequency questionnaire (FFQ) (22), comprises of 168-item a trained nutritionist administered these FFQ. The FFQ consisted of a list of foods with standard serving sizes. Participants were asked to report their frequency and amount of each food item consumed during the previous year on a daily (e.g., bread), weekly (e.g., rice, meat), or monthly (e.g., fish) basis. Portion sizes of the consumed foods were converted to grams using household measurements (23). Nutritionist IV computer software was used for the nutrient analysis of the diets. The database of this software was modified for Iranian foods.

Nutrient Adequacy Ratios (NAR)

For calculating the NAR, the ratio of daily individual intakes to the standard recommended amounts for the subject's sex and age category was used. The standard recommended amounts are based on RDA (Recommended Daily Allowances) (24). We calculated the NAR for three key nutrients, including zinc, vitamin C, and riboflavin according to the above-mentioned method. The prevalence of nutrient deficiency was estimated using NAR. NAR lower than one is considered as a deficiency.

Assessment of other covariates

International Physical Activity Questionnaire (IPAQ, short form) were obtained by using an interview-based questionnaire from all participants about all the vigorous and moderate elements over the last 7 days, considering the time spent on these activities, that was used to assess physical activity of the study subjects across a variety of different domains including leisure-time, domestic, work, and transport-related physical activity and time spent on light, moderate, high and very high-intensity activities. The level of physical activity of participants was calculated as Met.h/d (25). For height measurements, subjects were in a standing position without shoes, in contact with the wall with their head, shoulders, heels, and hips, and their height was recorded to the nearest 0.1 cm.

Statistical analysis

All statistical analysis was performed using the IBM SPSS software version 22.0 (SPSS, Chicago, IL, USA) and p-values less than 0.05 were considered statistically significant. Normal distribution of data was checked by the Kolmogorov-Smirnov test. An independent sample t-test was used for assessed differences between groups with the low and standard intake of nutrients. RMR/FFM was analyzed after adjusting for FFM. The differences between RMR/FFM groups and dietary intake of nutrients were assessed by the Binary logistic regression were performed to adjust for confounders effects such as age, energy intake, and physical activity (METs/d). Results

were presented as odds ratios (ORs) and 95% confidence intervals (CIs) compared with the RMR groups.

Results

Study population characteristics

A total of 293 healthy overweight and obese women were enrolled in this cross-sectional research. The mean age, height, weight, and BMI of the study participants were 36.39 years (SD = 8.71), 161.84 cm (SD = 5.85), 80.22 kg (SD = 11.28), and 30.77 kg/m² (SD = 3.79), respectively (Table 1) the mean body composition, RMR components, biochemical and anthropometric characteristics of subjects are shown in table 1.

Table.1 Study population characteristics			
Parameters	Minimum	Maximum	Mean ± SD
Age (years)	18	56	36.39 ± 8.71
Height (cm)	147.50	179.00	161.84 ± 5.85
Weight (kg)	59.50	122.40	80.22 ± 11.28
BMI (kg/m ²)	25.00	40.70	30.77 ± 3.79
RMR parameters			
RMR measure (kcal/day)	952.00	2467.00	1569.60 ± 255.70
RQ	0.73	0.99	0.85 ± 0.04
RMR/FFM (kcal/day/kg)	21.50	45.86	33.74 ± 4.48
V. O ₂	0.14	0.35	0.22 ± 0.036
V. CO ₂	0.01	0.30	0.19 ± 0.034
Body composition parameters			
Body fat mass (kg)	19.40	59.40	33.52 ± 7.74
Fat free mass (kg)	35.30	67.70	46.68 ± 5.50
Blood parameters			
FBS (mg/dl)	67.00	137.00	87.39 ± 9.76
Insulin (mIU/ml)	6.67	65.89	15.59 ± 6.02
HOMA	1.29	16.59	3.40 ± 1.52
ISQUICKI	0.39	0.68	0.54 ± 0.04
RMR, resting metabolic rate; RQ, respiratory quotient; FFM, fat-free mass; V. O ₂ , Oxygen consumption; V. CO ₂ , carbon dioxide consumption; FBS, fasting blood sugar; HOMA, homeostasis model assessment; ISQUICKI, insulin sensitivity quantitative insulin sensitivity check index.			
N = 293			
Data are indicated as Mean ± SD otherwise indicated			

Participant's characteristics between standard and deficiency of daily nutrient intakes

Dietary intake of three nutrients including riboflavin, vitamin C, and zinc of 293 participants were categorized based on nutrient adequacy ratios (NAR) and divided into two groups, standard and deficiency (Table 2). The RMR indicated a significant association with zinc (P = 0.001), that demonstrates people who consume higher zinc had higher RMR. Moreover, other factors like RMR/FFM (P = 0.06), V. O₂ (P = 0.001), V. CO₂ (P = 0.007), body fat mass (P = 0.02), FFM (P = 0.006), height (P = 0.005), and weight (P = 0.006) had a significant relationship with zinc. Besides, riboflavin had a significant association with body fat mass (P = 0.05), however, there were showed no relationship between vitamin C and participant characteristics (P > 0.05).

