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Original article

Metabolic syndrome and calcium: the effects on body composition and biochemical parameters among premenopausal women

Gozde Aritici, Murat Bas

Acıbadem Mehmet Ali Aydınlar University, Health Sciences Faculty, Department of Nutrition and Dietetics, Istanbul, Turkey - E-mail: gozde.aritici@acibadem.edu.tr

Summary. *Aims:* The objective of this study is to investigate the association of the dietary calcium intake with the risk of metabolic syndrome among the premenopausal women. *Methods:* The cross-sectional study was conducted between August and December 2015. One hundred and forty-six premenopausal women, from 19 to 52 years old, participated in the study. The diet section of this study was based on the 3-day self-reported nutrient intake of the recipients. All participants agreed to participate and be submitted to clinical, dietary, anthropometric and biochemical evaluations at the Endocrinology Department at Baskent University Hospital in Ankara. Multiple logistic regression models were used to estimate multivariable odds ratios (ORs) and 95% CIs comparing different dietary intake levels of calcium. *Results:* Participants in 'the group without metabolic syndrome' exhibited significantly higher BMI, waist circumferences, body fat and visceral fat ($p<0.001$) when they were compared with the group with metabolic syndrome. Systolic blood pressure, diastolic blood pressure, low density lipoprotein-cholesterol and triglyceride level were higher in the group with metabolic syndrome than the group without metabolic syndrome ($p<0.001$). Compared to women without metabolic syndrome, women with metabolic syndrome had lower serum calcium level and dietary calcium intake ($p<0.001$). In multiple logistic regression analysis, serum calcium level within normal range was positively associated with the risk of having metabolic syndrome (odds ratio 2.59, 95% confidence interval 0.59-1.51). *Conclusions:* This study suggests that high dietary calcium intake and high serum calcium level are associated with a decreased risk of metabolic syndrome among Turkish premenopausal women. These findings may lead to an effective approach to the reduction of the risk of metabolic syndrome by means of dietary therapy and especially by means of the consumption of dairy products.

Key words: serum calcium level, dietary calcium intake, metabolic syndrome, obesity

Introduction

Metabolic syndrome, a clustering phenomenon of metabolic phenotypes such as abdominal obesity, dyslipidaemia, hypertension and insulin resistance, is an important precursor of cardiovascular disease and type 2 diabetes. Metabolic syndrome is a major public health problem in both developed and developing countries, and the prevalence of diseases related to metabolic syndrome shows an increasing trend (1,2). The prevalence of metabolic syndrome around the world is in the range of 7.9-43% in males and 7-56% in females (3-5). It was reported that the prevalence of metabolic syndrome varies between 23.7% and 32.2% in males, 38.6% and 45.0% in females in previous studies conducted in different parts of Turkey (6-10).

The precise aetiology of metabolic syndrome remains unclear, but it is known as a complicated inter-

action between genetic, metabolic and environmental factors. Among modifiable environmental factors, dietary habits are at prime importance in the prevention and treatment of metabolic syndrome. A number of individual foods and nutrients (e.g. fats, meat, fruits, vegetables, fish and dietary fibre) have been reported to be associated with metabolic syndrome (11,12). Recent studies (13-15) have shown that dairy consumption is inversely associated with body weight, hypertension, glucose homeostasis and type 2 diabetes. Although the underlying mechanisms remain incomplete, calcium and vitamin D, which are two major components of dairy products, have been postulated to be primarily responsible for the beneficial effect of dairy consumption on body weight and insulin sensitivity (16). Zemel et al. (17) found an inverse relationship between dietary calcium and fat mass in both sexes after the adjustment for total energy intake, physical activity, age and ethnic origin. With the meta-analysis of five clinical studies in women, Davies et al. demonstrated an inverse relationship between BMI and dietary calcium (18). Other studies have found an inverse relationship between calcium consumption and both adiposity and cardiovascular disease (19).

Dairy products are the main source of the dietary calcium, and different mechanisms have been proposed to explain the role of calcium in the risk for suffering MetS (20). However, there is an evidence that calcium which is provided as a food supplement or which is taken as a fortification decreases LDL-c and triglyceride concentrations, and increases HDL-c concentrations as well (21). The potential hypolipidemic mechanisms of calcium may occur via: (i) the inhibition of fat absorption accompanying an increased faecal fat excretion; (ii) the inhibition of the absorption of bile acids; (iii) a calcium-induced increase in the conversion of cholesterol to bile acids (22).

