Original Article

Association of dietary fiber with high sensitivity C-reactive proteinin type 2 diabetes mellitus

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Abstract:

Introduction: Hs-CRP is a nonspecific marker of the inflammatory response has been associated with development of type 2 diabetes mellitus. Cardiovascular disease is a major consequence of diabetes. DM confers a 2-4 fold rise in cardiovascular risk compared with general population. One of the many modifiable risk factors for both cardiovascular disease and diabetes is diet. Fiber is an important dietary factor that may modify the risk of both diseases. *Material & methods*: The current study is an attempt to explore the association of dietary fiber on inflammatory marker, hs-CRP in type2 diabetic subjects. Total 80 diabetic subjects were included in this study of which 40 were taking more dietary fiber and 40 were taking relatively low dietary fiber. Serum hs-CRP was measured by chemiluminescent immunometric assay (DPC Biermann Gmbh., Germany). Nutrient information was calculated using a pretested food recall questionnaire prepared by nutritionists for usual Bangladeshi food articles. *Results:* Hs-CRP was significantly higher in subjects taking low dietary fiber. *Conclusion:* So, low dietary fiber consumption maybe a possible causal factor of raised CRP. Type 2 diabetic patients who took less dietary fiber in their diets had elevated blood CRP levels.

Key words: Hs-CRP: High sensitivity C- reactive protein, Dietary fiber, T2DM: Type 2 Diabetes Mellitus.

Introduction

Diabetes mellitus is a fast expanding global health problem. Hs-CRP is a nonspecific marker of the inflammatory response has been associated with development of type 2 diabetes mellitus. In type 2 diabetes mellitus increased hs- CRP was found¹. Cardiovascular disease is a major consequence of diabetes. DM confers a 2-4 fold rise in cardiovascular risk compared with general population². Further more cardiovascular morbidity and mortality is increase in patients with elevated CRP levels³. Creactive protein (CRP) is a marker of inflammation recently recognized as an independent predictor of future coronary heart disease^{+*}. Based on data from the 1988 to 1994 third National Health and Nutrition Examination Survey (NHANES III), the prevalence of elevated CRP concentrations (>3.0 mg/L) was 13.7% for men and 27.3% for women'. Lifestyle factors that influence CRP concentrations may provide an important intervention opportunity to reduce

the risk of cardiovascular disease, diabetes, and their complications. One of the many modifiable risk factors for both cardiovascular disease and diabetes is diet. Fiber is an important dietary factor that may modify the risk of both diseases¹⁰⁻¹⁴. Dietary fiber intake is associated with decreased oxidation of lipids, which in turn is associated with decreased inflammation". It has been postulated that a lowfiber diet with highly refined carbohydrates can contribute to hyperglycemia, which increases the proinflammatory cytokines plasma interleukin (IL) 6 (IL-6), tumor necrosis factor?, and IL- 18^{16} . IL-6 is a primary determinant of CRP production; thus, consistently elevated concentrations of IL-6 might result in elevated CRP concentrations. Again, chronic low grade inflammation in diabetes is associated with the dietary pattern. On the contrary, in a cross-sectional study among British population¹, a dietary pattern characterized by high intake of fruits and vegetables was inversely associated with features of metabolic

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syndrome. We already know some benefits of dietary fibers to human health. It seems that the ingestion of fibers also brings benefits in inflammatory processes¹⁸⁻²⁰ that have been associated with chronic disorders such as the metabolic syndrome (MS), obesity, type² *diabetes mellitus* (T2DM), cancer and cardiovascular diseases (CVD)^{21,22}. The current study was an attempt to explore the association of dietary fiber on inflammatory marker, hs-CRP in type 2 diabetic subjects. The objective of the study was to find out the influence of diet in CRP level in type 2 diabetes mellitus.

