Mediatory role of inflammatory markers on the relationship between dietary energy density and body compositions among obese and overweight adult women: A cross-sectional study

Niki Bahrampour [1], Atieh Mirzababaei [2], Farideh Shiraseb [3], Khadijeh Mirzaei [*4]

[1] Department of Nutrition, Science and Research Branch, Islamic Azad University (SRBIAU), Tehran, Iran

[2] Department of Community Nutrition, School of Nutritional Sciences and Dietetics, Tehran University of Medical Sciences (TUMS), Tehran, Iran

[3] Department of Community Nutrition, School of Nutritional Sciences and Dietetics, Tehran University of Medical Sciences (TUMS), Tehran, Iran

[4] Department of Community Nutrition, School of Nutritional Sciences and Dietetics, Tehran University of Medical Sciences (TUMS), Tehran, Iran

[*]Corresponding author, Faculty Member, Department of Community Nutrition, School of Nutritional Sciences and Dietetics, Tehran University of Medical Sciences, Tehran, P.O. Box 14155-6117, Iran. Email: mina_mirzaei101@yahoo.com; mirzaei_kh@tums.ac.ir

Tel:+98-21-88984837 ex. 122

Fax:+98-21-88984861

Disclosures relevant to this paper

The authors declare that they do not have any conflict of interest.

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Abstract

Aims: Obesity is a global issue. Energy density (ED) can influence on body compositions (BCs). Consumption of HED (high energy density) foods can increase body fat mass (BFM) and inflammatory markers. This study was performed to assess mediatory role of high-sensitive C-reactive protein (hs-CRP), transforming growth factor-beta (TGF-β) and plasminogen activator inhibitor- 1 (PAI-1) on the relationship between ED and BC in women with overweight and obesity.

Methods: This study was a cross-sectional research among 391 women. Body composition analyzer (BIA) and food frequency questionnaire (FFQ) was used to assess BCs and food intake of individuals. Blood samples and serum level of hs-CRP, PAI-1 and TGF- β were collected. ED per one gram of foods were calculated and divided to quartiles. Linear logistic regression tests were used to investigate the association between BCs across quartiles of ED intake.

Results: Results demonstrate skeletal muscle mass (SMM), total body water (TBW), intracellular water (ICW), fat free mass (FFM), visceral fat area (VFA) and fat free mass index (FFMI) was seem to be under the effect of hs-CRP among ED intakes. TBW, extracellular water (ECW), FFM with PAI-1, bone mineral content (BMC) with PAI-1 and TGF-beta, and skeletal lean mass (SLM) with hs-CRP were inversely associated. Fat right arm (FRA), fat right arm (FLA), fat right and left leg (FRL,FLL), fat trunk, TBW, ICW, ECW, BFM, FFM, SMM, SLM, waist circumference (WC), FFMI and FMI were positively under the influence of TGF-beta after following higher ED food intakes.

FRA, FLA, FRL, FLL, fat trunk, ICW, BFM, SMM, SLM, WC, FFMI and FMI were positively under the influence of PAI-1.

Conclusions:

All adipose tissue content of subcategories of BC were strongly associated with ED intake in the mediatory role of PAI-1 and TGF-beta.

Keywords: body compositions, diet, energy density, inflammatory markers

What's known?

As we know inflammatory markers are in related with body compositions from the past studies. In addition dietary energy density can directly effect on BCs especially on body fat content.

What's new?

Actually the mediatory role of inflammatory markers (hs-CRP, TGF-beta and PAI-1) on changing different BC subcategories due to consumption of various ED groups is unknown. We investigate the relationship between ED and BCs under the role of inflammatory markers.

Introduction

Obesity, a multifactorial disease, is a developing global issue (1). According to World Health Organization (WHO) worldwide obesity ranking, there are more than 1.9 billion overweight with body mass index (BMI) above 25 kg/m^2 and more than 650 million obese with BMI above 30 kg/m^2 adults over 18 years in 2016 and the prevalence of obesity is 21.4% in Iran according to meta-analysis (2–4). In addition prevalence of obesity and body fat percentage are higher than men among women (5,6). Fat accumulation is already seen as gynoid type in women (7).

Generally, body compositions (BCs) has higher accuracy than BMI for determining obesity(8). Studies showed that BC balance is changed in obesity. Xiongfei Liang et al. reported that ECW can increase as a result of adipose tissue increasing (6). It has been suggested fat distribution especially visceral fat could affect human health (9), activate innate immune response (10,11) and secret inflammatory cytokines from adipose tissues (12). Increasing plasma level of high-sensitive C-reactive protein (hs-CRP), transforming growth factor-β (TGF-beta) and plasminogen activator inhibitor- 1(PAI-1) can be related with having high ED diet and body fat mass in obese individuals (13–15).

