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Research Article

High sensitivity C-reactive protein in metabolic syndrome

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ABSTRACT

Background: Presence of metabolic syndrome in an individual substantially increases his risk of developing cardiovascular disease and type 2 diabetes mellitus. Occurrence of both obesity and type 2 DM have reached epidemic proportions in India. Metabolic syndrome is considered to be a proinflamatory state associated with low grade systemic inflammation. C- reactive protein is a robust biomarker of this chronic systemic inflammation. Higher values of high sensitivity C- reactive protein (hs-CRP) are associated with metabolic syndrome and its components and provides additional prognostic information on future development of cardiovascular events in them.
Methods: 50 patients aged 18 years and above with metabolic syndrome, and 50 age and sex matched controls attending OPD or admitted to medicine department wards of Bangalore Medical College were enrolled for this cross sectional study. The new IDF criteria were used for the diagnosis of metabolic syndrome. A fasting blood sample was drawn for estimation of hs-CRP, blood glucose and lipid profile. Waist circumference, height and weight were measured at the same time. The results were tabulated and analysed.
Results: There was a statistically significant difference in values of various demographic parameters like BMI, waist circumference, BP and biochemical parameters like blood sugar, lipid profile between cases and controls. Patients with metabolic syndrome had higher mean value of hs-CRP (8.3±1.04 Vs 1.6±0.79mg/l) with a p value <0.001.
Conclusions: Patients with metabolic syndrome had significantly higher levels of hs-CRP when compared to controls and hs-CRP levels increased linearly with increasing number of metabolic syndrome components. Hence hs-CRP can probably be used as a surrogate marker of chronic inflammation in patients with metabolic syndrome.

Keywords: High sensitivity C-reactive protein, Metabolic syndrome, Cytokines

INTRODUCTION

The metabolic syndrome (MetS) is clustering of cardio-vascular risk factors in an individual, which includes abdominal obesity, hypertension, glucose intolerance, dyslipidemia, and insulin resistance, and it is associated with an increased propensity for diabetes and cardiovascular disease.[1] Inflammation plays a pivotal role both in the development of insulin resistance and metabolic syndrome.[2] Developing a robust biomarker that can predict metabolic syndrome instead of examining individual variable features will be important from a population standpoint of view in screening, monitoring the natural history of the disease, and measuring the response to therapeutic interventions. There is now abundant evidence that high concentrations of high sensitivivity C-reactive protein (hs-CRP), a proinflamatory cytokine is associated with insulin resistance and metabolic syndrome and may predict onset of diabetes mellitus and cardiovascular events, independent of other traditional risk factors. There are suggestions to include hs-CRP as one of the diagnostic criteria for metabolic syndrome.[3] According to many experts, the increasing burden of obesity is the driving force behind the rising prevalence of the metabolic syndrome.[4] Adipose tissue in obese people is insulin

resistant, which raises nonesterified fatty acid levels, worsening insulin resistance in muscle and altering hepatic glucose metabolism. This adipose tissue of obesity also exhibits abnormalities in the production of several adipokines that may separately affect insulin resistance and/or modify risk for atherosclerotic cardiovascular disease. These include increased production of inflammatory cytokines, plasminogen activator inhibitor- 1, and other bioactive products. At the same time the potentially protective adipokine, adiponectin, is reduced.[5]

Ridker et al evaluated in a large-scale population cohort of the women health survey (WHS), the potential interrelationships between hs-CRP, the metabolic syndrome and incident cardiovascular events (CVEs).[6] In the 8-year prospective follow-up of 14,719 women in the WHS, an hs-CRP of more than 3 mg/l in patients with MetS predicted a greater age-adjusted relative risk (RR) for future cardiovascular events. Furthermore, they reported that at all levels of severity of the metabolic syndrome, hs-CRP added prognostic information with regard to subsequent risk of incident cardiovascular events and was additive to the Framingham risk score. Thus, it has been proposed that hs-CRP be added as a criterion for diagnosing metabolic syndrome and for creation of an hs-CRP-modified CHD risk score.[7] When measured with new "high sensitivity" CRP assays, levels of hs-CRP less than 1, 1 to 3, and greater than 3 mg/L(milligrams per liter) discriminate between individuals with low, moderate, and high risk for future CHD events and stroke.[8]

