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Nutrient patterns and their relationship to Metabolic Syndrome in Iranian adults

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What is already known on this subject?

The global prevalence of metabolic syndrome is increasing and the impact of this condition on potential co-morbidities such as cardiovascular disease is high.

There is evidence for a relationship between nutrient patterns and metabolic syndrome and its components in Iranian adults.

What this study adds?

The present study investigates the association between nutrient patterns and metabolic syndrome in the general adult population of Iran.

Our findings indicate a nutrient pattern characterised by dietary protein, carbohydrate, starch, glucose, fructose, sucrose, maltose was associated with higher odds of MetS in both genders.

Nutrient patterns and their relationship to metabolic syndrome

Background: The prevalence of metabolic-syndrome (MetS) is increasing globally. It is associated with a significant risk of developing type 2 diabetes-mellitus and cardiovascular-disease.

Methods: The relationship between adherence to several different dietary-patterns and the presence of MetS was explored in an Iranian population sample of 5764 subjects.

Results: We observed that the prevalence of MetS was 13% and 18% in men and women, respectively. There were three main dietary-patterns, the first pattern was characterized by protein, carbohydrate, starch, glucose, fructose, sucrose, maltose, dietary-fiber, potassium, calcium, magnesium, phosphorus, iron, zinc, manganese, thiamine, riboflavin, carotene, vitamin c, and lactose; second representative of fat, saturated-fat, monounsaturated-fat, polyunsaturated-fat, cholesterol, sodium, calcium, zinc, phosphorus, iodine, vitamin-D, chloride, betaine, niacin; third consisting of copper, selenium, vitamin A, riboflavin, vitamin B12. In this dietary pattern, individuals in first quintile had a higher consumption of total fat, saturated fatty acid, monounsaturated fatty acid, poly unsaturated fatty acid, Cholesterol and vitamin A. In the second pattern, individuals in the fifth quintile ate less carbohydrate, dietary

fiber, glucose, Fructose, potassium compared to first quintile. We found that individuals in the first quintile in pattern 3 had higher intakes of protein, zinc, and calcium compare to other quintiles.
Conclusions: We have found that a nutrient pattern which mostly characterized by dietary protein, carbohydrate, starch, glucose, fructose, sucrose, maltose was associated with a higher risk of MetS in both genders, while a pattern which was represent of copper, selenium, Vitamin A, riboflavin, vitamin B12 was associated with greater odds of Mets, in women.

Keywords: nutrient pattern, metabolic syndrome, factor analyses

Introduction:

Metabolic syndrome (MetS) is characterized by a clustering of abdominal obesity, insulin resistance, hypertension, dyslipidemia, and impaired glucose tolerance, features that contribute to an increased risk of diabetes mellitus[1] and cardiovascular disease[1, 2].
The prevalence of Mets has been increasing globally. According to the National Health and Nutritional Examination Survey (NHANES) [3], the prevalence of MetS among adults in the United States was approximately 23% between 1988 to 1994, and increased to approximately 34% between 2003 to 2006, although the criterion for fasting blood glucose was updated to 100 mg/dl [4]. An increased prevalence of MetS has also been reported in Asia. This increase in Asia over recent decadeshas been attributed to the adoption of Western lifestyles [5]. Dietary pattern analysis has recently emerged as a method for examining diet–disease relationships [6]. In this approach, statistical methods are used to combine multiple foods or nutrients to derive single-exposure variables, or dietary patterns [7]. It has been suggested that such dietary patterns may provide a better insight into the relationships between diet and disease [6] and may be more predictive of chronic disease risk than the intake of individual nutrients or foods [7]. Furthermore, the effects associated with single nutrients or foods may be too small to be detectable, while there may be significant associations between dietary patterns and risk of

obesity, diabetes, cardiovascular disease and some cancers[7]. There have been some recent studies examining the effect of specific foods and dietary patterns on MetS [8-11]. For example a high intake of dietary fiber, calcium, vitamin D, whole grains, fruits, and vegetables have been reported to have independent protective effects against risk of Mets[12-14]..Whilst dietary pattern analysis has been criticised for potential errors due to subjectivity and differences between ethnic populations [15], healthy dietary patterns, such as the Mediterranean diet or prudent diets characterized by high intakes of whole grains or fish, vegetables, and fruits, have shown favourable effects on metabolic abnormalities[12, 14, 16]. Few studies on the association between dietary patterns and features of the MetS have been conducted in Asian populations. In this present study, the association between adherence to several dietary patterns and the presence of MetS was explored in Iranian adults.

Materials and Methods

Population:

Men and women aged 35-65 years from an urban population (n = 5764) were recruited using a stratified – cluster sampling method from the Mashhad stroke and heart atherosclerosis disorder (MASHAD) study, Mashhad, Iran. Every area was divided into 9 locations centered upon Mashhad Healthcare center divisions in Iran. Families were identified by the indigenous population authorities who also provided the information brochures of the study to participants. Communal leaders who were acquainted with the families in these communities also helped with the identification and enrolment of potential participants. Eligible participants were contacted by telephone to organize an appointment for the physical examination. Non-responders were also contacted and information was sought regarding their demographic and diabetes and hypertension status. The demographic, anthropometric and lifestyle data were collected by two expert health care professionals and a nurse. Exclusion criteria were pregnancy and lactation, established cardiovascular disease or diabetes, consumption of dietary supplements. Smoking habit was classified into two categories: current smoker or non-smoker. Each participant provided written informed consent, and the study was approved by the ethics committee of Mashhad University of Medical Sciences.