A growing number of studies are being published about the role of diet on prevention of obesity (16). Regardless of the micronutrient content, almost many of weight loss diets have been suggested to reduce total daily energy expenditure (17). In Westerterp-Plantenga et al. study observed that obese women usually consume more high energy density (HED) foods with larger amounts in comparison of non-obese women (18). Energy density(kcal/g) (ED) of foods which is identified as energy of one gram of foods (ranges between 0 kcal/g to 9kcal/g for fat) can effect on BCs like body fat mass (BFM) and this method may be one of the best methods of assessing calorie intake (19). Consumption of HED foods can increase body fat mass and inflammatory markers, on the contrary low energy density (LED) foods are more nutrient dense, satiety suppressor and body fat reducer (20–22). Ahra Ko et al. and colleagues(23) have shown that high level of hs-CRP can be a reason of low consumption of fruits and vegetables (LED category).

Little is known about ED of food and alteration of BC. Thus, this study was performed to assess mediatory role of hs-CRP, TGF-beta and PAI-1 on the relationship between ED and BC in women with overweight and obesity.

Method

Study population

This study was a cross-sectional research in which 391 healthy, overweight and obese women 18-48 years were participated. Participants were chosen with multistage cluster random sampling in health care centers in districts of Tehran, Iran. Existence BMI under 25 kg/m^2, experience of any ongoing or previous chronic disease like diabetes and cardiovascular disease, smoking, alcohol or medicine consumption and being pregnant or lactated were exclusion criteria in present study. The total energy range between 800-4000 kcal/d was acceptable (24).

Other variables assessment

Education, socio-economic status, marital status, number of family members, number of people that had history of weight loss in past year and annual income levels were collected by demographic questionnaire. Blood pressure of subjects were also measured.

Body compositions and anthropometric measurement

Body composition analyzer (InBody770 scanner; InBody, Seoul, Korea) was used to assess BCs such as body fat mass (BFM), fat free mass (FFM), bone mineral content (BMC), fat mass index (FMI), fat free mass index (FFMI), skeletal muscle mass (SMM), soft lean mass

(SLM), total body fat (TBF), visceral fat area (VFA), visceral fat level (VFL), fat left leg (FLL), fat right leg (FRL), fat left arm (FLA), fat right arm (FRA), trunk fat, total body water (TBW), extracellular water (ECW), intracellular water (ICW) fat mass index (FMI), fat free mass index (FFMI), body mass index (BMI) by following the manufacturer's protocol (25). Height of participants was measured with Seca 216 to the nearest 0.1 cm in standing position without shoes. Body weight were measured by digital scales with a light cloth for individuals (with an accuracy of 0.1 kg). Waist circumference (WC) and waist to hip ratio (WHR) were measured for all persons by experts.

Physical activity assessment

Physical activity (PA) was assessed using the short form of validate International Physical Activity Questionnaire (IPAQ) (26). The metabolic equivalent (METs) and MET-minutes per week (MET-min/wk) were measured by summing the activity hours per week.

Dietary data collection and evaluation of ED

147-item validated food frequency question (FFQ) was used to assess the average food intake of individuals over the past year (27). All dietary intakes such as energy, macronutrients and micronutrients were calculated by NUTRITIONIST IV software (version 7.0; N-Squared Computing, Salem, OR). Total energy intake was evaluated using foods and beverages reported except alcoholic drinks. ED of all food intakes was calculated by dividing total daily energy (in kilocalories) to weight of foods (in grams) eaten in one day (28,29).

Biochemical parameters measuring

Blood samples were collected in the morning from the participants while they were fasting for 12 hours by experts at the Nutrition and the Biochemistry Laboratory of the School of Nutritional Sciences Dietetics, TUMS. Samples of blood collected in parent tubes containing 0.1 EDTA, was taken following the standard protocol in a sitting position. Samples of serum were centrifuged for serum collection 10 min at 300 rpm, diluted in 1 ml tubes, and stored at

−80 °C until the analysis. Tests were analyzed utilizing the Auto-Analyzer BT 1500 (Selectra 2; Vital Scientific, Spankeren, Netherlands). Hs-CRP, PAI-1 and TGF-beta levels were measured by an immunoturbidimetric test with the Pars Azmoon kit (Pars Azmoon Inc. Tehran, Iran). Serum level of high-density lipoprotein cholesterol (HDL-C), fasting blood sugar (FBS), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL), total cholesterol (TC) and triglyceride (TG) was measured too.