As per the latest data available, around one third of Indians especially from urban areas have metabolic syndrome. Since hs-CRP levels provide additional prognostic information on cardiovascular risk in patients with metabolic syndrome, this study was undertaken to assess the same in an urban population from south India and also to study the association of hs-CRP levels with various components of metabolic syndrome.

METHODS

50 Patients aged 18 years and above with metabolic syndrome attending outpatient department or admitted in the medicine wards of Victoria hospital, and Bowring and Lady Curzon hospital, attached to Bangalore Medical College and Research Institute, over a two year period between November 2012 to November 2014 were enrolled. Similarly, 50 age and sex matched controls were also enrolled into this cross sectional case control study.

The new International Diabetes Federation definition criteria was used for the diagnosis of metabolic syndrome as given below.[9] Central obesity (defined as waist circumference ≥90cm for men and ≥80cm for women) plus any two of the following four criteria:

- raised TG level: ≥150 mg/dL (1.7 mmol/L), or specific treatment for this lipid abnormality
- reduced HDL cholesterol: <40 mg/dL (1.03 mmol/L*) in males and <50 mg/dL (1.29 mmol/L) in females, or specific treatment for this lipid abnormality
- raised blood pressure: systolic BP ≥130 or diastolic BP ≥85 mm Hg, or treatment of previously diagnosed hypertension.
- raised fasting plasma glucose (FPG) ≥100 mg/dL (5.6 mmol/L), or previously diagnosed type 2 diabetes mellitus.

Patients with acute infection, acute stroke, acute myocardial infarction, pregnant women, patients on steroids, and those with chronic infections or chronic inflammatory conditions like rheumatoid arthritis, systemic lupus, inflammatory bowel disease etc were excluded. Patients satisfying the inclusion criteria underwent relevant routine blood investigations which included estimation of fasting blood glucose, lipid profile and high sensitivity C- reactive protein levels. Blood samples were taken after 12 hours overnight fast. Waist circumference was measured at a point midway between 12th rib and top of iliac crest, at the end of normal expiration. The high sensitivity C-reactive protein was measured quantitatively using particle enhanced turbidimetric assay.

Statistical analysis

Data analysis was done with use of SPSS, version 13. Descriptive statistics was used to calculate the frequency, mean, and standard deviation. To examine the linear trend of the proportions, trend chi-square was used and to find the test of association chi-square was computed.

RESULTS

This was a cross sectional case control study in which 50 cases of metabolic syndrome and 50 age and sex matched controls were enrolled. There were statistically significant differences between cases and controls in values of various demographic parameters like waist circumference, BMI, BP, and biochemical parameters FBS and Lipid profile and hs-CRP values as shown in Table 1. As highlighted in the last row of Table 1 patients with metabolic syndrome had higher mean value of hs-CRP (8.3±1.04 Vs 1.6±0.79 mg/L) with a p value <0.001 which was statistically significant.

On subgroup analysis, 36 (72%) patients with metabolic syndrome belonged to high risk group with a mean hs-CRP value >3 mg/L compared to 9 (18%) controls. Whereas, the low to moderate risk category was composed of majority 41 (82%) controls Vs 14(28%) cases as given in Table 2 and Figure 1.

Table 1: Showing comparison of demographic profile and other variables of cases and controls.