Anthropometric assessment:

Body weight and height were measured with subjects in light clothing and without shoes. Body mass index (BMI) was calculated as weight (kilograms) divided by height*height (squared meters). Waist circumference was measured at the midpoint between the lowest rib margin and the iliac crest during minimal respiration. Resting blood pressure was taken three times by a trained technician using a standardized protocol. The average of three recorded measurements was used in all data analyses. For blood pressure measurements, the subjects remained seated for 15 minutes and as a minimum of two readings were taken using a standard mercury sphygmomanometer. The mean values of the closest two readings were calculated.

Biochemical assessment

Total cholesterol, triglycerides, low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), glucose and FBG were measured using an auto-analyzer (Ependorf, Germany), as described previously[17].

Metabolic syndrome:

The diagnosis of MetS was based on the definition of the International Diabetes Federation: waist circumference (WC) ≥80 for women or ≥94 cm for men in the presence of two or more of the following components: fasting plasma glucose ≥100 mg/dl; systolic (or diastolic) blood pressure ≥130 (or ≥85) mm Hg; HDL cholesterol <50 mg/dl for women or <40 mg/dl for men; triglyceride ≥150 mg/dl [21].

Dietary assessment:

Dietary information was collected using a 24-hour recall questionnaire, administered by a trained dietary interviewer during face-to-face interview [1]. Individual nutritional intakes were assessed with the use of the Dietplan6 software (Forest field Software Ltd., UK) that was used to analyze the macro and micro nutrient intake. The variables selected for the purpose of this study were total energy intake, crude and energy adjusted intake of all macronutrients. Macronutrients were also considered as a percentage of total caloric intakes.

Assessment of physical activity:

Physical activity levels were assessed using the James and Schofield human energy requirements equations [22]. Physical activity level was calculated as the total energy expenditure (TEE) and ratio of the BMR (Basal Metabolic Rate) over a twenty-four hour period. Questions on physical activity were based on the James and Schofield equations, and were selected from those used in the Scottish Heart Health Study (SHHS) /MONICA questionnaire (Bolton-Smith et al., 1992). Questions assessed the time spent on activities during work (including housework), outside work, and in bed (resting and sleeping).

Statistical analysis:

Statistical analysis was performed using SPSS version 16.0 (SPSS® Inc., Chicago, IL). Nutrient intake was expressed in grams, milligrams and micrograms. It was also adjusted for total energy intake through the residual method [23]. Energy-adjusted nutrient intakes were calculated as the residuals from the regression model, with absolute nutrient intake as the dependent variable and total energy intake as the independent variable [23]. Factor analysis with orthogonal transformation (varimax procedure) was applied to derive nutrient patterns based on the 40 nutrients and bioactive compounds. Factors were retained for further analysis based on their natural interpretation and eigenvalues on the Scree test [31]. In this study, we retained factors with eigenvalues >3 as this cut off could result in more interpretable dietary patterns. In addition, factors with eigenvalues ≤3 did not explain sufficient amounts of overall variation. We computed the factor score for each nutrient pattern by summing up intakes of nutrients weighted by their factor loadings [31]. Each participant received a factor score for each identified pattern. As simple linear dose–response relationships are unlikely to be found in nutritional epidemiology [24], we categorized the subjects based on quintiles of nutrient pattern scores. Continuous and categorical demographic variables were compared across quintiles of nutrient pattern scores using analysis of variance and Chi-square tests, respectively. We computed age-, gender- and energy-adjusted intakes of food groups and nutrients using analysis of covariance (ANCOVA). Comparison of dietary intakes across categories of nutrient pattern scores was done using ANCOVA with Bonferroni correction. Means of anthropometric measures across quintiles of nutrient pattern scores were calculated in different models for both genders. First, adjustments were done for age (continuous), and energy intake (continuous). In the second model, we further controlled for marital status, education, smoking status, and physical activity. All these analyses were done using analysis of covariance with Bonferroni correction. To determine any association between nutrient patterns and Mets, we used binary logistic regression, with the adjustments as mentioned above. Again, these analyses were done for both genders. In these analyses, the first quintile of the nutrient pattern scores was considered as the reference category. To compute the overall trend of odds ratios across increasing quintiles of nutrient pattern scores, we used the quintiles of each pattern as an ordinal variable in the logistic regression models. Statistical significance was defined as a two-tailed p-value <0.05.

