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PII: S0009-9120(17)30131-5
DOI: doi: 10.1016/j.clinbiochem.2017.03.016
Reference: CLB 9506

To appear in: *Clinical Biochemistry*

Received date: 10 February 2017
Revised date: 13 March 2017
Accepted date: 13 March 2017

Please cite this article as: Sayyed Saeid Khayyatzadeh, Seyyed Mohammad Reza Kazemi-Bajestani, Mohammad Bagherniya, Mehraneh Mehramiz, Maryam Tayefi, Mahmoud Ebrahimi, Gordon A. Ferns, Mohammad Safarian, Majid Ghayour-Mobarhan , Serum high C reactive protein concentrations are related to the intake of dietary macronutrients and fiber: Findings from a large representative Persian population sample. The address for the corresponding author was captured as affiliation for all authors. Please check if appropriate. Clb(2016), doi: 10.1016/j.clinbiochem.2017.03.016

Serum high C reactive protein concentrations are related to the intake of dietary macronutrients and fiber: Findings from a large representative Persian population sample

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Running title: dietary intake and hs-CRP levels

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Acknowledgment

This study was approved and founded by Mashhad University of Medical Sciences (MUMS). The authors have no conflict of interest to disclose.

Serum high C reactive protein concentrations are related to the intake of dietary macronutrients and fiber: Findings from a large representative Persian population sample

Abstract

OBJECTIVE: Serum high-sensitivity CRP is a marker of inflammation and an independent predictor of chronic diseases. However, the effect of diet on serum hs-CRP is unclear. The aim of this study was to investigate the relationship between dietary macronutrient intake and serum hs-CRP.

DESIGN AND METHODS: We recruited 9778 adults, aged 35–65 years as part of the MASHAD study. Dietary intake was determined using 24-hour dietary recall and several biochemical parameters including serum hs-CRP were measured. Analysis of covariance was used for assessment of crude and energy-adjusted nutrients across quartiles of serum hs-CRP. To find the association of dietary nutrients intake and serum hs-CRP level, we used logistic regression in different model.

RESULTS: Unadjusted and adjusted multivariate analyses indicate that there was a significant positive association between dietary protein and sodium intake and serum hs-CRP concentrations. There was also a positive association with dietary fat and cholesterol and serum hs-CRP in the adjusted models. There was a significant inverse association between dietary carbohydrate and fiber consumption and serum hs-CRP in both crude and adjusted models.

CONCLUSION: We have found a significant positive association between the dietary intake of fat, protein, cholesterol and sodium and hs-CRP level, and an inverse correlation between dietary carbohydrate and fiber and serum hs-CRP in a large representative Iranian population.

Keywords: hs-CRP; Dietary intake; inflammation; cardiovascular disease, fiber

Introduction

An independent and direct association has been reported between serum inflammatory markers and chronic diseases such as obesity (1), diabetes (2), metabolic syndrome (3) and cardiovascular disease (CVD) (3, 4). C-reactive protein (CRP), is an acute phase protein, and an inflammatory marker, secreted by liver in response to high levels of pro-inflammatory cytokines such as interleukin 6 (IL-6) (5). Serum high-sensitivity CRP (hs-CRP) is an independent predictor of diabetes, metabolic syndrome and CVD (3, 6, 7). Findings of a previous prospective, nested case–control study, within a large population sample of healthy women, showed that among 12 inflammatory factors, hs-CRP was the strongest predictor of CVD risk (8). A strong positive correlation between serum hs-CRP with a marker of oxidative stress has also previously been reported within a Iranian population (9). Kazemi-Bajestani et al reported that serum hs-CRP is an independent predictor of angiographically-defined coronary artery disease (10).
Risk factors such as smoking (11), a high body mass index (BMI), high waist circumferences (12) and low levels of physical inactivity (13) appear to be correlated with serum hs-CRP. However, there is conflicting data for the relationship between dietary intake and the level of serum hs-CRP.

In some previous reports, serum hs-CRP concentrations were associated with dietary intake (14, 15). High intakes of some foods or nutrient such as fruits and vegetables (14), fish and poultry (16), dietary fiber (17), oleic acid (18) were inversely related to serum hs-CRP, while, a direct correlation was found between consumption of red meat (19), trans fat (20) and saturated fat (21) and hs-CRP in other reports. Previous studies, have also reported that there is no significant association between consumption of fiber (22), carbohydrate, protein and total fat, mono unsaturated fatty acid, poly unsaturated fatty acid, cholesterol (21), trans fatty acid (23), eicosapentaenoic acid, docosahexaenoic acid (24) and serum hs-CRP. Taken together it seems that the relationship between dietary intake especially dietary nutrients and serum level of hs-CRP is unclear. To the best of our knowledge, there are very few data investigating the relationship between hs-CRP and dietary intakes in a large population sample of adults without a history of a cardiovascular event, particularly within an Asian population. The current study was carried out to examine the association between dietary macronutrient intake and serum hs-CRP among a representative large adult population in Iran.