Recent studies support the inverse relation between dietary calcium intake, adiposity, insulin resistance and dyslipidaemia in the general population (17,18). Therefore, the objectives of this study were to investigate the association of dietary calcium intake with the risk of metabolic syndrome among postmenopausal women.

Materials and Methods

Study population

The cross-sectional study was conducted between August and December 2015. It was conducted among women who were healthy and thus did not have any health problems at that time. One hundred and forty-six premenopausal women, 19 to 52 years old, participated in the study. It was prospectively examined the medical records and nutritional status. All participants agreed to participate and submitted to clinical, dietary, anthropometric, and biochemical evaluations at the Endocrinology Department at Baskent University Hospital in Ankara. Ethical approval was granted by the Research Ethics Review Committee of Baskent University, Ankara, Turkey. The women who used vitamin and mineral supplementation, entered menopause, pregnant and lactation, used statin and metformin were excluded.

Clinical and anthropometric characteristics

Height, weight, waist and hip circumferences were measured between 08.00 am and 10.00 am after a 12-h fast. Height was measured using a stadiometer (Seca 703, Germany) accurate to ±0.5 cm, and weight was obtained with a digital calibrated scale (Jawon IOI 353, Biodynamics Corp., Seattle, WA, USA), accurate to ±0.1 kg, with the participants wearing light clothes and no shoes. BMI was calculated using the standard equation (kilograms per metre squared). Waist circumference was measured in the standing position, midway between the lower margin of the last rib and the iliac crest, at mid exhalation. Hip circumference was measured at the widest point of the hip/buttocks area with the measuring tape parallel to the floor. Waist-to-hip ratio was determined by dividing waist circumference by hip circumference. Anthropometric measurements were taken twice and mean values were used in all analyses. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured twice in the sitting position, with an interval of 15 minutes between the measurements, by means of standard sphygmomanometers of appropriate width, after a rest period for 30 minutes.

Biochemical analysis

Percentage of body fat was estimated by electrical bioimpedance using a Jawon IOI 353 body fat analyzer (Biodynamics Corp., Seattle, WA, USA). We stratified adiposity as global adiposity (excessive adipose tissue, independent of site) and abdominal adiposity. BMI and percentage of body fat were used as parameters of global adiposity. Waist circumference and waist-to-hip ratio were used to evaluate abdominal adiposity.

Blood samples were collected after a 12-h fasting period. Biochemical evaluation included glucose, total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, triacylglycerol, calcium, phosphorous, HbA1C, parathyroid hormone and vitamin D. Fasting plasma glucose, total cholesterol, HDL-cholesterol, LDL-cholesterol, TG, HbA1C, phosphorous and calcium levels, which were measured with original kits using an Abbott-Aeroset Autoanalyzer (Architect C-8000, Chicago, Illinois, USA), were recorded. Parathyroid hormone and fasting plasma insulin levels, which were measured with original kits using an Perfect Plus 400 Autoanalyzer (Mindray, UK), were recorded.

Diagnosis of Metabolic Syndrome

Metabolic syndrome was diagnosed according to NCEPATP III (23) (National Cholesterol Education Program Adult Treatment Panel III). Thus, a participant had MS if he or she had three or more of the following: (i) abdominal obesity: waist circumference >102 cm in men and >88 cm in women; (ii) plasma triglycerides: ≥150 mg/dL; (iii) plasma HDL cholesterol: <40 mg/dL in men and <50 mg/dL in women; (iv) systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥85 mmHg or the use of antihypertensive medicine; (v) plasma glucose ≥110 mg/dL or the use of antidiabetic medicine/insulin.

Dietary assessment

The diet section of this study was based on the 3-day self-reported nutrient intake of the recipients. These three days included a day from the weekend and the previous or following next two days (Sunday, Monday and Tuesday or Thursday, Friday and Saturday). During the interview, the food models and the photos of common Turkish dishes at various portions, as well as household cups and measures, were used to assess the type and amount of food and beverages consumed during the previous day (24). The energy and nutrient composition of the diets were calculated using the Nutrition Information System (BeBiS) program (25). This database contains Turkish food composition tables for all food, including cooked Turkish dishes. Participants were asked to describe the serving size of each food item and the proportions of common standard measures (e.g. tea and tablespoons, cups of tea).

Statistical analysis

Data are reported as mean ± SD for continuous variables and as numbers or a percentage for categorical variables. Clinical and biochemical characteristics were compared using the Student's t test and the chi-square test when the variables were continuous and categorical, respectively. The Pearson correlation test was used to evaluate associations between serum and dietary calcium and components of metabolic syndrome. Logistic regression analyses were carried out to calculate the odds ratios of having metabolic syndrome and its components (dependent variables) according to the serum and dietary calcium level with the adjustment for potential risk factors (independent variables). Statistical analyses were performed using SPSS software, version 16.0 (SPSS Inc., Chicago, IL, USA).