Result:

The prevalence of the MetS based on the IDF was 13% and 18% in men and women respectively. Our statistical analysis showed three main dietary patterns in the middle age population: 1- identified as the pattern one , and was characterized by protein, carbohydrate, starch, glucose, fructose, sucrose, maltose, dietary fiber, potassium, calcium, magnesium, phosphorus, iron, zinc, manganese, thiamin, riboflavin, carotene, vitamin c, and lactose . Pattern two was characterised by total fat, saturated fat, monounsaturated fat, polyunsaturated fat, cholesterol, Sodium, calcium, zinc, phosphorus, iodine, vitamin D, chloride, betaine, niacin . Third pattern was consisting of copper, selenium, Vitamin A, riboflavin, vitamin B12. These three patterns explained 51.8 % of variance in dietary nutrient consumption. Anthropometrical, clinical and socioeconomic characteristics based on the quintiles of nutrient pattern are shown in Table 1. For the first and second dietary patterns, individuals in the first quintile were younger than third and fifth(p<0.001), however we failed to find any significant difference for age in the third pattern between quintile (p=0.881). There were significant differences for education between quintiles in the first and second dietary pattern groups but not in the third. Moreover we found significant differences for physical activity levels between the quintiles for all the dietary patterns. Table 2 shows the multivariable-adjusted intakes of selected food groups and nutrients based on the nutrients pattern. In the first dietary pattern the individuals in the first quintile had a higher consumption of total fat, SFA, MUFA, PUFA, Cholesterol and vitamin A. Within the second pattern individuals in the fifth quintile ate less carbohydrates , dietary fiber, glucose , Fructose, potassium compared to the first quintile. We found that individuals in the first quintile in pattern 3 had higher intakes of protein, zinc, and calcium compare to other quintiles. Multivariable-adjusted means of cardio-metabolic factors based on the gender and across the quintiles and patterns are shown in table 3. within the first pattern we observed a significant difference for crude model (unadjusted) across quintile in both gender for waist circumference (WC). Moreover in first pattern experienced the significant change across the quartile for WC even after partially or fully adjustment and again in both men and women. Interestingly, within the second pattern in male , WC failed to be significant in crude model but when the confounders were taken into account got significant, in contrast for systolic blood pressure (SBP) after partially or fully adjustment we failed to find the significant differences across the quintiles. We used logistic regression to examined the strength of the association for both gender by using unadjusted, partially and fully adjusted model. Men within the first dietary pattern were 35 % more likely to have MetS (OR: 1.35, 95%CI: 1.02-1.79). For women after partial adjustment for confounders, we found that the association was greater for the first dietary pattern (OR: 1.3495%, CI: 1.07-1.66). For the second dietary pattern, we found no effect of the food pattern for men or women even after adjustment for potential confounders within the third pattern for women we found that they have 30 % more tendency to have the MetS, in the third quintile after full adjustment (OR: 1.3, 95%CI: 1.05-1.62).

Discussion:

To the best of our knowledge this is the first study in the Middle East region to assess the association between dietary patterns and MetS. Using Principal component factor analysis (PCFA), we identified three major dietary patterns in a sample of Iranian middle-aged men and women. In this study, we found a significant association between adherence to the first nutrient pattern (consisting of protein, carbohydrate, starch, glucose, fructose, sucrose, maltose, dietary fiber, potassium, calcium, magnesium, phosphorus, iron, zinc, manganese, thiamin, riboflavin, carotene, vitamin c, and lactose) and odds of having MetS in both genders. Moreover, the third nutrient pattern (characterized by copper, selenium, vitamin A, riboflavin, vitamin B12) was positively associated with the risk of MetS among women but not for the men. No significant associations were found between for second dietary pattern in either men or women. Although associations between dietary patterns and risk of chronic conditions have received increased attention, few data are available linking patterns of nutrient intake and risk of non-communicable diseases [4–6, 8–11]. The present study revealed, for the first time, the existence of three major nutrient patterns in a large Middle Eastern population. Previous studies on nutrient patterns have reported similar associations with different types of cancer [4–6, 9, 10, 26, and 32] and osteoporosis [11]. Nutrients included in the nutrient pattern analyses in previous studies varied between 19 and 30 nutrients and differed amongst studies based on the outcome variable(s) of interest. We attempted to include a maximum number of MetS-related nutrients and bioactive compounds (more than 45 in total) in our analysis. For example, in contrast to previous studies, we included mono and disaccharides such as fructose, glucose and sucrose in the factor analysis, since there is a large body of evidence relating monosaccharide intake to Mets-factor development [33, 34]. In the first pattern due to having high amount of the protein, carbohydrate, starch, glucose, fructose, sucrose, and maltose could be regarded as Western patterns. The combination of MetS- inducing nutrients and those protecting against MetS development in this nutrient pattern makes interpretation somewhat difficult; however, taken together, our findings on the association between nutrient patterns and MetS support previous findings on the link between dietary patterns and MetS or its components [45–47], and underline the validity of the nutrient pattern approach in assessing diet–disease relations. Furthermore, our findings indicate that complex, previously unrecognized, interactions may take place between highly loaded nutrients (both MetS-inducing and protective) that require much further research. Finally, the direct association that we found between nutrients loaded in the first and third pattern and Mets might provide an excellent basis from which to evaluate MetS-protective effects of multiple-nutrient supplementation in future studies. For example: vitamin A, vitamin C, magnesium, calcium and potassium, they may help support health and wellness and potentially reduce the risk of chronic diseases [13]. MetS has been associated with greater intake of key nutrients. Zinc is involved in the synthesis, storage, and release of insulin. Dietary zinc intake was inversely associated with MetS [24]. Some studies have shown that increased dietary magnesium intake was associated with lower risk of the MetS [25, 26]. Moreover, some other nutrients in this pattern, such as thiamine [20] have been positively related to MetS components. B-vitamins (which found in both first and third pattern) may stimulate appetite; thus, their long-term consumption may trigger excessive energy intake and weight gain and energy intake is the main factor for the elevated BP [43]. Starch and free sugars were also highly represented in this the first nutrient pattern. In contrast to free sugars, there is a controversy about the association between starch consumption and Mets among studies because starch is a complex carbohydrate mostly present in solid foods with fiber and other food components [34, 44]. Although there is also some discrepancy for some nutrients which is in line with our finding, some study showed that vitamin A had a positive relationship with IR, UA, and MetS [54]. Samara et al.