Material and Methods

Study participants

This study was conducted in a population sample of 9778 men and women aged between 35-65 years from the Mashhad stroke and heart atherosclerosis disorder (MASHAD) study. The participants were selected from an urban population using a stratified-cluster sampling method. Exclusion criteria included: a history of a cardiovascular event, or surgery, heart failure, cancer, autoimmune diseases and inflammatory diseases; also pregnancy, lactation and dietary supplement use. The demographic and life style data were collected using standard questionnaires and face-to-face interviews. The study design, sample selection and characteristics of study population has been previously published elsewhere (25).

Informed, written consent was provided by all participants. Ethical committee of Mashhad University of medical science approved the protocol of the current study.

Anthropometric and biochemical assessment

Anthropometric measurements including weight, height, and waist and hip circumference were obtained by qualified nurses. Body mass index (BMI) was computed as weight (Kg) divided by height in meters squared. We measured resting blood pressure three times using a standardized protocol. The mean of three recorded measurements was reported as subject's blood pressure. Fasting blood were collected early in morning after a 12 h fast and stored at -80° C. Serum triglycerides, total cholesterol, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), fasting blood glucose and hs-CRP were measured using enzymatic methods (Pars Azmun, Karaj, Iran). The standard protocols of anthropometric and biochemical assessment have been reported previously (25).

Dietary assessment

The dietary intake of participants was assessed by a trained interviewer using a 24-recall method. Dietplan6 software was applied for assessment of nutritional intakes of population (Forestfield Software Ltd., UK). We adjusted the reported dietary intake for total energy; therefore, dietary intakes of participant were presented using two models.

Assessment of metabolic disorders

Metabolic syndrome was defined based on International Diabetes Federation (IDF) (26). Hypertension was defined if subject's blood pressure was equal or more than 140/90 mmHg. The individuals with Fasting blood glucose ≥ 126 mg/dl or under treatment with existing oral hypoglycemic agents and insulin treatment were considered as diabetic. Obesity was defined as a body mass index ≥ 30 kg/m2, and abdominal obesity as waist circumference > 88 cm for women and > 102 cm for men.

Statistical analyses

Statistical analysis was applied using SPSS version 16.0 (SPSS_ Inc., Chicago, IL, USA). We checked normality of data using the Kolomogorov-Smirnov test. Chi-squared analysis was performed to test the distributions of participants in categorical variables across quartiles of serum hs-CRP. To examine significant differences in continuous variables across quartiles of serum hs-CRP, we used covariance analyses (ANCOVA). Subjects in the 1^{st} quartile (lowest level of hs-CRP) were considered as the reference group. ANCOVA was used for the assessment of crude and energy-adjusted nutrients across quartiles of serum hs-CRP. To find the association of dietary nutrients intake and serum hs-CRP level, we used logistic regression in different models. In model I, adjustments were made for age, gender and energy intake. We additionally controlled for current smoking, physical activity levels and body mass index in model II. P values were considered significant at <0.05.

Results

Baseline characteristics of study population

General characteristics of the study participants across quartile categories of hs-CRP levels are shown in Table 1. The median interquartile ranges of hs-CRP were 0.72 (0.59-0.85) mg/L in the first quartile, 1.30 (1.14-1.4) mg/L in the second quartile, 2.29 (1.92-2.81) mg/L and 6.63 (4.61-11.95) mg/L in the third and fourth quartiles, respectively (Table 1). The first quartile of serum hs-CRP categories was considered to be the reference group, in the univariate and multivariate analysis. Forty percent (3911) of the participants were men. The percentage of male participants decreases significantly from the 1st quartile (29.4%) to the 4th quartile (20.8%) of the hs-CRP quartiles ($p<0.001$). The subjects in the first quartile for serum hs-CRP, were significantly younger than other quartiles (46.9±8.2 y 1st vs 47.6±8.2 y 2nd, 48.7±8.1 y 3rd and 49.0±8.3 y in 4th $p<0.001$, Table 1). The mean value of several risk factors include hip and waist circumference, BMI, general and abdominal obesity and metabolic syndrome rose with quartiles (Table 1). Furthermore, current smoking ($p<0.05$) status was significantly higher among 4th quartile of hs-CRP category in compare to the 1st quartile.