Statistical analysis

Data analysis was performed using the SPSS version 23 (SPSS Inc., Chicago IL, USA). The Kolmogorov–Smirnov test was used to determine the data normality. Quantitative data were reported as the mean ± standard deviation (SD) and qualitative variables were showed as number and percent. ED were calculated and divided to quartiles. One-way Analysis of variance (ANOVA) and Chi-square tests were used to compare quantitative and qualitative variables across different quartiles of ED. To determine the relationship between ED and BCs and inflammatory markers, linear regression was utilized in crude model and adjusted model. Age, energy, physical activity, BMI, education level, history of weight loss, family members and economic status were confounder variables. The results are reported as a percentage change (β) with 95% confidence intervals (95% CI). To analysis of specific differences between ED groups, Bonferroni Post-hoc test was used to show variables differences between ED quartiles. P-value less than 0.05 showed the significance.

Results

Study population and general characteristics

General and anthropometric variables of the study subjects are reported across the ED quartiles in **Table 1**. The mean±SD age, weight, and BMI of participants were 36.79±9.14 (y), 80.69±11.78 (kg), and 31.10±4.12 (kg/m²) respectively.

Among ED quartiles, a significant difference was found in age, PA, number of people who had a history of weight loss in the past year, and income status before and after adjusting confounders (age, BMI, energy intake) ($P<0.05$). Besides TG blood level of participants was statistically significant among ED groups ($P=0.01$) **(Table 1)**. Other variables did not show a positive significant relationship between the ED quartiles. The mean±SD of ED, BFM and SLM was 9756±24751 (kcal/d), 33.59±8.19 (kg) and 43.97±5.26 (kg).

Dietary intake of macronutrient and food components according to the ED quartiles

Dietary intakes of participants are shown in ED quartiles in **Table 2**. Carbohydrate (P= 0.02), saturated fat (SFA) (P= 0.002), total fiber (P= 0.02), Iron (P= 0.03) and Copper (P= 0.002) intake were significant different among ED quartiles in crude model. Finally the significance disappeared after adjusting for potential confounders ($P>0.05$). Fruits, vegetables, legumes, dairy products, refined grains, protein, total fat, polyunsaturated fatty acids (PUFA), monounsaturated fatty acids (MUFA), and caffeine consumption remained significant in ED quartiles even after adjustment of total energy intake ($P<0.05$). Among micronutrients, daily intake of sodium, potassium, calcium, phosphorus, magnesium, zinc, copper, manganese selenium, and vitamins of A, C, D, E, B1, B2, B6, B12 and k was statistically significant in crude model and after adjustment among ED quartiles ($P \leq 0.05$).

Association of body compositions and inflammatory markers serum level among ED quartiles

As can be seen in **Table 3** no significant relationship between ED and BC subcategories and inflammatory markers was seen in crude model. The mean of BCs subcategories and serum level of inflammatory markers were not statistically significantly different between the ED groups even after controlling for potential confounding variables like age, PA, marital, income, job, education, and economic status (P> 0.05). All means of body fat content subgroups had an upper level in the highest ED quartile. Also mean±SD of serum level of PAI-1, TGF- beta, and hs-CRP were 16.66±31.77, 79.80±52.22, 4.34±4.79 mg/dl respectively after adjustment all confounders among overweight and obese women.

Logistic regression analysis examining ED quartiles in relationship with BC subcategories among participants

The relationship between ED quartiles and body compositions in crude model and adjusted model l and 2 are reported in **Table 4**. Logistic regression test demonstrate a positive association between highest ED quartiles and FRA, FRL, FLL, BFM and SMM in all three models (P< 0.05). Also a significance positive relationship between ED of food intakes and FLA (β= 0.22, 95% CI: 0.03-0.41, P= 0.02), TBW (β= 0.03, 95% CI: 0.05-1.39, P= 0.03), ICW (β= 0.45, 95% CI: 0.04-0.87, P= 0.03), FFM (β= 0.98, 95% CI: 0.07-1.89, P= 0.03) and SLM (β= 0.95, 95% CI: 0.09-1.80, P= 0.03) were observed in model 2 after adjusting for age, PA, job, education, marital status, family members, history of having weight loss, economy and income status). Mentioned BCs were significant at first in crude model but these significances were disappeared in model 1 after adjusting for age, PA, job, education and marital status (P> 0.05). Even many other BC subcategories like ECW and BMC had a marginal positive significant association with higher ED consumption. WC (β= 1.78, 95%CI= 0.19-3.37 P= 0.02), FFMI (β= 0.23, 95%CI= 0.01-0.46 P= 0.04), FMI (β= 0.55, 95%CI= 0.08-1.03 P= 0.02) and trunk fat (β= 0.68, 95%CI= 0.13-1.23 P= 0.01) were just positively associated with ED food intakes in model 2.