Variable	Cases	Controls	P value
Age (years)	50.76±10.35	50.78±10.57	0.992
Sex ratio(males/females)	23/27	22/28	1
Height (meters)	1.564±.08	1.635±0.09	<0.001
Waist circumference (centimeters)	101.56± 9.99	80.18±5.89	<0.001
BMI	29.78±4.06	20.78±2.08	<0.001
Systolic BP (mmHg)	135.16±14.99	112.96±11.13	<0.001
Diastolic BP (mmHg)	85.24±10.49	70.88±7.04	<0.001
Fasting blood glucose (mg/dl)	166.22±72.3	85.22±8.67	<0.001
Total cholesterol (mg/dl)	204±42.77	153.18±23.91	<0.001
LDL-cholesterol (mg/dl)	114.74±40.16	79.16±2.83	<0.001
HDL-cholesterol (mg/dl)	39±9.79	49.48±7.11	<0.001
Triglycerides (mg/dl)	226.64±101.25	121.88±20.09	<0.001
VLDL-cholesterol (mg/dl)	47.80±23.93	23.83±6.04	<0.001
High sensitivity C reactive protein (hs-CRP) (mg/l)	8.3±1.04	1.6±0.79	<0.001

Table 2: Distribution of hs-CRP values among different risk groups of cases and controls.

	Risk category	Cases	Control	Total
hs-CRP risk_groups	Low risk group (hs-CRP<1 mg/l)	3	24	27
	Moderate risk group (hs-CRP1to3mg/l)	11	17	28
	High risk group (hs-CRP>3mg/l)	36	9	45
	Total	50	50	100

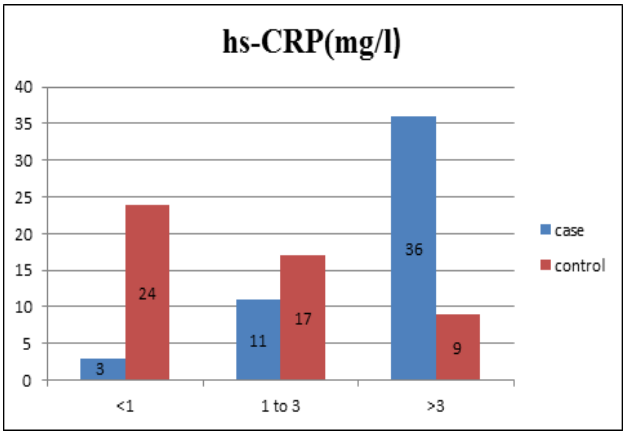

Figure 1: hs-CRP values among cases and controls.

DISCUSSION

Among the novel risk factors for cardiovascular disease currently under investigation, high-sensitivity C-reactive protein (hs-CRP) is most promising. To date, various prospective and cohort epidemiologic studies have demonstrated that hs-CRP independently predicts future cardio vascular risk and development of type 2 diabetes mellitus, with additive prognostic information beyond that is available from the Framingham Risk Score. In contrast to several other biomarkers that also reflect biological aspects of inflammation and insulin resistance, hs-CRP measurement is relatively inexpensive, standardized, widely available, and has a decade-to-decade variation similar to that of cholesterol. Given the consistency of prognostic data for hs-CRP and the practicality of its use in outpatient clinical settings, the time has come for a careful consideration of adding hs-CRP as a laboratory criterion for diagnosing metabolic syndrome and for the creation of an hs-CRP-modified coronary risk score useful for global risk prediction in both men and women.[10]

In the present study, there was higher mean concentration of hs-CRP in patients with metabolic syndrome (8.3±1.04 mg/l v/s 1.6±0.79 mg/l) and there was a linear increase in the values with increasing number of components of the metabolic syndrome. Patients having 2, 3, and 4 risk factors had a mean hs-CRP of 7.217.40, and 9.92 mg/L respectively. Bo et al also found similar findings, the mean hs-CRP for those with 0, 1, 2, 3, 4, 5 components of the metabolic syndrome were1.9, 1.8, 2.9, 4.1, 4.1, and 5.3 mg/L (p = 0.001).[11]