Table.2 Participants' Characteristics between Standard and Deficiency of Daily Nutrient Intakes									
Parameters	Nutrient								
	Vitamin c			Zinc			Riboflavin		
	NAR <1	NAR ≥1	P-value	NAR <1	NAR ≥1	P-value	NAR <1	NAR ≥1	P-value
	n=30	n=250		n=36	n=244		n=11	n=269	
	10.2%	85.3%		12.3%	83.3%		3.8%	91.8%	
Age (years)	34.90±8.62	63.60±8.53	0.30	38.05±9.13	36.18±8.44	0.22	31.63±8.41	36.62±8.50	0.08
Height (cm)	161.63±6.27	161.32±5.82	0.78	158.78±6.33	161.74±5.70	0.005	160.27±8.16	161.40±5.76	0.53
Weight (kg)	77.54±9.28	80.32±11.13	0.19	75.35±8.78	80.71±11.10	0.006	75.61±14.41	80.20±10.80	0.17
BMI (kg/m ²)	29.78±3.29	30.87±3.78	0.13	29.91±3.40	30.88±3.78	0.15	29.30±4.03	30.81±3.72	0.19
RMR parameters									
RMR measure (kcal/day)	1500.2±307.28	1580.2±247.49	0.17	1437.5±288.33	1591.7±244.25	0.001	1450.6±301.44	1576.5±252.59	0.10
RQ	0.86±0.03	0.85±0.04	0.16	0.86±0.042	0.85±0.041	0.39	0.858±0.03	0.854±0.04	
RMR/FFM (kcal/day/kg)	00.04±5.60	33.92±4.36	0.32	32.50±5.10	34.02±4.39	0.06	31.79±2.93	33.91±4.54	0.12
V. O ₂	0.21±0.04	0.22±0.03	0.13	0.20±0.04	0.22±0.03	0.001	0.20±0.04	0.22±0.03	0.13
V. CO ₂	0.18±0.04	0.19±0.03	0.22	0.17±0.04	0.19±0.03	0.007	0.17±0.04	0.19±0.03	0.16
Body composition parameters									
Body fat mass (kg)	31.80±6.66	33.65±7.77	0.21	30.79±6.66	33.84±7.74	0.02	29.15±7.10	33.63±7.66	0.05
Fat free mass (kg)	45.63±5.26	46.76±5.44	0.28	44.27±4.74	46.98±5.44	0.006	45.55±7.70	46.69±5.33	0.49
Blood parameters									
FBS (mg/dl)	86.50±10.59	87.51±9.64	0.60	87.93±11.62	87.30±9.34	0.73	83.30±7.33	87.57±9.81	0.17
Insulin (mIU/ml)	14.75±4.77	15.70±6.30	0.44	15.37±4.15	15.62±6.41	0.83	18.28±10.03	15.47±5.93	0.40
HOMA	3.17±1.17	3.42±1.59	0.41	3.35±1.05	3.40±1.61	0.84	3.81±2.33	3.38±1.50	0.38
ISQUICKI	0.55±0.045	0.54±0.049	0.49	0.540±0.03	0.545±0.05	0.58	0.53±0.05	0.54±0.04	0.70
RMR, resting metabolic rate; RQ, respiratory quotient; FFM, fat-free mass; V. O ₂ , Oxygen consumption ; V. CO ₂ , carbon dioxide consumption ; FBS, fasting blood sugar; HOMA, homeostasis model assessment; ISQUICKI, insulin sensitivity quantitative insulin sensitivity check index.									
N=293									
Data are indicated as Mean ± SD otherwise indicated									
P-values are from independent sample t-test									