hs-CRP levels and dietary intake

The association between the serum hs-CRP concentration and dietary intake is shown in Table 2. There were no significant associations between hs-CRP levels and crude dietary intake of nutrients, although after adjustment for total energy, a significant correlation was found between the dietary intakes of fat, cholesterol, protein and sodium correlated and hs-CRP level ($p<0.01$) (Table 2). Adjusted and unadjusted risks of elevated hs-CRP across dietary intake quartiles are presented in Table 3. The ability of dietary intake of specific macronutrients to predict increase risk of hs-CRP elevation based on quartile distribution was determined using multiple regression models. In comparison to the 1st quartile, intake of protein was positively associated with serum hs-CRP level in 4th quartile in all crude (95% CI1-1.02; $p<0.01$), model I (adjusted for age, sex, energy intake) (95% CI 1.02-1.04; $p<0.001$) and model II (additionally adjusted for current smoking habit, physical activity levels and body mass index) (OR=1.01, 95%CI 1-1.01; $p<0.05$) analysis (Table 3).

Whilst in the unadjusted model, there was no significant association between hs-CRP quartile and dietary fat or cholesterol intake, there were significant positive associations in both adjusted models, for the 3rd and 4th quartiles of cholesterol intake and serum hs-CRP concentration (Table 3). Individuals who consumed more fat were more likely to have higher levels of serum hs-CRP (Table 3). In both unadjusted and adjusted models, there were significant inverse associations between the dietary intake of carbohydrate and fiber and serum hs-CRP concentrations. Individuals in the highest quartile for carbohydrate intake had lower serum hs-CRP concentrations [crude: OR=0.99 (95% CI 0.99-1; $p<0.05$ and model 1) and model II: OR=0.99 (95% CI 0.99-0.99; $p<0.001$)]. Likewise, individuals with higher intakes of fiber had a lower serum hs-CRP level (differences between 1st quartile as a reference and 3th ($p<0.01$) and 4th ($p<0.001$) quartiles of serum hs-CRP were significant different (as shown in Table 3). There was a significant positive association between habitual dietary sodium intake and increasing quartile of hs-CRP levels in all three analyses (crude, model I and model II) (Table 3.).

Discussion

Based on the current study, the consumption of some dietary items were associated with the concentrations of serum hs-CRP in a representative population of Iranian adults. Higher intakes of protein, fat, cholesterol and sodium were positively associated with serum hs-CRP circulation using multivariate analysis. However, our results indicated that higher intakes of carbohydrate and fiber were

associated with lower concentrations of serum hs-CRP. There have been few studies examining the relationship between dietary nutrients and hs-CRP in a large representative population particularly among Asian countries. Adjusted analyses show that there was a significant positive association between intake of fat and cholesterol and serum hs-CRP. A review of experimental data has previously shown that both quantity and quality of fat in diet could affect the postprandial inflammatory response. This study showed that a diet with a higher percentage of saturated fat and higher ratio of n-6 to n-3 poly unsaturated fatty acids are associated with an enhanced inflammatory profile (27). Similarly, the role of saturated and trans fatty acids in increasing hs-CRP circulating has been reported by some of earlier studies (20, 21). A previous study in rats reported that a high fat diet caused a significant increase in serum hs-CRP (28). To explain the relationship between dietary fat and hs-CRP level, it has been suggested that serum IL-6 concentration may increase following a high fat diet (29), and as previously mentioned, IL-6 increases hepatic secretion of hs-CRP (5). With respect to the result found about consumption cholesterol and hs-CRP, it should be noted that a Western type diet, characterized by a high content of fat and cholesterol, increases serum cholesterol (30). This condition leads to an accumulation of cholesterol in immune cells such as macrophages, which increases the inflammatory response (30). In another rodent study, it has been shown that dietary cholesterol leads to hepatic inflammation suggesting dietary cholesterol should be considered as a salient factor of hepatic inflammation (31).