Materials and Methods: Bangladeshi subjects were selected purposively from the Out-Patient Department (OPD) of BIRDEM. Type 2 diabetes mellitus was diagnosed based on the criteria of WHO (defined as fasting blood glucose ? 7.0 mmol/L (126 mg/dl) 2-h postprandial glucose ? 11.1 mmol/L (200 mg/dl). Informed written consent was taken from each subject. With all aseptic precaution, fasting venous blood (6 ml) was taken from each subject. The sera of selected subjects were aliquoted and kept frozen at -70°C until analysis. Serum hs-CRP was assayed by chemiluminescent immunometric method (DPC Biermann Gmbh., Germany). Nutrient information was calculated using a pretested food recall questionnaire prepared by nutritionists for usual Bangladeshi food articles. The consumption was recorded on a weekly, monthly and more than a month basis. Data analysis of the dietary

parameters was carried out using software developed and previously used in the research studies using standard nutrients values of Bangladeshi foods. Dietary history was taken by means of dietary recall. Here a questionnaire, prepared by the nutritionists was introduced which dealt with dietary habits, frequency of eating and type of cooking medium. The consumptions of carbohydrate, protein, fat and dietary fiber were recorded on a daily, weekly and monthly basis. Dietary parameters were analyzed by special software. Statistical analysis was done by SPSS (version 12). All the data were expressed as mean \pm SD (standard deviation), median (range) as appropriate. The statistical significance of differences between the values were assessed by t-test and Mann-Whitney u-test (as appropriate). Correlation was also analyzed among the parameters. A two-tailed *p*-value of <0.05 was considered statistically significant.

The Research Prol The research protocol was approved by 'Ethics Committee' of BIRDEM.

Results and observations: A total 80 diabetic subjects were included in this study of which 40 were taking more dietary fiber and 40 were taking relatively low dietary fiber. In Tables I and II, hs-CRP was significantly (p=0.000) higher in subjects taking low dietary fiber. There was significant negative correlation found between CRP of subjects taking high, and low intakes of dietary fiber.

Variable	Patient taking high fiber (n = 40)	Patient taking low fiber (n = 40)	t/p value
CRP (mg/l)	7.3 ± 8.6	17.4 ± 20	12.621/0.000
T. Calorie (Kcal/d)	3877 ± 1499	4543 ± 1411	2.047/0.044
Carbohydrate (gm/d)	272 ± 83.7	307± 62.9	2.138/0.036
Protein (gm/d)	74.6 ± 23.8	83.5± 23.7	1.677/0.097
Fat (gm/d)	322 ± 138	379 ± 111	2.027/0.046
Dictary Fiber (gm/d)	16.8 ± 3.7	7.1±3	12.627/0.000

Table I: Composition of Dietary Intakes of the study subjects.

Results were expressed as Mean \pm SD as appropriate t-test was performed as the test of significance at 5% level of significance level. n = number of subjects

Variable	Patients taking	Patients taking	z/p value
	high fiber (n - 40)	low fiber (n - 40)	_
CRP (mg/dl)	4.4 (1.2-49.4)	12.4 (2.4-127)	4.735/0.000
T. calorie (Kcal/d)	3568 (1597-8675)	4320 (2349-7765)	2.440/0.015
CHO (gm/d)	235 (132-443)	324 (178-420)	2.084/0.037
Protein (gm/d)	75(30-120)	85 (32-176)	1.401/0.161
Fat (gm/d)	324 (80-620)	358 (213-654)	1.699/0.089
Dietary fiber (gm/d)	16.4(2.8-25)	6.8 (3-16.4)	7.108/0.000

Results are expressed as median (range); Mann- Whitney 'u' test was performed as the test of significance at 5% significance level. n = number of subjects

 Variables
 r value
 p value

 High and low intake of dietary fiber
 -0.533***
 0.000

 T. caloric
 0.185
 0.100

0.108

0.259*

0.339

0.021

Table III: Relation of CRP with different parameters of the study subjects

Fat 0.099 0.382 Results were expressed as correlation coefficient (Spearman rho) r values;