Results

In total, one hundred and fourty-six individuals agreed to participate in the study. Table 1 indicates the clinical and biochemical characteristics of the participants. The participants in 'the group without metabolic syndrome' were compared with the subjects in 'the group with metabolic syndrome' and this study exhibited significantly higher BMI, waist circumferences, body fat and visceral fat ($p<0.001$). Systolic blood pressure, diastolic blood pressure, low density lipoprotein-cholesterol and triglyceride level were higher in the group with metabolic syndrome than the group without metabolic syndrome ($p<0.001$). Compared to the women who were in the group without metabolic syndrome, the women who were in the group with

metabolic syndrome had lower serum calcium level and dietary calcium intake (p<0.001).

Serum calcium levels and dietary calcium intake according to the presence or absence of metabolic syndrome and the abnormalities of its individual components are presented in Table 2. Subjects with metabolic syndrome, high abdominal obesity, high BP and low HDL-C had lower serum calcium levels and dietary calcium intake than those without abnormalities (p<0.05).

Table 3 showed the Pearson's correlation coefficients between serum calcium and dietary calcium intake and components of metabolic syndrome. The correlation analysis indicated that the serum calcium had positive correlations with the WC, total fat mass, visceral fat mass, systolic BP, diastolic BP, TG, LDL-C and TC (p<0.001). The correlation analysis indicated that the serum calcium has an inverse relationship with BMI and serum HDL-C (p<0.001). Also, the correlation analysis showed that the dietary calcium intake had negative correlations with the WC, total fat mass, visceral fat mass, systolic BP and diastolic BP (p<0.001), and had positive correlations with the HDL-C (p<0.001).

The logistic regression analysis was applied after the adjustment of age, body mass index, alcohol intake, cigarette smoking and exercise. Subjects in the high dietary calcium intake had a lower odds ratio for prevalent metabolic syndrome, abdominal obesity, low HDL-C and high BP than those in the low calcium group (Table 4). The evaluated odds ratio (ORs) of having metabolic syndrome in relation to serum calcium level, low serum calcium level in women had a 2.59-fold increased risk of metabolic syndrome as compared with high serum calcium levels in women.

Table 1. Basic clinical and biochemical characteristics of study population

	Women without metabolic syndrome (n=83)	**Women with metabolic syndrome (n=63)**
Age (yr)	33.3±7.5	36.3±8.3**
BMI (kg/m²)	23.4±3.6	30.7±4.8*
Dietary calcium intake (mg/d)	631.7±131.6	743.07±174.2*
WC (cm)	78.9±7.7	94.4±6.8*
Total fat mass (kg)	20.4±7.8	27.8±8.9*
Visseral fat (kg)	14.2±4.6	10.3±3.8*
Systolic BP (mmHg)	110.9±11.9	136.3±13.7*
Diastolic BP (mmHg)	71.3±8.6	84.2±8.6*
Fasting glucose (mg/dL)	88.2±7.1	90.8±11.8
TG (mg/dL)	78.9±33.2	119.0±56.2*
HDL-C (mg/dL)	59.2±11.4	43.0±6.2*
LDL-C (mg/dL)	106.5±29.6	126.7±31.8*
Ca (mg/dL)	9.31±0.35	9.10±0.31*
Vitamin D (μg/dL)	24.9±9.8	22.4±9.4
P (mg/dL)	3.52±0.43	3.49±0.38
Parathyroid hormone (pg/dL)	49.6±22.5	53.7±25.7

BMI, body mass index; WC, waist circumference; BP; blood pressure; HDL-C, high density lipoprotein-cholesterol; LDL-C, low density lipoprotein-cholesterol; TG, triglyceride; TC, total cholesterol; Ca, calcium; P, Phosphor
**p<0.001; **p<0.05*

Table 2. Mean serum calcium levels and dietary calcium intake according to presence/absence of metabolic syndrome or abnormalities in its components.