Our results show a positive significant association between protein intake and serum hs-CRP level. It is possible that this relationship is caused by a Western-type dietary pattern which is very common among Iranian population (32-35) and contains high levels of red meat and processed meat (16). A significant relationship between high intake of red and processed meats as a high source of protein and high level of hs-CRP was found by several earlier studies (19, 36). In the previous study conducted in Iran after adjusting for protein intake the significant association between red meat and hs-CRP was attenuated (36) suggesting protein content of red meat might lead to high serum hs-CRP. Nevertheless, results of some previous studies are not in line with our findings related to dietary protein intake and hs-CRP (21, 37), which might be due to differences in the sample size, age, region and ethnic groups applied in these studies. It is worth noting that some sources of protein in the diet such as egg, red meat and full-fat dairy products contain high levels of cholesterol, saturated and trans fatty acids and as we mentioned above high intake of these food items (cholesterol, saturated and trans fatty acids) is accompanied by elevated hs-CRP level, which might be a better explanation for our findings about protein, fat and cholesterol and serum hs-CRP. The positive association between carbohydrate and fiber consumption and hs-CRP level was another finding of the current study. Although findings of some previous studies are not consistent with our results in relation to the association between dietary carbohydrate (21) and fiber (22) with hs-CRP concentration; there is growing evidence showing an inverse relationship between dietary fiber and serum hs-CRP (38-41). The beneficial effect of fiber on serum level of hs-CRP are proposed to be related to weight reduction, modifying the secretion, turnover or metabolism of insulin and glycemic control, or alterations in serum adiponectin, interleukin-6, free fatty acids and triglycerides (38, 42, 43). A previous clinical trial study proposed that ad libitum low-fat, high-carbohydrate intake lead to weight loss and decreased hs-CRP significantly (44). It appears that a high carbohydrate diet especially when fat is replaced by high quality carbohydrate diet, which contains large

amounts of fibers, may result in favorable change in hs-CRP level. These results support the potential importance of high dietary fibers to prevent several chronic diseases including diabetes, metabolic syndrome and cardiovascular disease.

We also found a positive association between dietary sodium intake and hs-CRP values. As previously suggested, the possible mechanisms of sodium in enhancing the inflammatory response might be attributed to direct role of sodium in stimulation the gene expression of several inflammatory factors (45, 46). In line with our finding, a previous observational study found that there was an association between sodium intake and serum CRP which may influenced by BMI (47). Zhu et.al, investigated the association between habitual sodium intake and inflammatory status and reported a significant direct association between higher sodium intake and adipocyte dysfunction and inflammation among adolescents (48). However, there are few data investigating dietary sodium intake and hs-CRP level in a large healthy population.

This study had some limitations. First of all, this is a cross-sectional study. Like other studies with this design, it is not possible to imply causation from the data on associations. A self-measured questionnaire was used to obtain dietary intakes of the study participants, which may lead to reporting bias. Finally, 24-hour recalls were used to obtain dietary intakes, which relies on memory and under-reporting, or over reporting of some dietary data may lead to inaccuracies, although this method has been widely applied.

Conclusion

We have found a significant positive association between macronutrient intake of fat and protein, as well as a habitual high sodium dietary intake and elevated concentrations of serum hs-CRP. Furthermore, we found an inverse relationship between consumption of carbohydrate and fiber and serum hs-CRP in a large representative Iranian adult population, suggesting that through manipulating diet, serum level of hs-CRP as one the most well-known inflammatory biomarker, might be modified. In future, further studies, particularly longitudinal intervention studies may be required.

References:

1. Ramos EJ, Xu Y, Romanova I, Middleton F, Chen C, Quinn R, et al. Is obesity an inflammatory disease? Surgery. 2003;134(2):329-35.
2. Jung UJ, Choi M-S. Obesity and its metabolic complications: the role of adipokines and the relationship between obesity, inflammation, insulin resistance, dyslipidemia and nonalcoholic fatty liver disease. International journal of molecular sciences. 2014;15(4):6184-223.
3. Haffner SM. The metabolic syndrome: inflammation, diabetes mellitus, and cardiovascular disease. The American journal of cardiology. 2006;97(2):3-11.
4. Theuma P, Fonseca VA. Inflammation and emerging risk factors in diabetes mellitus and atherosclerosis. Current diabetes reports. 2003;3(3):248-54.
5. Pepys MB, Hirschfield GM. C-reactive protein: a critical update. The Journal of clinical investigation. 2003;111(12):1805-12.
6. Ridker PM. High-sensitivity C-reactive protein potential adjunct for global risk assessment in the primary prevention of cardiovascular disease. Circulation. 2001;103(13):1813-8.
7. Ridker PM. Clinical application of C-reactive protein for cardiovascular disease detection and prevention. Circulation. 2003;107(3):363-9.
8. Ridker PM, Hennekens CH, Buring JE, Rifai N. C-reactive protein and other markers of inflammation in the prediction of cardiovascular disease in women. New England Journal of Medicine. 2000;342(12):836-43.
9. Razavi A, Baghshani MR, Rahsepar AA, Ardabili HM, Andalibi MSS, Parizadeh SMR, et al. Association between C-reactive protein, pro-oxidant–antioxidant balance and traditional cardiovascular risk factors in an Iranian population. Annals of clinical biochemistry. 2013;50(2):115-21.
10. Kazemi-Bajestani S, Azarpazhooh M, Ebrahimi M, Vedadian P, Esmaeili H, Parizadeh S, et al. Serum high sensitivity CRP concentrations predict the presence of carotid artery plaque in individuals without a history of cardiovascular events. Nutrition, metabolism, and cardiovascular diseases: NMCD. 2015;25(4):434.
11. Bermudez EA, Rifai N, Buring JE, Manson JE, Ridker PM. Relation between markers of systemic vascular inflammation and smoking in women. American Journal of Cardiology. 2002;89(9):1117-9.
12. Huffman FG, Whisner S, Zarini GG, Nath S. Waist circumference and BMI in relation to serum high sensitivity C-reactive protein (hs-CRP) in Cuban Americans with and without type 2 diabetes. International journal of environmental research and public health. 2010;7(3):842-52.
13. Yu Z, Ye X, Wang J, Qi Q, Franco OH, Rennie KL, et al. Associations of physical activity with inflammatory factors, adipocytokines, and metabolic syndrome in middle-aged and older chinese people. Circulation. 2009;119(23):2969-77.
14. Ko A, Kim H, Han C-J, Kim J-M, Chung H-W, Chang N. Association between high sensitivity C-reactive protein and dietary intake in Vietnamese young women. Nutrition research and practice. 2014;8(4):445-52.
15. Galland L. Diet and inflammation. Nutrition in Clinical Practice. 2010;25(6):634-40.
16. Lopez-Garcia E, Schulze MB, Fung TT, Meigs JB, Rifai N, Manson JE, et al. Major dietary patterns are related to plasma concentrations of markers of inflammation and endothelial dysfunction. The American journal of clinical nutrition. 2004;80(4):1029-35.
17. Ma Y, Griffith JA, Chasan-Taber L, Olendzki BC, Jackson E, Stanek EJ, et al. Association between dietary fiber and serum C-reactive protein. The American journal of clinical nutrition. 2006;83(4):760-6.
18. Yoneyama S, Miura K, Sasaki S, Yoshita K, Morikawa Y, Ishizaki M, et al. Dietary intake of fatty acids and serum C-reactive protein in Japanese. Journal of epidemiology. 2007;17(3):86-92.