The association of the mediating effect of some inflammatory factors on BCs between ED quartiles

The association between BCs and ED in the relationship of inflammatory markers is shown in **Table 5**. The positive association was remained between FRA (β= 0.24, 95%CI= 0.009-0.48, P= 0.04), FLA (β= 0.23, 95%CI= -0.001-0.47, P= 0.05), trunk fat (β= 0.82, 95%CI= 0.10-1.54, P=0.02), BFM (β= 1.84, 95%CI= 0.11-3.57, P= 0.03), WC (β= 2.33, 95%CI= 0.26-4.39, P= 0.02), FMI (β= 0.60, 95%CI= 0.01-1.20, P= 0.04) and ED food intakes after entering hs-CRP. These variables were not under the effect of hs-CRP. Also, VFA (β= 8.20, 95%CI= 0.40-15.99, P= 0.03) was positively associated with hs-CRP between ED intakes. SMM, TBW, ICW, FFM, VFA and FFMI was seem to be under the effect of hs-CRP among ED intakes. TBW, ECW, FFM with PAI-1, BMC with PAI-1 and TGF-beta, and SLM with hs-CRP were inversely associated among increasing ED intakes (P> 0.05). FRA, FLA, FRL, FLL, fat trunk, TBW, ICW, ECW, BFM, FFM, SMM, SLM, WC, FFMI and FMI were positively under the influence of TGF-beta after following higher ED food intakes.

FRA, FLA, FRL, FLL, fat trunk, ICW, BFM, SMM, SLM, WC, FFMI and FMI were positively under the influence of PAI-1.

Discussion

This study is the one that was designed to assess the relationship between the energy density of food intake and body compositions under the influence of inflammatory markers. After adjusting confounders results showed that consumption of higher ED foods is significantly related to fat mass subcategories all over the body and WC in women. In addition, SMM, TBW, ICW, FFM, and FFMI were under the effect of hs-CRP among the density of energy intakes. SLM was inversely correlated with ED intakes under the mediatory role of hs-CRP. A raised hs-CRP that is as a result of obesity, can damage mitochondria, muscle tissue and decrease SLM (30). In addition, VFA is more active than subcutaneous fat in aspect of metabolic rate which can be a reason for increasing hs-CRP (31).

In line with this study, a systematic review study which is searched between studies with subjects that have the same ranged age with this study found that lower energy density might be related to lower BMI and other obesity parameters (20). In other systematic review studies, Arango-Angarita et al., found a positive relationship between dietary ED of foods and adiposity using FMI as the indicator among adolescents (32). Getting more ED is one of the consequences of getting a high-fat content diet (33). High energy density foods like the one that is found in the western diet which includes sweetened beverages, red meat, refined grains, and fast foods can lead to reduce BMC and increase bone fracture through functions of excessive added sugar, sodium, and saturated fats in the body. As can be seen this study showed a marginal inverse significant association between BMC and ED under the effect of PAI-1 in overweight and obese subjects (34,35). Many studies suggest that TGF-beta can play a role in loss of bone mineral density by affecting on osteoblasts(36). Aydin et al. showed hs-CRP blood level and BCs (VFL, TBF, and total muscle mass) increasingly align with each other especially in the woman (37). High plant diets and Mediterranean diet which contain more fruits and vegetables and less high ED foods are more tend to decrease hs-CRP and PAI-1 level and healthier liver in humans (37,38). Also the number of fruits and vegetable consumed was significantly different in both total woman and highest quartile. Adding beverages include milk and sweetened drinks and caffeine into calculating ED can affect body fat (39). In agreement with Yamauchi et al. positive relationship between fat distribution in both arms and ED intake may be because of lower muscle content compared with legs (40). Besides more fat distribution in legs in women may be related to hormonal interventions in obese women (41).