revealed that calcium levels were positively related to TG and negatively to HDL-c in women [55]. As with many other Middle Eastern countries, in recent decades, the Iranians have been experiencing a rapid nutrition transition characterized by adopting unhealthy Westernized dietary patterns instead of their own healthier traditional ones [27, 28]. Interestingly, during the same period of time, there has been a significant rise in the prevalence of non-communicable disease risk factors such as hypertension, especially among youth [3, 27, 39, and 46]. Our finding regarding the positive association of the Western dietary pattern with MetS is therefore of great significance, as it suggests that this nutrition transition could be a major reason for the alarming increase in the prevalence of MetS among adolescents in the Middle Eastern countries and particularly in Iran. Iran is a Middle Eastern country which, over the past four decades, has experienced rapid socio-demographic change and urbanization, so that more than 60 % of its population is currently urban dwelling with a very young structure [28]. However, these dramatic changes have been failed to appropriately couple with a steady and significant economic growth, as Iran still remains a lower middle income country [28]. These unsynchronized socio-demographic and economic transitions, along with the potential impact of globalization on cultural values regarding food choices, have led to a substantial shift in recent decades in the food baskets of urban families in particular, in favour of inexpensive dietary energy sources and decreased dietary quality (both of which are among the major characteristics of the Western dietary pattern), as food consumption patterns and dietary quality are extremely income- and culture- dependent [28]. So, it may not be a surprising finding that a substantial proportion of Iranian adolescents are following a Western dietary pattern. The Western pattern in Asian countries is not exactly the same as that followed by Western populations [31, 40]. Even Asians who consume substantial quantities of meat or animal-based foods still adhere to a rice-based diet, which contributes to the maintenance of a low-fat diet compared with Western countries. We assume that Westernized patterns will not become associated with metabolic syndrome abnormalities unless the staple foods change. However, these patterns should be monitored. Within the first pattern we observed the significant difference for crude model across quintile in both gender for WC. Moreover in this pattern there was a significant change across the quintile for WC even after adjustment in both men and women. Several studies have reported that the high intake of carbohydrates among Asian populations was associated with the risk of type 2 diabetes mellitus [16], cardiovascular disease [17], and metabolic syndrome among those who were metabolically obese with normal body weight [18]. However, the adoption of Western patterns involving the high consumption of animal products such as meat, processed meat, and eggs in Asian countries has also been reported to have increased the risk of diabetes [19], hypertriglyceridemia [20], cardiovascular disease [21], and obesity in young people [22] because of the high intake of saturated fat associated with this diet. Moreover, several studies reported that dietary patterns high in staple foods were associated with a greater risk for type 2 diabetes mellitus in Chinese women [34] and that high-carbohydrate diets were associated with insulin resistance and dyslipidemia in South Asia [35]. In addition, white rice was reported to be associated with an increased risk for diabetes in Japanese [36] and American individuals [37] and for ischemic stroke in Chinese individuals [38]. Future studies are necessary to explore the effect of carbohydrate quality in staple foods or the effect of fiber contents in grain foods on the risk of metabolic syndrome. Another possible explanation is the limitation in the practical utility of the definition of metabolic syndrome. A recent report claimed that metabolic syndrome might be considered useful as an educational concept with limited clinical utility because no accepted central underlying mechanisms have been suggested [3]. Although an inverse association between dietary fiber [44], potassium [48] and zinc [24] and MetS has been reported in previous studies, the presence of free sugars in this nutrient pattern may have resulted in an

MetS-inducing effect; thus, it appears that free sugars increase the odds of MetS even when co-ingested with nutrients that may assist to protect against the development of MetS. Although assessment of the effects of individual nutrient intakes in the framework of a nutrient pattern is impossible, it appears that nutrients with greater factor loadings, along with the synergistic effects of other nutrients, determine the contribution of a given pattern to MetS. Thus, based on our findings, people should be clinically advised not to consume large amounts of simple sugars in their diets, regardless of overall energy intake. The reasons for the observed gender disparity in the associations between nutrient patterns with MetS are unclear, but may, at least in part, in the differential influence of gonadal steroids on body composition and appetite; behavioural, socio-cultural and genetic factors may also play a role [50]. Another reason for this discrepancy might be the difference in accuracy of dietary assessment among females and males. Thus, actual food choices [51], self-reported preferences for foods [52] and accuracy of dietary assessment [53] may all vary by gender. For example, European women appear to eat more fruit, vegetables and dietary fiber than men [51]; gender was reported to be the most personal characteristic that related to intake measurement errors for food groups [53]. This may especially be the case for FFQs based on the Willett format; for these, a tendency to underestimate and overestimate nutrient intakes in men and women, respectively, has been reported [54].