Association of riboflavin, vitamin C and zinc and RMR/FFM among obese women

Table 3 shows multivariate-adjusted models with 95% confidence intervals for prevalence of higher RMR/FFM across the median of dietary intake of riboflavin, vitamin C, and zinc. As shown in Table 3, the RMR/FFM showed a significant association with riboflavin, vitamin C, and zinc in the crude model. For riboflavin, in the crude model before adjustment for the confounders, showed a statistically significant relationship ($\beta = 1.59$; 95% CI: 1.04–23.26, $P = 0.04$). After controlling for the potential confounders such as age, energy intake, and physical activity, the association change to marginal significance ($\beta = 1.52$; 95% CI: 0.91–23.04, $P = 0.06$). Moreover, differences in vitamin C and RMR/FFM was marginal significant ($\beta = 0.75$; 95% CI: 0.95–4.77, $P = 0.06$). But after controlling for the potential confounders, the association disappeared ($\beta = 0.48$; 95% CI: 0.66–3.96, $P = 0.28$). Differences in zinc and RMR/FFM were also significant in the crude model ($\beta = 0.78$; 95% CI: 1.04–4.61, $P = 0.03$), but after adjustment for the potential confounders, the association disappeared ($\beta = 0.66$; 95% CI: 0.78–4.86, $P = 0.15$).

Table.3 Association of riboflavin, vitamin C and zinc and RMR/FFM among obese women				
RMR/FFM		B	OR (95% CI)	P-value
Crude Model	Riboflavin	1.59	4.93 (1.04–23.26)	0.04
Model1 ^a		1.75	5.80 (1.21–27.77)	0.02
Model2 ^b		1.71	5.55 (1.11–27.59)	0.03
Model3 ^c		1.52	4.58 (0.91–23.04)	0.06
Crude Model	Vitamin C	0.75	2.13 (0.95–4.77)	0.06
Model1 ^a		0.82	2.27 (1.01–5.13)	0.04
Model2 ^b		0.79	2.20 (0.93–5.19)	0.07
Model3 ^c		0.48	1.62 (0.66–3.96)	0.28
Crude Model	Zinc	0.78	2.19 (1.04–4.61)	0.03
Model1 ^a		0.71	2.04 (0.96–4.33)	0.06
Model2 ^b		0.71	2.04 (0.87–4.76)	0.09
Model3 ^c		0.66	1.95 (0.78–4.86)	0.15
P-values are from binary logistic regression				
Model 1: Adjusted for age. ^b Model2: Further adjusted for energy intake. ^c Model3: Further adjusted for physical activity (METs/d).				

Discussion

The results of the cross-sectional analysis conducted in 293 obese women showed a significant association between vitamin C, zinc, and riboflavin intake and the RMR/FFM. RMR was distinct in standard or deficiency consumption of vitamin C, zinc, and riboflavin.

The findings of the current study indicate that the amount of zinc consumed has been associated with RMR which higher intakes of zinc enhance RMR in person. This finding is in the same line with a study by Maxwell which demonstrates that zinc as an essential factor in several enzymes, involved with energy metabolisms such as pyruvate carboxylase, lactate dehydrogenase, carbonic anhydrase and aldolase (26). However, fifty percent of the conducted researches only investigated the association between adiposity and zinc. Zinc plays an important role in growth, reproduction tissue repair and cellular immunity (27). Some studies state that zinc is connected with obesity (28). Zinc deficiency may increase fat deposition and decrease lean mass accrual (29). The association between adiposity and zinc status may be attributed to the correlation between zinc metabolism and leptin too (29). Adipose tissue is associated with energy storage and also functions as an endocrine organ to release free fatty acids and adipokines, such as leptin (6). Moreover, zinc has different functions in the metabolism of energy and works as a component of several enzymes crucial to the metabolism of carbohydrates, proteins, and lipids, through both structural and catalytic functions essential for hormone receptor activation and tissue formation. Zinc is also involved in the metabolism of hormones that take part in the progress of obesity, especially insulin, and seems to be connected with the mechanisms of insulin resistance usually present among obese people (12, 30, 31). Previous investigations recommend a negative association between RMR and insulin resistance (32, 33). Studies revealed subjects with obesity and impaired glucose tolerance showed higher RMR levels than those with obesity and normal glucose tolerance (34). The physiological mechanisms responsible for the increased RMR in individuals with insulin resistance are poorly known. Several mechanisms have been suggested to demonstrate the elevated RMR, plasma glucagon, increases in protein turnover, containing futile substrate cycling, and sympathetic nervous system activity (35). The other recommended mechanisms that showed the relationship between insulin resistance and RMR were an increase in gluconeogenesis. It has been suggested that an increase in free fatty acid concentration in individuals with insulin resistance contributes to the extreme rates of gluconeogenesis and consequently to enhanced rate energy expenditure in these persons (36).