CHO

Protein



Discussion: Hs- CRP is now well accepted as a maker for chronic subclinical inflammation and is raised in diabetic subjects. Among the carbohydrates the dietary fiber are claimed to have a unique role in determining insulin secretion or sensitivity. The role of high fiber carbohydrates in influencing insulin sensitivity in randomized feeding studies is found to

References:

- Duncan BB, Schmidt MI, Pankow JS, Ballantyne CM, Couper D, Vigo A, Hoogeveen R, Folsom AR, Heiss G. Low-grade systemic inflammation and the development of type 2 diabetes: the Atherosclerosis Risk in Communities study. *Diabetes* 2003; **52**:1799 –1805.<u>http://dx.doi.org/10.2337/diabetes.52.7.1799</u> PMid:12829649
- 2. American Heart Association. Heart disease and stroke statistical update. Dallas,TX. American Heart Association 2004.
- 3 Ridker PM, Buring JE, Cook NR, Rifai N. C-reactive protein, the metabolic syndrome, and risk of incident cardiovascular events: an 8-year follow-up of 14719 initially healthy American Women. *Circulation* 2003;

be inconsistent also. Our hypothesis was that persons consuming higher amount of dietary fiber would have lower concentrations of CRP. In addition, this study provides evidence that dietary fiber is associated with CRP concentrations. The mechanism between dietary fiber and inflammation is unclear. In a recent review article¹⁰, King suggested that dietary fiber decreases lipid oxidation, which in turn is associated with decreased inflammation. Normal bowel flora also contributes to a healthy intestinal environment, which helps to prevent inflammation¹⁰. The antiinflammatory effects of fiber are intriguing, because prior work had focused on the ability of fiber to reduce other substances that cause inflammation (eg, the inhibition of hyperglycemia and its effects on lipids, particularly LDL cholesterol).

The relation of dietary patterns and CRP have been explored in some other studies^{16,23}. In conclusion, this study provides important information about the relation between dietary fiber and CRP. Increased consumption of dietary fiber appears to be strongly associated with lower CRP concentrations and vice versa.

Conclusion: The study revealed that CRP, an inflammatory marker, in type 2 diabetic subjects is significantly more in subjects taking less dietary fiber compared to diabetic subjects taking more dietary fiber. This dietary fiber maybe is the possible causal factor of raised inflammatory marker more in diabetic patients who are taking less dietary fiber.

107:391-397.<u>http://dx.doi.org/10.1161/</u> 01.CIR.0000055014.62083.05PMid:12551861

- Ridker PM, Buring JE, Shih J, Matias M, Hennekens CH. Prospective study of C-reactive protein and the risk of future cardiovascular events among apparently healthy women. *Circulation* 1998;98:731–3. PMid:9727541
- Koenig W, Sund M, Frohlich M, et al. C-reactive protein, a sensitive marker of inflammation, predicts future risk of coronary heart disease in initially healthy middle-aged men: results from the MONICA (Monitoring Trends and Determinants in Cardiovascular Disease) Augsburg Cohort Study, 1984 to 1992. *Circulation* 1999;**99**:237–242. PMid:9892589