19. Montonen J, Boeing H, Fritsche A, Schleicher E, Joost H-G, Schulze MB, et al. Consumption of red meat and whole-grain bread in relation to biomarkers of obesity, inflammation, glucose metabolism and oxidative stress. European journal of nutrition. 2013;52(1):337-45.
20. Lopez-Garcia E, Schulze MB, Meigs JB, Manson JE, Rifai N, Stampfer MJ, et al. Consumption of trans fatty acids is related to plasma biomarkers of inflammation and endothelial dysfunction. The Journal of nutrition. 2005;135(3):562-6.
21. Arya S, Isharwal S, Misra A, Pandey RM, Rastogi K, Vikram NK, et al. C-reactive protein and dietary nutrients in urban Asian Indian adolescents and young adults. Nutrition. 2006;22(9):865-71.
22. Ma Y, Hébert JR, Li W, Bertone-Johnson ER, Olendzki B, Pagoto SL, et al. Association between dietary fiber and markers of systemic inflammation in the Women's Health Initiative Observational Study. Nutrition. 2008;24(10):941-9.
23. Mozaffarian D, Pischon T, Hankinson SE, Rifai N, Joshipura K, Willett WC, et al. Dietary intake of trans fatty acids and systemic inflammation in women. The American journal of clinical nutrition. 2004;79(4):606-12.
24. Poudel-Tandukar K, Nanri A, Matsushita Y, Sasaki S, Ohta M, Sato M, et al. Dietary intakes of α-linolenic and linoleic acids are inversely associated with serum C-reactive protein levels among Japanese men. Nutrition research. 2009;29(6):363-70.
25. Ghayour-Mobarhan M, Moohebati M, Esmaily H, Ebrahimi M, Parizadeh SMR, Heidari-Bakavoli AR, et al. Mashhad stroke and heart atherosclerotic disorder (MASHAD) study: design, baseline characteristics and 10-year cardiovascular risk estimation. International journal of public health. 2015:1-12.
26. Ebrahimi M, Kazemi-Bajestani SMR, Ghayour-Mobarhan M, Moohebati M, Paydar R, Azimi-Nezhad M, et al. Metabolic syndrome may not be a good predictor of coronary artery disease in the Iranian population: population-specific definitions are required. The Scientific World Journal. 2009;9:86-96.
27. Margioris AN. Fatty acids and postprandial inflammation. Current Opinion in Clinical Nutrition & Metabolic Care. 2009;12(2):129-37.
28. Ibrahim IAAE-H, El-Aziz MFMA, Ahmed AF, Mohamed MAE-A. Is the effect of high fat diet on lipid and carbohydrate metabolism related to inflammation? Mediterranean Journal of Nutrition and Metabolism. 2011;4(3):203-9.
29. Lundman P, Boquist S, Samnegård A, Bennermo M, Held C, Ericsson C-G, et al. A high-fat meal is accompanied by increased plasma interleukin-6 concentrations. Nutrition, Metabolism and Cardiovascular Diseases. 2007;17(3):195-202.
30. Tall AR, Yvan-Charvet L. Cholesterol, inflammation and innate immunity. Nature Reviews Immunology. 2015;15(2):104-16.
31. Wouters K, van Gorp PJ, Bieghs V, Gijbels MJ, Duimel H, Lütjohann D, et al. Dietary cholesterol, rather than liver steatosis, leads to hepatic inflammation in hyperlipidemic mouse models of nonalcoholic steatohepatitis. Hepatology. 2008;48(2):474-86.
32. Esmaillzadeh A, Kimiagar M, Mehrabi Y, Azadbakht L, Hu FB, Willett WC. Dietary patterns, insulin resistance, and prevalence of the metabolic syndrome in women. The American journal of clinical nutrition. 2007;85(3):910-8.
33. Esmaillzadeh A, Azadbakht L. Major dietary patterns in relation to general obesity and central adiposity among Iranian women. The Journal of nutrition. 2008;138(2):358-63.
34. Esmaillzadeh A, Kimiagar M, Mehrabi Y, Azadbakht L, Hu FB, Willett WC. Dietary patterns and markers of systemic inflammation among Iranian women. The Journal of nutrition. 2007;137(4):992-8.
35. Esmaillzadeh A, Azadbakht L. Food intake patterns may explain the high prevalence of cardiovascular risk factors among Iranian women. The Journal of nutrition. 2008;138(8):1469-75.