Another BC subcategories called VFA is usually higher in women than men (42) and this can lead to elevate hs-CRP level as a consequence of obesity (43). Also, VFA can be increased by a high-fat diet (44). In many studies same as this study, macro and micronutrients which are abundant in vegetables and fruits like manganese, potassium, magnesium, vitamin K, and B vitamins were correlated with VFA and VFL (45). First, lower consumption of magnesium may be related to higher hs-CRP serum levels in this study (46). This can be related to lower SLM following the hs-CRP effect because Mg can be more important even than protein intake (47). Second, vitamin A intake may reduce inflammation in the body. Lower intake of vitamin A can be seen in the highest quartile of ED in this study (48). Third, dietary total fat and PUFA can increase three mentioned inflammatory markers, inflammation and body fat directly(49–52). Forth consumption of LED foods that have high water content and low sodium and fat content maybe lead to lower body fat and balanced TBW and ECW (53,54).

Interestingly, findings show an inverse correlation between TBW, ECM, FFM, and PAI-1. Also all the fat content of BCs were associated with PAI-1 and TGF-beta. As we know more adipose tissue you have, more inflammatory cytokines exist. Inflammatory markers like TGF-beta can lead to existence of more body fat by effecting in secretion of insulin. Insulin is an anabolic hormone (55).

It is generally recommended that lower consumption of antioxidants, which are less in high ED foods and higher refined grains could reduce the production of pro-inflammatory cytokines by affecting the immune system and increases inflammation in the body, especially in obese people (56).

Unlike many studies, this present study had not linked WHR and higher ED intake in quartiles without the mediatory effect of inflammatory serum markers and after entering them. Although previous literature is inconsistent. The fact that all women in the study were overweight and obese could be one of the reasons for the insignificance. Another reason may be the underreporting of intake of animal fat and over-reporting of intake of fruits and vegetables in obese people (57). In addition lower PA may aggravate obesity and inflammatory markers among women (58) who consume the highest ED foods. In 2009, a prospective cohort study between 89,432 participants with a mean age of 53 years showed a weak relationship between ED and WC. Furthermore, no significant correlation was found with weight gain after following them for 6 years (59). Despite this study, Shahinfar et al. did not mention a relationship between ED and WC (60).

Finally the relationship between ED consumption and subsequent changes in BCs may lead to alter levels of inflammatory markers and vice versa. Consuming LED foods can reduce appetite and whole day energy intake. This may cause weight loss and decrease inflammation (61).

Conclusion

In conclusion, all adipose tissue content of subcategories of BC were strongly associated with ED intake in the mediatory role of PAI-1 and TGF-beta among overweight and obese women after following high ED diet. Further prospective studies are needed to confirm these results.

Strengths and Limitations

The strengths of this research are that few studies have been investigated about the association between ED intake of foods and whole BC subcategories among overweight and obese women. Especially using BIA for assessing BCs and observing the effect of these inflammatory markers on BCs in the relation of ED intakes were the nobility of this study.

The first limitation of this study that should be considered is the cross-sectional design. In addition dairy products in this study were not divided into low-fat and high fat because fat content of diaries may effect on ED consumption. FFQ was used in this study and this can be decrease the accuracy. The study population was limited to the woman and this can be reduce the generality. Further study with a large population of men and women and long-term cohort or randomized clinical trials study is needed to find the exact relationship between ED and BCs.

Abbreviation

ED: energy density, LED: low energy density, HED: high energy density, BC: body composition, PA: physical activity, BFM: body fat mass, FFM: fat-free mass, BMC: bone mineral content, FMI: fat mass index, FFMI: fat-free mass index, SMM: skeletal muscle mass, SLM: soft lean mass, TBF: total body fat, VFA: visceral fat area, VFL: visceral fat level, FLL: fat left leg, FRL: fat right leg, FLA: fat left arm, FRA: fat right arm, TBW: total body water, ECW: extracellular water, ICW: intracellular water, WC: waist circumference, WHR: waist to hip ratio, WHtR: waist to height ratio.

Ethics approval and consent to participate

This study approved by the ethics committee of Tehran University of Medical Sciences (TUMS) with the following identification: IR.TUMS.VCR.REC.1395.1597. All participants signed written informed consent forms. All experiments were performed in accordance with relevant guidelines and regulations.

Consent for publication

All authors listed approved the final manuscript and consent for publication.

Availability of data and materials

The data are not publicly available because of containing information that could compromise the privacy of the research. The data-sets used and analyzed during the current study available from the corresponding author Khadijeh Mirzaei on reasonable request.

Competing interests

The authors declare that there is no competing interest.

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Authors' contributions

The project was designed by NB and AM; AM collected the samples and analyzed the data; NB wrote the paper; FS reviewed and edited the paper; KHM conducted research and had primary responsibility for final content. All authors read and approved the final manuscript.

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