- Ridker PM, Hennekens CH, Buring JE, Rifai N. Creactive protein and other markers of inflammation in the prediction of cardiovascular disease in women. *N Engl J Med* 2000;**342**:836–843. <u>http://dx.doi.org/ 10.1056/NEJM200003233421202</u>PMid:10733371
- Rutter MK, Meigs JB, Sullivan LM, D'Agostino RB Sr, Wilson PW. C-reactive protein, the metabolic syndrome, and prediction of cardiovascular events in the Framingham Offspring Study. *Circulation* 2004; 110:380 –385. <u>http://dx.doi.org/10.1161/01.</u> <u>CIR.0000136581.59584.0E</u> PMid:15262834
- Sattar N, Gaw A, Scherbakova O, et al. Metabolic syndrome with and without C-reactive protein as a predictor of coronary heart disease and diabetes in the West of Scotland Coronary Prevention Study. *Circulation* 2003;**108**:414 –419.<u>http://dx.doi.org/ 10.1161/01.CIR.0000080897.52664.94</u> PMid:12860911
- Ford DE, Erlinger TP. Depression and C-reactive protein in US adults:data from the Third National Health and Nutrition Examination Survey. Arch Intern Med 2004;164:1010–1014.<u>http://dx.doi.org/10.1001/archinte.164.9.1010</u>PMid:15136311
- 10. King DE. Dietary fiber, inflammation, and cardiovascular disease. *Mol Nutr Food Res* 2005;**49**:594–600. http://dx.doi.org/10.1002/mnfr.200400112
- Liu S, Buring JE, Sesso HD, Rimm EB, Willett WC, Manson JE. A prospective study of dietary fiber intake and risk of cardiovascular disease among women. J Am Coll Cardiol 2002;39:49 –56. http://dx.doi.org/10.1016/S0735-1097(01)01695-3
- 12. Pereira MA, O'Reilly E, Augustsson K, et al. Dietary fiber and risk of coronary heart disease: a pooled analysis of cohort studies. *Arch Intern Med* 2004;**164**:370–376.<u>http://dx.doi.org/10.1001/arch-inte.164.4.370</u>PMid:14980987
- 13. Liu S. Whole-grain foods, dietary fiber, and type 2 diabetes: searching for a kernel of truth. *Am J Clin Nutr* 2003;**77**:527–529.PMid:12600838
- 14. Stevens J, Ahn K, Juhaeri, Houston D, Steffan L, Couper D. Dietary fiber intake and glycemic index and incidence of diabetes in African- American and white adults: the ARIC study. *Diabetes Care* 2002;25:1715–1721.<u>http://dx.doi.org/10.2337/</u> diacare.25.10.1715PMid:12351467

- Ajani UA, Ford ES, Mokdad AH. Dietary fiber and C-reactive protein: findings from national health and nutrition examination survey data. J Nutr2004;134:1181–1185.PMid:15113967
- 16. Esposito K, Marfella R, Ciotola M, et al. Effect of a Mediterraneanstyle diet on endothelial dysfunction and markers of vascular inflammation in the metabolic syndrome: a randomized trial. *JAMA* 2004;
 292:1440 1446.<u>http://dx.doi.org/10.1001/jama.292.12.1440</u> PMid:15383514
- Williams DE, Prevost AT, Whichelow MJ. A crosssectional of dietary patterns with glucose tolerance and other features of metabolic syndrome. *Br J Nutr* 2000;83: 255-266 <u>http://dx.doi.org/10.1017/</u> <u>S0007114500000337</u>
- Salman H, Bergman M, Djaldetti M, Orlin J, Bessler H. Citrus pectin affects cytokine production by human peripheral blood mononuclear cells. *Biomed Pharmacother*. 2008;62(9):579-82. <u>http://dx.doi.org/</u> <u>10.1016/j.biopha.2008.07.058</u>
- Ma Y, Hébert HR, 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. <u>http://dx.doi.org/10.1016/j.nut.2008.04.005</u> PMid:18562168 PMCid:2603616
- Ajani UA, Ford ES, Mokdad AH. Dietary fiber and C-reactive protein: findings from National Health and Nutrition Examination Survey Data. J Nutr. 2004;134(5):1181-5.PMid:15113967
- 21. Bulló M, Casas-Agustench P, Amigó-Correig P, Aranceta J, Salas-Salvadó J. Inflammation, obesity and comorbidities: the role of diet. *Public Health Nutrition* 2007;**10**(10A):1164-72.PMid:17903326
- Wellen K, Hotamisligil GS. Inflammation, stress, and diabetes. J Clin Invest. 2005;115(5):1111-1119. PMid:15864338 PMCid:1087185
- Lopez-Garcia E, Schulze MB, Fung TT, et al. Major dietary patterns are related to plasma concentrations of markers of inflammation and endothelial dysfunction. *Am J Clin Nutr* 2004;**80**:1029 –35. PMid:15447916