36. Azadbakht L, Esmaillzadeh A. Red meat intake is associated with metabolic syndrome and the plasma C-reactive protein concentration in women. The Journal of nutrition. 2009;139(2):335-9.
37. King DE, Egan BM, Geesey ME. Relation of dietary fat and fiber to elevation of C-reactive protein. Am J Cardiol. 2003;92(11):1335-9.
38. North C, Venter C, Jerling J. The effects of dietary fibre on C-reactive protein, an inflammation marker predicting cardiovascular disease. European journal of clinical nutrition. 2009;63(8):921-33.
39. King DE, Egan BM, Woolson RF, Mainous AG, Al-Solaiman Y, Jesri A. Effect of a high-fiber diet vs a fiber-supplemented diet on C-reactive protein level. Archives of Internal Medicine. 2007;167(5):502-6.
40. Bo S, Durazzo M, Guidi S, Carello M, Sacerdote C, Silli B, et al. Dietary magnesium and fiber intakes and inflammatory and metabolic indicators in middle-aged subjects from a population-based cohort. The American journal of clinical nutrition. 2006;84(5):1062-9.
41. Ajani UA, Ford ES, Mokdad AH. Dietary fiber and C-reactive protein: findings from national health and nutrition examination survey data. The Journal of nutrition. 2004;134(5):1181-5.
42. Qi L, Van Dam RM, Liu S, Franz M, Mantzoros C, Hu FB. Whole-grain, bran, and cereal fiber intakes and markers of systemic inflammation in diabetic women. Diabetes care. 2006;29(2):207-11.
43. Liu S, Manson JE, Buring JE, Stampfer MJ, Willett WC, Ridker PM. Relation between a diet with a high glycemic load and plasma concentrations of high-sensitivity C-reactive protein in middle-aged women. The American journal of clinical nutrition. 2002;75(3):492-8.
44. Kasim-Karakas SE, Tsodikov A, Singh U, Jialal I. Responses of inflammatory markers to a low-fat, high-carbohydrate diet: effects of energy intake. The American journal of clinical nutrition. 2006;83(4):774-9.
45. Telini LSR, de Carvalho Beduschi G, Caramori JCT, Castro JH, Martin LC, Barretti P. Effect of dietary sodium restriction on body water, blood pressure, and inflammation in hemodialysis patients: a prospective randomized controlled study. International urology and nephrology. 2014;46(1):91-7.
46. Dinarello CA, editor Hyperosmolar sodium chloride, p38 mitogen activated protein and cytokine-mediated inflammation. Seminars in dialysis; 2008.
47. Fogarty AW, Lewis SA, McKeever TM, Britton JR. Is higher sodium intake associated with elevated systemic inflammation? A population-based study. The American journal of clinical nutrition. 2009;89(6):1901-4.
48. Zhu H, Pollock NK, Kotak I, Gutin B, Wang X, Bhagatwala J, et al. Dietary sodium, adiposity, and inflammation in healthy adolescents. Pediatrics. 2014;133(3):e635-e42.