		n	Serum Calcium Levels (mg/dL)	Dietary Calcium Intake (g/day)
Metabolic syndrome	Yes	63	9.26±0.31*	631.71±131.65*
	No	83	9.05±0.28	743.07±174.17
Abdominal obesity	Yes	77	9.22±0.32*	645.69±131.08*
	No	69	9.05±0.05	750.07±184.05
High BP	Yes	53	9.28±0.30*	635.85±138.31*
	No	93	9.06±0.29	728.74±171.94
High TG	Yes	21	9.46±0.95*	687.18±165.29
	No	125	9.08±0.28	741.68±148.45
Low HDL-C	Yes	79	9.21±0.31*	659.68±159.95*
	No	67	9.06±0.31	736.69±164.94
High glucose	Yes	14	9.17±0.36	653.20±120.84
	No	132	9.13±0.31	699.45±170.07

*BP; blood pressure; HDL-C, high density lipoprotein-cholesterol; TG, triglyceride; *p<0.001; **p<0.05*

Table 3. Correlations of serum calcium levels and dietary calcium intake with parameters of metabolic variables and other characteristics

	Serum Calcium Levels (mg/dL)	Dietary Calcium Intake (g/day)
	r	r
Age (yr)	-0.053	-0.113
BMI (kg/m2)	-0195**	-0.130
WC (cm)	0.335*	-0.229*
Total fat mass (kg)	0.207**	-0.354*
Visseral fat mass (kg)	0.216**	-0.354*
Systolic BP (mmHg)	0.270*	-0.305*
Diastolic BP (mmHg)	0.300*	-0.288*
Glucose (mg/dL)	0.037	0.011
TG (mg/dL)	0.374*	0.139
HDL-C (mg/dL)	-0.244*	0.223*
LDL-C (mg/dL)	0.197**	-0.006
TC (mg/dL)	0.188**	0.107

*BMI, body mass index; WC, waist circumference; BP; blood pressure; HDL-C, high density lipoprotein-cholesterol; LDL-C, low density lipoprotein-cholesterol; TG, triglyceride; TC, total cholesterol *p<0.001; **p<0.05*

Discussion

In the present study, relationships were found between the serum calcium levels, dietary calcium intake and some components of the metabolic syndrome in premenopausal women.

The effects of dairy consumption on the risk of metabolic syndrome can be partially explained by calcium intake in dairy foods, and several studies have found that people with higher calcium intakes have a lower prevalence of metabolic syndrome and its components. Dietary calcium is known to play a key role in blood pressure control and adipocyte metabolism, and thus its effects on metabolic syndrome could be partially mediated by its effects on body fat, blood pressure and insulin sensitivity (2).

Inadequate intake of calcium is a global problem, especially among women, and it has been associated with several medical disorders, such as osteoporosis, hypertension, colon cancer, breast cancer and kidney stones. Based on recent research, increased dietary intake of calcium is currently recommended for the general population to lower the risk of these chronic diseases (26,27). In a large cohort study of 34,486

Table 4. Logistic regression analysis of metabolic syndrome or its components for serum calcium level and dietary calcium intake

	Serum Calcium Levels (mg/dL) OR (95% CI)	Dietary Calcium Intake (g/day) OR (95% CI)
Metabolic syndrome	2.59 (0.59, 1.51)*	0.35 (068, 1.93)**
Abdominal obesity	4.23 (0.51, 4.23)*	0.43 (0.57, 1.97)**
High BP	2.1 (0.62, 1.31)**	0.43 (0.76-1.78)*
High TG	1.87 (0.58, 1.09)	1.86 (0.59-1.11)
Low HDL-C	3.78 (0.55, 2.07)*	0.36 (0.61, 1.69)**
High glucose	2.61 (0.38, 1.10)	0.43 (0.94-2.19)

*BMI, body mass index; WC, waist circumference; BP; blood pressure; HDL-C, high density lipoprotein-cholesterol; LDL-C, low density lipoprotein-cholesterol; TG, triglyceride; Ca, calcium; P, phosphor p-value calculated by chi-square *p<0.001;*
***p<0.05*
Odds ratios (ORs) were adjusted for age, body mass index, alcohol intake, cigarette smoking and exercise.

postmenopausal women, higher intake of calcium, except vitamin D and milk products, was associated with reduced ischaemic heart disease mortality (28). On the other hand, several studies indicate that milk and milk products have hypolipidemic and anti-atherogenic effects, which could be related to not only calcium, but also other bioactive substances in milk (29,30).