A major strength of the study is it was performed in a large population. However the main limitation was the cross-sectional design and also the possibility of residual confounding bias due to unknown or unmeasured confounders (e.g., birth weight, feeding pattern during infancy, and family history of hypertension), although we adjusted the ANCOVA models with known confounding variables [65]. Next, there are a few other methods for identifying dietary patterns, some of which (e.g., reduced rank regression) are believed to be even more successful than the PCFA in deriving dietary patterns that are predictors of disease risk [13, 66-70]. Finally, the dietary pattern approach can be subjective and creates difficulties in replicating results in other populations. Nevertheless, this approach is useful for enhancing our understanding of the complex dietary variables implicated in chronic diseases [41].

In conclusion, We have found that a nutrient pattern which mostly characterized by a dietary protein, carbohydrate, starch, glucose, fructose, sucrose, maltose was associated with a higher risk of MetS in both genders, while a pattern which consisting of copper, selenium, vitamin A, riboflavin, vitamin B12 was associated with greater odds of Mets, in women. The results of this study could be therefore of major public health significance. However, before making any firm conclusion, additional large-scale prospective studies with adequate methodological quality are required to first confirm these findings.

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Table 1 General characteristics of participants across quintiles of major nutrient pattern scores

		First nutrient pattern				Second nutrient pattern				Third nutrient pattern			
		Q1	Q3	Q5	p [b]	Q1	Q3	Q5	p	Q1	Q3	Q5	p
Age (y)		48.9±8.2	48.8±8	48.4±8	0.002	49.6±7.9	48.9±8	48.4±8.5	0.01	48.7±7.7	48.9±8.1	48.7±8.3	0.88
Gender (Female %)		68.5	61.7	50.7	≤0.001	70.7	62.8	48.3	≤0.001	64.5	64.6	54.9	≤0.001
Current smoker (yes %)		20	22.8	22.1	0.44	23	20.2	22.4	0.05	21.6	21.8	20.7	
Education					≤0.001				≤0.001				0.32
	Less than high school (%)	47.5	45.1	40.9		49.7	46.6	39.8		45.5	44.7	45.8	
	High school (%)	36.3	38.4	40.5		35.2	36.6	40.6		36.4	36.6	38.7	
	More than high school (%)	16.2	16.5	18.6		15.1	16.8	19.6		18.1	18.7	15.5	
Job status					0.01				0.001				0.04
	Employed (%)	63.5	64.5	67.1		61.2	63.4	68.1		65.4	61.6	67.1	
	Unemployed (%)	13.9	11.2	9.2		14.9	10.5	8.8		12.6	13.6	11.1	
	Retired (%)	22	23.9	23		23.1	25.3	22.2		21.6	24.4	21.2	
Physical activity					≤0.001				≤0.001				0.08
	Inactive (%)	21.4	24.2	32		20.7	24.5	30.5		23.8	23.6	28	
	Low activity (%)	26.3	32	25.5		28.6	28.6	26.6		30.2	29.3	26.2	
	Active (%)	41.6	34.6	34.4		40.4	37.4	33.5		36.4	38.3	35.7	
	Extremely active (%)	10.7	9.2	8		10.4	9.5	9.4		9.6	8.8	10	

[a] Mean±standard deviation (SD)
[b] Obtained from ANOVA or Chi-square test, where appropriate

Table 2 Age, gender and energy-standardized nutrient intakes across quintiles of nutrient patterns' scores