Anubha Mahajan et al also had similar results where hs-CRP values were significantly elevated in subjects with

metabolic syndrome compared to subjects without metabolic syndrome (P=2.1×10−33 and1.1×10−40 for men and women, respectively).[12] A strong linear augmentation in hs-CRP values was observed as the number of components of metabolic syndrome increased from 0 to 5 with median hs-CRP levels of 0.87, 1.20, 1.71, 2.00, 2.47 and 2.82 mg/L. This suggests the fact that higher the number of components of metabolic syndrome in a patient, higher the values of hs-CRP and the risk of development of cardiovascular events.

CONCLUSION

From the results of the present study it can be concluded that, patients with metabolic syndrome have significantly higher levels of hs-CRP when compared to controls and hs-CRP levels increased linearly with increasing number of metabolic syndrome components. Hence hs-CRP can probably be used as a surrogate marker of chronic inflammation in patients with metabolic syndrome. There is accumulating evidence that elevated levels of the inflammatory marker hs-CRP are associated with increased risk for development of cardiovascular disease and diabetes mellitus. Adding hs-CRP values in the diagnostic criteria for metabolic syndrome has shown to improve future prediction of development of these diseases.

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Ethical approval: The study was approved by the institutional ethics committee

REFERENCES

1. Reaven GM. The insulin resistance syndrome: definition and dietary approaches to treatment. Ann Rev Nutr. 2005;25:391-406.
2. Devaraj S, Rosenson RS, Jialal I. Metabolic syndrome: an appraisal of the pro-inflammatory and procoagulant status. Endocrinol Metab Clin North Am. 2004;33:431-53.
3. Ridker PM, Wilson PW, Grundy SM. Should C-reactive protein be added to metabolic syndrome and to assessment of global cardiovascular risk. Circulation. 2004;109:2818-25.
4. Bergman RN, Van Citters GW, Mittelman SD, Dea MK, Hamilton- Wessler M, Kim SP, Ellmerer M. Central role of the adipocyte in the metabolic syndrome. J Investig Med. 2001;49:119–26.
5. You T, Yang R, Lyles MF, Gong D, Nicklas BJ. Abdominal adipose tissue cytokine gene expression: relationship to obesity and metabolic risk factors. Am J Physiol Endocrinol Metab. 2005;288:741–7.
6. Ridker PM, Pare G, Parker A, Loci related to metabolic-syndrome pathways including LEPR, HNF1A, IL6R, and GCKR associate with plasma C-reactive protein: the Women's Genome Health Study. Am J Hum Genet. 2008;82:1185–92.
7. Ridker PM, Wilson PW, Grundy SM. Should C-reactive protein be added to metabolic syndrome and to assessment of global cardiovascular risk. Circulation. 2004;109:2818–25.
8. Paul M Ridker. C-Reactive Protein: A Simple Test to Help Predict Risk of Heart Attack and Stroke. Circulation. 2003;108:81-5.
9. International Diabetes Federation. Worldwide definition of the metabolic syndrome. Available at: http://www.idf.org/webdata/docs/IDF_Meta-syndrome_definition.pdf. Accessed August 24, 2005.
10. Vidyasagar S, Abdul razak UK, Prashanth CK, Varma DM, Bairy KL. Highly sensitive C reactive protein in metabolic syndrome. JIACM. 2013;14:230-4.
11. Bo S,Gentile L, Ciccone G, Baldi C, Benini L, Dusio F, et al. The metabolic syndrome and high c reactive protein: prevelance and difference by sex in a southern European population based cohort. Diabetes Metab Res Rev. 2005;21;515-24
12. Mahajana A, Jaiswala A, Tabassum R, Podder A, Ghosh S, Madhu SV, et al. Elevated levels of C-reactive protein as a risk factor for Metabolic Syndrome in India. Atherosclerosis. 2012;220:275–8.

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