In the QUEBEC family study, LDL-cholesterol and the ratio of total- to HDL-cholesterol were negatively correlated with calcium intake (19). Some trials have also shown a significant improvement in serum lipids profile with calcium supplementation on energy-restricted diets in obese women (31) or while consuming their usual diets in the group of adults with hypercholesterolemia or in normal older women compared to placebo (32-34). In our study, in the low dietary calcium group, LDL-C levels were higher and HDL-C levels were lower than that in the high dietary calcium group, and serum calcium levels were significantly different between women with high HDL-C and with low HDL-C. In one fairly large cross-sectional study in 5,394 men and 4,800 women, a linear increase of both total cholesterol and HDL cholesterol with serum calcium levels were found, independent of confounding factors such as age, blood pressure, body weight, fat and cholesterol intake (35). In hyperlipidemic patients, Carlson et al. (36) found a 10% decrease in serum cholesterol during calcium treatment, but there was no change in triglycerides. In our study, the TG levels were raised with high serum calcium levels and subjects with high TG had higher calcium level than those without high TG, which is in line with the results of other human studies (37). However, in this study, dietary calcium intake was not associated with TG levels. In contrast, intake of dietary calcium was negatively associated with TG levels in other studies (38,39).

In a randomized, placebo-controlled trial in 32 obese adults, plasma glucose, which was applied after a glucose tolerance test, was significantly lower in a diet supplemented with calcium from dairy products compared with the control group at the end of the experiment, which lasted 24 weeks. Additionally, plasma insulin was lower after calcium intake from dairy products (40). In this study, serum calcium levels and dietary calcium intake are not associated with glucose levels, insulin and insulin resistance. These findings are in contrast to the results from previous studies (41,42).

A highly significant association between serum calcium and both systolic and diastolic BP was found in postmenopausal women. When the importance of calcium in all aspects of physiology is considered together with the huge amount of research which was done on hypertension, there are remarkably few studies on the relationship between total serum calcium levels and BP. However, in a few available studies (43), the results are similar to those presented in this study. The results of our study confirm the inverse association between dietary calcium and blood pressure, in that a greater intake of calcium was associated with a reduction in blood pressure. Several studies reported that serum calcium levels were positively related to BP in epidemiologic studies (44,45). A higher dietary Ca intake reduced the risk of hypertension in women aged over 45 in the American Women's Health Study, and a Ca intake over 1000 mg/day lowered the risk of hypertension (multivariate relative risk = 0.87) (46). Similarly, in this study, dietary calcium intake was inversely associated with BP in women. A meta-analysis of 23 observational studies estimated that each 100 mg increase in daily calcium intake would produce a low-

ering of 0.39 mmHg in systolic and 0.35 mmHg in diastolic blood pressure (47).

Dietary calcium plays a partial role in the regulation of energy metabolism. High-calcium diets attenuate adipocyte lipid accretion, increase lipolysis and preserve thermogenesis during caloric restriction (48). Intracellular calcium can also act directly on adipocytes to regulate lipid metabolism and insulin-stimulated glucose uptake and storage (49). An inverse relationship between dietary calcium (and/or dairy products) and adiposity indices has been found in several epidemiologic studies in the general population (19,50). In a population-based prospective study with 43,000 adult subjects, overweight was less common in individuals who consumed high quantities of milk products compared with the low consumers (50,51). This negative association between milk consumption and body weight was not observed in adults at normal weight. In our study, there was no significant correlation between body mass index or body weight and dietary calcium intake, but there was a negative association between serum calcium level and body mass index. In contrast, there was a significant correlation between the dietary calcium intake and serum calcium level and the abdominal obesity and total body fat in participants. A recently published cross-sectional survey, carried out in a very large Portuguese population (n = 39,640), showed that high milk consumption was associated with significantly lower body mass index in the entire population but postmenopausal women (52).

A limitation of our study was that we did not measure ionized calcium, but total serum calcium, which might be affected by serum albumin and pH. Also, because of the cross-sectional design of this study, it was not possible to establish a cause–effect relationship between serum calcium and dietary calcium intake and metabolic syndrome. Therefore, prospective or longitudinal studies are necessary to elucidate elaborately the association between serum calcium level and dietary calcium intake and metabolic syndrome.

As a conclusion, this study suggests that high dietary calcium intake and high serum calcium level is associated with a decreased risk of metabolic syndrome among Turkish premenopausal women. These findings may lead to an effective approach to the reduction of the risk of metabolic syndrome by means of dietary therapy and especially by means of the consumption of dairy products.

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Correspondence:
Gozde Aritici
Acıbadem Mehmet Ali Aydınlar,
University Health Sciences Faculty,
Department of Nutrition and Dietetics, İçerenköy Mahallesi
Kayışdağı Caddesi No:32, Istanbul, Turkey
Tel. +90 216 5004238
E-mail: gozde.aritici@acibadem.edu.tr