This study found a significant association between vitamin C and RMR. It showed women with higher intake of vitamin C had higher RMR. This result is in line with previous studies which showed that the increase in blood vitamin C concentrations associated with the change in RMR/FFM (37). In contrast, some other studies have shown that vitamin C administration significantly decreased RMR (38). A potential mechanism for this correlation could be because of ascorbic acid modulation on lipolysis in the interior of adipocytes and inflammatory response (39). Vitamin C, an antioxidant, regulates glucocorticoid metabolism and gene expression involved in adipogenesis (40). Ascorbic acid decreased weight gain and reduced total body weight and adipose tissue. This decrease correlated with low expression of genes involved in adipogenesis, adipocyte differentiation and metabolism of glucocorticoids (13). In an *in-vitro* assay, it was perceived that vitamin C inhibited glucose uptake and lactate production, and decreased glycerol release and caused a consistent reduction of leptin secretion in a dose-dependent manner (13). In this study, we also found that women who consumed a diet with higher riboflavin were more likely to have higher RMR. Low riboflavin intake is prevalent in many parts of the world, especially in developing countries (41). Investigations have shown that riboflavin deficiency causes a pathological pro-inflammatory response of macrophages [9–10]. Considering the dietary restrictions, restrictions on food intake or common dietary mistakes perceived among obese people, changes in the micronutrient intake leading to their deficiency are possible. Suitable riboflavin content is necessary to perform the effector function of macrophages. We observed inhibition in macrophages

proliferation, intensification of apoptosis incidence, and also the reduction in phagocytosis efficiency [9]. Furthermore, resting reactive oxygen species production was raised while respiratory burs, a key ingredient of intracellular killing, were destroyed. Considering the significant function of adipocytes in the creation of obesity-related chronic inflammation to be justifiable to verify the influence of riboflavin deficiency on adipocytes function in the context of pro-inflammatory activation (42).

To the best of our knowledge, it is the first study that assesses the possible relationship between nutrients and RMR in obese women. The major limitation of this study was the participants in the same-sex sample that it is not possible to generalize the results to men population. Because of the study type, cross-sectional study, we could not determine the causality, certainly; further randomized clinical trials and prospective observational studies are needed to confirm the effect of these nutrients on RMR. Another limitation for assessing dietary intakes from FFQ is misclassification. Albeit we controlled for the effect of the potential confounder by the statistical methods, because of unknown confounder cannot be excluded residual confounding will affect.

Conclusions

In conclusion, we could find a significant association between dietary intake of zinc, riboflavin, and vitamin C and change in RMR/FFM in overweight and obese women, although after controlling for ranges of potential confounding factors the meaningful decreased.

Abbreviations

RMR: Resting Metabolic Rate; DBM: Double Burden of Malnutrition; NAR: Nutrient Adequacy Ratio; MAR: Mean Adequacy Ratio; BMI: Body Mass Index; FFM: Fat-Free Mass;

ELISA: Enzyme-Linked Immuno-Sorbent Assay; HOMA: homeostasis model assessment; ISQUICKI: Insulin Sensitivity Quantitative Insulin Sensitivity Check Index; FFQ: Food Frequency Questionnaire; RDA: Recommended Daily Allowances; IPAQ: International Physical Activity Questionnaire; RQ: Respiratory Quotient; FBS: Fasting Blood Sugar.

Declarations

Ethics approval and consent to participate

All procedures involving human subjects were approved by the Ethics Commission of Tehran University of Medical Sciences (IR.TUMS.VCR.REC.1395.1597), and all participants signed written informed consent.

Consent for publication

This is formally to submit the article entitled "The association between deficiency of nutrient on resting metabolic rate in overweight and obese women: a cross-sectional study" prepared by the Tehran University of Medical Sciences for review and, hopefully, publication in your prestigious journal. The authors would like to advise that all authors listed have contributed to the work. All authors have agreed to submit the manuscript to Nutrition & Metabolism. No part of the work has been published before. There is no conflict of interest in this paper.

Availability of data and materials

Participants in this study did not agree to the public sharing of their data so supporting data is not available.

Competing interests

All authors declared that they have no competing interests

Funding

This study is funded by grants from the Tehran University of Medical Sciences (TUMS). (Grant ID:97-03-161-41155).

Author's contributions

SFS, AM, AA and FSh wrote the Manuscript, KhM had full access to all the data in the study and was responsible for the integrity and accuracy of the data. All authors have read and approved the final manuscript.

Acknowledgment

We are extremely grateful to all the participants who took part in this study and the school of Nutritional and Dietetics at Tehran University of medical sciences.

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