Table 1. Demographic and biochemical characteristics of individuals by quartile of serum hs-CRP concentration				
	1st quartile (N=2446) 0.72(0.59-0.85) mg/l	**2nd quartile (N=2463) 1.30(1.14-1.4) mg/l**	**3rd quartile (N=2427) 2.29(1.92-2.81) mg/l**	**4th quartile (N=2442) 6.63(4.61-11.95) mg/l**
Age(y)	46.9±8.2	47.6±8.2	48.7±8.1	49.0±8.3***
Gender (male) (%)	1149 (29.4%)	1058 (27.1%)	890 (22.8%)	814 (20.8%) ***
Current smoking (%)	475 (22.6%)	544 (25.9%)	534 (25.5%)	545 (26.0%)*
Physical activity (PAL)	1.59±0.27	1.57±0.28	1.57±0.27	1.58±0.29
Hip circumference (cm)	100.6±7.8	102.8±8.5	104.9±9.08	106.5±10.5***
Body mass index (kg/m^2)	26.0±4.1	27.2±4.3	28.7±4.4	29.8±5.2***
Waist Circumference (cm)	90.7±10.9	94.7±11.1	96.9±11.7	98.6±12.8***
General obesity (%)	777 (35.6%)	1067 (48.4%)	1257 (58.5%)	1396 (63.6%)***
Abdominal obesity (%)	1358 (62.1%)	1649 (74.7%)	1736 (80.7%)	1803 (82%)***
Metabolic syndrome (%)	634 (16.7%)	862 (22.7%)	1085 (28.5%)	1220 (32.1%) ***

Values expressed as mean ± SD for variables with normal distribution, and median and interquartile rang for non-normally distributed data.

*p<0.05, **p<0.01, ***p<0.001

General obesity was defined as body mass index ≥ 30 kg/m2, and abdominal obesity as waist circumference > 102 cm for men and >88 cm for women.

Table 2. Nutrient intake across quartiles for serum hs-CRP concentration				
	quartiles for serum hs-CRP			
	Q1	**Q2**	**Q3**	**Q4**
Energy (Kcal/day)	2061±627	2034±618	2011±608	2037±617
Fat (g/day)				
Crude	78±31.4	77.6±31.9	76.8±30.6	78.8±31.07
Energy adjusted	38.2±10.3	38.5±10.6	38.5±10.2	39.3±10.4**
SFA (g/day)				
Crude	20.4±8.7	20.04±8.6	20.1±8.6	20.4±8.9
Energy adjusted	10.2±3.4	10.1±3.3	10.3±3.5	10.2±3.4
PUFA (g/day)				
Crude	26.8±13.5	26.6±14.04	26.4±13.5	27.1±14.1
Energy adjusted	13.3±5.6	13.4±5.9	13.4±5.7	13.6±5.9
MUFA (g/day)				
Crude	20.9±8.8	20.6±9.1	20.4±8.6	21.2±9.1
Energy adjusted	10.4±3.1	10.3±3.2	10.4±3.1	10.6±3.3
Trans fat (mg/day)				
Crude	0.98±0.63	0.96±0.61	0.96±0.61	0.99±0.61
Energy adjusted	0.49±0.28	0.48±0.28	0.49±0.28	0.50±0.27
Cholesterol (mg/day)				
Crude	241.1±164	238.9±163.2	243.7±163.8	247.9±159.9
Energy adjusted	119.1±77.6	120.1±78.7	124.4±82.5	125.6±78.3**
Carbohydrate (g/day)				
Crude	267.6±88	263.2±87.4	261.5±87.6	260.2±90.6
Energy adjusted	133±26.3	132.1±26.9	132.2±25.9	129.5±26.8**
Dietary fiber (g/day)				
Crude	19.1±9.8	18.8±9.7	18.4±9.8	18.2±10.05
Energy adjusted	9.6±4.4	9.7±4.7	9.3±4.2	9.2±4.4**
Protein (g/day)				
Crude	76.1±28.5	76.4±28.3	75.2±27.7	77.1±28.2
Energy adjusted	37.3±9.3	37.9±9.3	37.9±9.3	38.5±10**
Potassium (mg/day)				
Crude	3087±1145	3064±1152	3066±1183	3103±1217
Energy adjusted	1554±477	1564±488	1566±474	1559±482
Sodium (mg/day)				
Crude	2608±2173	2531±2051	2693±2421	2793±2448
Energy adjusted	1266±975	1242±924	1319±1054	1372±1113**
Calcium (mg/day)				
Crude	918±398	901±389	915±396	905±409
Energy adjusted	462±174	461±172	461±177	458±178
Magnesium (mg/day)				
Crude	266±104	267±110	265±109	269±114
Energy adjusted	134±42	136±46	135±42	135±43
Selenium (mg/day)				