	First nutrient pattern				**Second nutrient pattern**				**Third nutrient pattern**			
	Q1	**Q3**	**Q5**	***p*** [c]	**Q1**	**Q3**	**Q5**	***p***	**Q1**	**Q3**	**Q5**	***p***
Energy (Kcal/day) [a]	1426±14 [b]	1777±14	2557±14	<0.001	1479±14	1779±14	2558±14	<0.001	1827±17	1775±17	2186±17	<0.001
Energy density (Kcal/gram) [a]	1.06±0.01	0.96±0.01	1.04±0.01	<0.001	0.89±0.01	1±0.01	1.13±0.01	<0.001	1.02±0.01	0.99±0.01	1.06±0.01	<0.001
Fat (g/day)	84.9±0.5	69.7±0.5	54.6±0.5	<0.001	55±0.5	68.4±0.5	89.7±0.5	<0.001	74.5±0.6	70.6±0.6	65.5±0.6	<0.001
Carbohydrate (g/day)	205.3±1.4	242.9±1.4	278.9±1.4	<0.001	284.1±1.2	245.7±1.2	188.3±1.2	<0.001	250.4±1.5	240.2±1.5	233.6±1.5	<0.001
Protein (g/day)	69±0.6	68.1±0.6	68.9±0.6	0.87	62.5±0.6	68.5±0.6	75±0.6	<0.001	50.4±0.5	68.6±0.5	86.7±0.5	<0.001
Dietary fiber (g/day)	11.4±0.2	16.1±0.2	25.6±0.2	<0.001	20.8±0.2	17.1±0.2	13.6±0.2	<0.001	16.9±0.2	16.7±0.2	19±0.2	<0.001
Glucose (g/day)	12.4±0.4	17.1±0.4	24.1±0.4	<0.001	28.4±0.4	16.7±0.4	9.1±0.4	<0.001	30.1±0.4	15.5±0.4	9.9±0.4	<0.001
Fructose (g/day)	14.1±0.5	20.1±0.5	27.7±0.5	<0.001	32.2±0.5	19.4±0.5	11.2±0.5	<0.001	33.6±0.5	18.1±0.5	12.2±0.5	<0.001
SFA (g/day)	21.7±0.1	18.4±0.1	14.2±0.1	<0.001	13.5±0.1	17.8±0.1	23.8±0.1	<0.001	17.8±0.2	18.8±0.2	17.7±0.2	<0.001
PUFA (g/day)	30.4±0.3	23.6±0.3	16.9±0.3	<0.001	17.5±0.3	23.3±0.3	31.7±0.3	<0.001	27.7±0.3	23.9±0.3	19.9±0.3	<0.001
MUFA (g/day)	23.9±0.1	19.5±0.1	14.6±0.1	<0.001	14.6±0.1	18.9±0.1	25.5±0.1	<0.001	20±0.1	19.8±0.1	18.3±0.1	<0.001
Cholesterol (mg/day)	321.6±5.1	220.9±5.1	136.5±5.1	<0.001	161.2±5.2	215.4±5.2	313.8±5.2	<0.001	148.5±5.1	218.3±5.1	324.6±5.1	<0.001
Potassium (mg/day)	2299±24	2774±24	3512±24	<0.001	3001±27	2830±27	2732±27	<0.001	2524±26	2794±26	3227±26	<0.001
Sodium (mg/day)	4178±216	2620±216	2500±217	<0.001	2412±213	2394±212	6134±214	<0.001	4840±215	2998±215	2278±215	<0.001
Zinc (mg)	8.7±0.08	8.9±0.08	9.9±0.08	<0.001	8.5±0.08	9.1±0.08	9.7±0.08	<0.001	6.9±0.07	9.2±0.07	11.2±0.07	<0.001
Vitamin D (μg/day)	2.8±0.06	1.8±0.06	1.4±0.06	<0.001	1.4±0.06	1.8±0.06	2.9±0.06	<0.001	1.4±0.06	1.8±0.06	2.9±0.06	<0.001
Calcium (g/day)	749.4±9.7	872.1±9.6	948±9.7	<0.001	833±9.9	856.3±9.9	874.9±9.9	0.02	710.2±9.5	863.2±9.5	971.7±9.5	<0.001
Vitamin A (μg/day)	954.3±59.5	273.4±59.4	212.5±59.7	<0.001	893.9±59.8	337.3±59.5	269.6±60	<0.001	165.8±58.4	201.3±58.4	1333±58	<0.001

a Energy was not adjusted
b Data are mean±standard error (SE)
c Obtained from ANCOVA

Table 3 Gender-stratified multivariable-adjusted means for components of metabolic syndrome across quintiles of nutrient pattern scores												
Variables	First nutrient pattern				Second nutrient pattern				Third nutrient pattern			
	Q1	Q3	Q5	*p*	Q1	Q3	Q5	*p*	Q1	Q3	Q5	*p*
Men												
Waist circumference												
Crude	92.7±0.5	94.5±0.5	95.5±0.4	<0.001	95±0.5	94.7±0.5	93.7±0.4	0.4	94.9±0.5	93.7±0.5	94.9±0.4	0.36
Model I[a]	92.8±0.6	94.6±0.5	95.4±0.5	0.01	95.6±0.6	94.9±0.5	92.8±0.4	0.009	94.9±0.5	93.8±0.5	94.7±0.4	0.5
Model II [b]	92.9±0.5	94.6±0.4	95±0.4	0.005	95.2±0.5	94.8±0.4	93.2±0.4	0.053	94.5±0.4	93.6±0.4	94.8±0.4	0.39
Triglycerides												
Crude	148.8±5.1	154±4.6	161.9±4.1	0.17	159±5.3	148.8±4.7	148.4±4	0.1	164.9±4.8	156.1±4.8	144.8±4.2	0.03
Model I[a]	149.2±5.6	153.6±4.7	162.2±4.7	0.36	162±5.5	150.6±4.7	143.5±4.5	0.01	164.8±4.8	157.1±4.8	143.9±4.3	0.02
Model II [b]	149.5±5.5	154±4.6	161±4.7	0.5	160.7±5.5	150.3±4.7	145±4.5	0.03	163.8±4.8	156.1±4.8	144.3±4.3	0.04
HLD-C												
Crude	38.1±0.4	38.4±0.4	38.1±0.3	0.87	38.5±0.4	38.6±0.4	38±0.3	0.82	38.1±0.4	38±0.4	38.8±0.3	0.57
Model I[a]	37.8±0.4	38.3±0.4	38.5±0.4	0.86	38.3±0.4	38.5±0.4	38.3±0.3	0.99	38.1±0.4	37.9±0.4	38.9±0.3	0.34
Model II [b]	37.9±0.4	38.3±0.4	38.5±0.4	0.88	38.5±0.4	38.4±0.4	38.2±0.3	0.98	38.2±0.4	37.9±0.4	38.9±0.3	0.42
Fasting Blood glucose												
Crude	89.8±1.8	89.2±1.7	92.3±1.5	0.69	87.7±1.9	88.3±1.7	94.7±1.4	0.01	89.2±1.7	92.5±1.7	93±1.5	0.15
Model I[a]	91.7±2	89.5±1.7	90.6±1.7	0.94	87.4±2	88±1.7	95±1.6	0.03	89.3±1.7	92.5±1.7	92.3±1.5	0.29
Model II [b]	91.4±2	89.7±1.6	90±1.7	0.97	86.9±1.9	87.9±1.7	95.4±1.6	0.01	89.3±1.7	92.3±1.7	92.4±1.5	0.25
Systolic Blood Pressure												
Crude	121.6±0.9	123.1±0.8	123.3±0.7	0.55	124.4±0.9	123.8±0.8	120.8±0.7	0.009	120.8±0.8	124.3±0.8	123±0.7	0.051
Model I[a]	120.7±0.9	122.7±0.7	124.4±0.8	0.04	124.3±0.9	123.5±0.8	121.1±0.7	0.07	121±0.8	123.7±0.8	123.1±0.7	0.08
Model II [b]	120.7±0.9	122.8±0.7	124.2±0.8	0.04	124.2±0.9	123.5±0.8	121.2±0.7	0.11	120.9±0.8	123.7±0.8	123.1±0.7	0.07
Diastolic Blood Pressure												
Crude	79.6±0.5	80.7±0.5	80.8±0.4	0.39	81.5±0.5	81.3±0.5	79±0.4	0.001	79.6±0.5	80.8±0.5	80.3±0.4	0.43