Crude	38.4±21.9	39.6±22.7	38.01±21.3	38.8±22.06
Energy adjusted	19.4±10.7	20.4±11.5	19.5±10.3	19.9±10.9
Copper (mg/day)				
Crude	1.29±0.59	1.3±0.6	1.29±0.59	1.31±0.66
Energy adjusted	0.64±0.23	0.66±0.23	0.65±0.22	0.65±0.27
Folate (µg/day)				
Crude	260±118	262±118	260±117	260±124
Energy adjusted	129±57	130±56	129±55	129±55
Vitamin C (mg/day)				
Crude	94.3±76.4	91.9±77.6	93.8±79.9	94.9±81.7
Energy adjusted	47.9±39.5	47.6±41.5	48.9±42.9	48.5±42.3
Vitamin E (mg/day)				
Crude	23.2±12.2	23.4±13.5	21.9±11.9	22.5±13.4
Energy adjusted	10.5±4.8	10.7±5.6	10.1±4.7	10.4±5.5
Vitamin D (µg/day)				
Crude	1.42±1.1	1.39±1.13	1.36±1.08	1.39±1.07
Energy adjusted	0.7±0.54	0.69±0.55	0.69±0.56	0.69±0.5
Carotene (µg/day)				
Crude	2407±2503	2202±2410	2342±2494	2366±2621
Energy adjusted	1219±1266	1140±1231	1203±1263	1191±1318
SFA: Saturated fatty acid MUFA: Mono unsaturated fatty acid PUFA: Poly unsaturated fatty acid *p<0.05 *p<0.05, **p<0.01, ***p<0.001				

Table 3. Multivariate odds ratio for serum hs-CRP quartiles of dietary intakes				
	hs-CRP			
	1	2	3	4
Protein(g)				
Crude	1	1 (0.99-1.00)	0.99 (0.99-1.00)	1.01 (1.00-1.02)**
Model I	1	1.01 (1.00-1.02)	1.003 (0.99-1.007)	1.03(1.02-1.04)***
Model II	1	1.00 (1.00-1.01)	1.00 (0.99-1.01)	1.01 (1.00-1.01)*
Fat(g)				
Crude	1	1 (0.99-1.00)	0.99 (0.99-1.00)	1 (0.99-1.00)
Model I	1	1 (0.99-1.00)	1 (0.99-1.01)	1.01 (1.00-1.01)**
Model II	1	1.00 (0.99-1.01)	1.00 (0.99-1.01)	1.01 (1.00-1.02)**
Cholesterol (mg)				
Crude	1	1 (0.99-1.00)	1 (1.00-1.00)	1 (1.00-1.00)
Model I	1	1 (0.99-1.00)	1.001 (1.00-1.002)**	1.001 (1.00-1.002)**
Model II	1	1 (1.00-1.00)	1.001 (1.00-1.002)**	1.002 (1.00-1.003)**
Carbohydrate(g)				
Crude	1	0.99 (0.99-1.00)	0.99 (0.99-1.00)	0.99 (0.99-1.00)*
Model I	1	0.99 (0.99-1.00)	0.99 (0.99-1.00)	0.99 (0.99-0.99)***
Model II	1	0.99 (0.99-1.00)	0.99 (0.99-1.00)	0.99 (0.99-0.99)***
Fiber(g)				
Crude	1	0.99 (0.98-1.00)	0.99 (0.98-1.00)*	0.99 (0.98-0.99)*
Model I	1	0.99 (0.98-1.01)	0.97 (0.96-0.99)*	0.97 (0.95-0.98)**
Model II	1	0.99 (0.98-1.01)	0.97 (0.95-0.99)*	0.96 (0.94-0.98)**
Sodium (mg)				
Crude	1	1 (1.00-1.00)	1 (1.00-1.00)	1.01 (1.00-1.00)*
Model I	1	1 (1.00-1.00)	1 (1.00-1.00)	1.01 (1.00-1.00)*
Model II	1	1 (1.00-1.00)	1 (1.00-1.00)	1.01 (1.00-1.00)*

a Model I: Adjusted for age, sex, energy intake
b Model II: Additionally, adjusted for current smoking, physical activity levels and body mass index
* p<0.05, **p<0.01, ***p<0.001

Highlights

The study included 9778 adults aged 35-65 years

Greater prevalence of metabolic syndrome, general and abdominal obesity in subjects with higher serum hs-CRP level

A significant positive association between the dietary intakes of fat, protein, cholesterol and sodium with hs-CRP level

An inverse correlation between dietary carbohydrate and fiber with serum hs-CRP level