Model I[a]	79±0.6	80.5±0.5	81.6±0.5	0.01	81.7±0.6	81.3±0.5	78.7±0.4	0.001	79.6±0.5	80.6±0.5	80.4±0.4	0.49
Model II [b]	79±0.6	80.5±0.5	81.4±0.5	0.02	81.7±0.6	81.3±0.5	78.9±0.4	0.003	79.5±0.5	80.6±0.5	80.4±0.4	0.38
Women												
Waist circumference												
Crude	95±0.4	97.3±0.4	95.7±0.5	0.001	97±0.4	96.4±0.4	95.7±0.5	0.4	95.7±0.4	96.8±0.4	96.6±0.4	0.36
Model I[a]	94.9±0.4	97.2±0.4	96.3±0.6	0.004	96.6±0.4	96.5±0.4	96.1±0.6	0.98	95.8±0.4	96.9±0.4	96.8±0.5	0.22
Model II [b]	95±0.4	96.8±0.3	97±0.5	0.005	96.6±0.3	96.4±0.3	96.4±0.5	0.93	95.6±0.3	96.9±0.3	97±0.4	0.07
Triglycerides												
Crude	131.9±2.9	142.5±3.1	135	0.01	142.7±2.9	140.3±3.1	135.2±3.5	0.42	139.8±3	140.3±3	135.6±3.3	0.55
Model I[a]	128.9±3.2	142.2±3.1	142.1±4	0.009	140.3±3.1	140.5±3	137.8±4.2	0.96	139.7±3	140.8±3	137.1±3.3	0.78
Model II [b]	128.8±3.2	142.1±3.1	143.6±4	0.007	140.4±3.1	140.6±3	138.2±4.2	0.95	139.8±3	141.1±3	137.8±3.3	0.71
HLD-C												
Crude	44.5±0.3	44 ±0.3	43.6±0.3	0.26	43.6±0.3	44.1±0.3	43.2±0.4	0.21	43.1±0.3	44.1±0.3	44.2±0.3	0.02
Model I[a]	44.5±0.3	44±0.3	43.7±0.4	0.26	43.4±0.3	44.1±0.3	43.4±0.4	0.2	43.1±0.3	44.1±0.3	44.3±0.3	0.02
Model II [b]	44.5±0.3	44.1±0.3	43.6±0.4	0.23	43.4±0.3	44.1±0.3	43.4±0.4	0.23	43.1±0.3	44.1±0.3	44.3±0.3	0.03
Fasting Blood glucose												
Crude	89.5±1.3	91.7±1.3	92.7±1.5	0.4	87.6±1.2	89.6±1.3	96.8±1.5	<0.001	88.4±1.3	89.5±1.3	95.6±1.4	0.002
Model I[a]	91.4±1.4	92±1.3	89.9±1.7	0.47	86.4±1.3	89.9±1.3	97.2±1.8	<0.001	88.6±1.3	90.1±1.3	94±1.4	0.006
Model II [b]	91.4±1.4	91.6±1.3	90.1±1.7	0.57	86.6±1.3	89.8±1.3	97.1±1.8	0.001	88.6±1.3	90.3±1.3	94±1.4	0.01
Systolic Blood Pressure												
Crude	121.7±0.7	123.2±0.7	120.8±0.8	0.2	122.7±0.7	122.1±0.7	121.3±0.8	0.77	121.7±0.7	122.8±0.7	121.7±0.8	0.66
Model I[a]	121.9±0.7	123.3±0.7	121.2±0.9	0.08	122.1±0.7	122.3±0.7	121.1±0.9	0.9	121.8±0.7	123.2±0.7	121.9±0.7	0.29
Model II [b]	122.1±0.7	123.2±0.7	121.5±0.9	0.2	122.1±0.7	122.2±0.7	121.5±0.9	0.98	121.7±0.7	123.2±0.6	122±0.7	0.18
Diastolic Blood Pressure												
Crude	78.5±0.4	79.3±0.4	78.7±0.5	0.52	79.5±0.4	79.6±0.4	77.6±0.5	0.02	78.9±0.4	79±0.4	78.8±0.4	0.9
Model I[a]	78.3±0.4	79.4±0.4	79.2±0.6	0.2	79.5±0.4	79.8±0.4	77±0.6	0.01	78.9±0.4	79.2±0.4	78.9±0.4	0.8
Model II [b]	78.4±0.4	79.3±0.4	79.4±0.5	0.32	79.6±0.4	79.7±4	77.2±0.6	0.01	78.8±0.4	79.2±0.4	79±0.4	0.68

a Model I: adjusted for age, energy intake and energy density
b Model II: additionally adjusted for current smoking, job status, education level and physical activity

Table 4 Odds ratio (95 % CI) for Metabolic Syndrome according to quintiles (Q) of nutrient patterns, stratified by gender												
Variables	**First nutrient pattern**				**Second nutrient pattern**				**Third nutrient pattern**			
	Q 1	**Q3**	**Q5**	***p*-trend**	**Q 1**	**Q3**	**Q5**	***p*-trend**	**Q 1**	**Q3**	**Q5**	***p*-trend**
Men												
Crude	1	1. 26(0.94-1.7)	1.35(1.02-1.79)	0.003	1	0.99(0.74-1.34)	0.77(0.58-1.02)	0.057	1	0.79(0.59-1.05)	0.91(0.69-1.19)	0.6
Model I[a]	1	1.27(0.93-1.72)	1.42(1.01-2.01)	0.005	1	0.97(0.72-1.31)	0.66(0.48-0.91)	0.01	1	0.79(0.59-1.05)	0.9(0.69-1.19)	0.53
Model II [b]	1	1.32(0.95-1.82)	1.4(0.97-2.01)	0.008	1	0.99(0.72-1.36)	0.72(0.51-1.01)	0.06	1	0.78(0.57-1.06)	0.94(0.7-1.25)	0.86
Women												
Crude	1	1.23(1-1.51)	0.93(0.75-1.16)	0.77	1	0.94(0.77-1.15)	0.8(0.65-1)	0.08	1	1.23(1-1.51)	0.97(0.78-1.2)	0.91
Model I	1	1.34(1.07-1.66)	1.2(0.9-1.6)	0.04	1	1.06(0.86-1.31)	1.02(0.77-1.36)	0.65	1	1.27(1.03-1.56)	1.04(0.83-1.3)	0.42
Model II	1	1.3(1.03-1.63)	1.22(0.91-1.64)	0.055	1	1.05(0.85-1.31)	1.04(0.78-1.4)	0.6	1	1.3(1.05-1.62)	1.03(0.82-1.3)	0.57

a Model I: adjusted for age, energy intake and energy density
b Model II: additionally adjusted for current smoking, job status, education level and physical activity

New Table based on comment of reviewer. clinical and demographical characteristics of participants based on metabolic syndrome status			
	Metabolic syndrome subjects (n:3300)	**Healthy subjects (n:2464)**	**p-value**
Age (y)	50.1± 7.8 [a]	47.9±8.1	<0.001 [b]
Gender (female) %	47.9	52.1	<0.001
Current smoker (Yes) %	21.8	20.8	<0.39
Weight(kg)	76.4±12.5	69.02±12.05	<0.001
BMI (kg/m^2)	29.9±4.1	26.6±4.4	<0.001
Waist circumference (cm)	101.1±9.7	91.5±11.6	<0.001
Systolic blood pressure(mmHg)	130.3±19.3	116.4±16.9	<0.001
Diastolic blood pressure(mmHg)	84.05±11.5	76.1±11.02	<0.001
LDL(mg/dl)	119.2±36.9	117.4±32.6	0.05
HDL(mg/dl)	38.6±7.6	44.2±10.05	<0.001
Glucose(mg/dl)	101.2±45.2	82.7±25.2	<0.001
Total cholesterol(mg/dl)	197.5±40.2	186.4±36.5	<0.001
Triglyceride(mg/dl)	171 (121-221)	101 (73-129)	<0.001
hs-CRP(mg/dl)	1.9 (0.55-2.45)	1.3 (0.43-1.73)	<0.001
Uric acid (mg/dl)	4.9±1.4	4.4±1.2	<0.001

a Mean±standard deviation (SD)
b Obtained from ANOVA, Chi-square test or Mann-Whitney test, where appropriate