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ORIGINAL ARTICLE

ROLE OF HIGH SENSITIVE C - REACTIVE PROTEIN IN METABOLIC SYNDROME

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ABSTRACT: The metabolic syndrome is a cluster of cardiovascular risk factors associated with an increased risk for developing cardiovascular disease and type-2 diabetes mellitus. However, worldwide there is no accepted criterion for the diagnosis of metabolic syndrome. Further, in light of many recent findings indicating that elevated levels of inflammatory markers, such as high-sensitivity C-reactive protein (hs-CRP), increase risk of diabetes and CVD, it has also been proposed that inflammation, as measured by such markers, be included in the definition of the syndrome. There are data indicating that elevated hs-CRP levels predict development of the metabolic syndrome, at least in women. Among apparently healthy men and women, the levels of high-sensitivity-CRP (hs-CRP) of<1, 1–3 and >3 mg/l distinguish between those at low, moderate and high risk of future cardiovascular disease. We report a study conducted on fifty selected patients between age groups 20 – 55 years admitted in our institute during the period from November 2011 to October 2013.The study was mainly aimed at evaluating the relation of high sensitive c reactive proteins in the components of metabolic syndrome.

KEYWORDS: metabolic syndrome, C - reactive protein.

INTRODUCTION: The metabolic syndrome is a constellation of abnormalities generally considered to include abdominal obesity, high blood glucose/impaired glucose tolerance, dyslipidemia, and high blood pressure that together increase risk of overt diabetes mellitus and cardiovascular disease (CVD) [1]. However, worldwide there is no accepted criterion for the diagnosis of metabolic syndrome. Metabolic syndrome is also considered a pro inflammatory state[2,3] and measurement of inflammatory markers like high-sensitivity C-reactive protein (hs-CRP) [4] might improve the prediction of cardiovascular disease and diabetes in patients with metabolic syndrome. The National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III) identifies various components of metabolic syndrome in adults and defines it as having three or more of the following: abdominal obesity (waist circumference.102 cm for men and.88 cm for women), triglyceride levels 150 mg/dL, high- density lipoprotein (HDL) cholesterol, 40 mg/dL for men and, 50 mg/dL for women, blood pressure 130/85 mm Hg, and fasting plasma glucose 100–125 mg/dL.

Low-grade inflammation may be part of the "common soil" underlying the metabolic syndrome, Type 2 diabetes and cardiovascular disease. Low-grade chronic inflammation is associated with cardiovascular disease, diabetes, insulin resistance, features of the metabolic syndrome and the metabolic syndrome itself [5]. IL-6 is a pro-inflammatory cytokine produced by adipose tissue, endothelial cells, macrophages and lymphocytes. C-reactive protein (CRP), an acute-phase reactant, is synthesized in the liver largely in response to IL-6. Recent studies indicate that inflammation, as measured by IL-6 and CRP, predicts not only cardiovascular events, but also the development of diabetes.

Recently, CRP and pro-inflammatory cytokines have been shown to predict Type 2 diabetes in diverse populations with varying risk factors. These associations are markedly reduced after adjustment for BMI or other factors related to insulin resistance, but an independent predictive value was retained in some studies [6].

MATERIALS AND METHODS: From November 2011 to October 2013, 50 randomly selected patients admitted in our institution with features suggestive of central obesity (waist circumference of >80cm –females &>90cm males and with or without hypertension, diabetes or any other clinical abnormality) were included in the test group. Control group mainly included females with waist circumference less than 80cm, and males less than 90cm and without hypertension, diabetes or any other abnormality. The patients included in the test group were 50 selected from in and out patients admitted in our institution. Control group individuals were selected from the outpatient clinic of our hospital. The patients were taken on basis of random selection from medical OPD, diabetic awareness camps conducted in our hospital and inpatients.

Every patient completed a detailed questionnaire about the relevant history and thorough clinical examination was performed on all patients.

Physical parameters like blood pressure (systolic and diastolic), waist circumference were recorded in both the test and control groups. Waist circumference was recorded at the level of the umbilicus with a plastic anthropometric tape. Systolic and diastolic blood pressure was measured using a mercury sphygmomanometer by auscultatory method following the American heart association protocol.

Blood samples were collected to analyze chemical parameters like fasting plasma glucose, lipid profile (Total triglycerides, total cholesterol, HDL cholesterol, LDL cholesterol) and high sensitive c reactive proteins. The study protocol was approved by local ethics committee and informed consent was taken from all individuals from all the individuals.

RESULTS: The subjects in both the test and control group were evaluated for baseline clinical and biochemical parameters. Subjects with hs-CRP above 10 mg/liter were excluded from the study because such an elevation in hs-CRP might also result from a possible systemic infection. Significant higher levels of BMI, waist circumference, systolic and diastolic pressure, hs-CRP, fasting blood glucose, total cholesterol, TG and LDL-C, low levels of HDL-C were observed among the cases compared to controls. None of the controls had any vascular events (retinopathy, neuropathy, peripheral vascular disease, ischemic heart disease). In all cases with high waist circumference, total cholesterol, LDL-C and triglycerides, significant increase with increasing hs-CRP levels was noticed.

The hs-CRP levels were significantly higher in patients with metabolic syndrome (5.94 ± 2.277mg/L) than in those (0.869± 0.22mg/L) without it. The difference in the levels of hs-CRP between both the groups was statistically significant to indicate a possible association of high levels of inflammation in patients with metabolic syndrome. A correlation of levels of hs-CRP with that of anthropometric variables revealed an association between hs-CRP levels and waist circumference >90cm in males and >80cm in females. Male and female patients with metabolic syndrome had higher levels of WC of 94.82± 9.14 and 94.82±9.14 respectively. Mean BMI value in test group was 26.86±3.44 in males and 27.29±4.86 in females which was statistically significant.

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DISCUSSION: This prospective cohort study provides evidence supporting low-grade inflammation as part of the "common soil" leading to development of the metabolic syndrome, diabetes and cardiovascular disease. There are data indicating that elevated hs-CRP levels predict development of the metabolic syndrome, at least in women. Metabolic syndrome is a cluster of cardio metabolic risk factors. It is frequently associated with an acute phase reaction, suggestive of a low grade inflammatory status of vascular endothelium. In fact the markers of acute phase response, including serum amyloid A, CRP and IL-6, the main mediator of the response, have been shown to be elevated in patients with metabolic syndrome.

CRP concentrations at the high end of the normal range not only predicted increased risk of diabetes, but also the metabolic syndrome. Non-diabetic men with CRP levels greater than or equal to 3 mg/l at baseline were 3.2 to 3.4 times more likely to develop the metabolic syndrome as defined by the NCEP and the WHO. This increased risk was not explained by lifestyle factors, but adjustment for BMI attenuated the association, particularly for the NCEP definition. It is to be expected that obesity weakens the association, since adipose tissue is a major source of pro-inflammatory cytokines such as IL-6 and TNF-α. Attenuation of the association after adjustment for factors related to insulin resistance also suggests that inflammation is an integral part of the disturbances in insulin, glucose and lipid metabolism that underlie the metabolic syndrome. Inflammation may also mediate the development of the metabolic syndrome in part through these underlying metabolic disturbances.

In vitro and small human studies have suggested several mechanisms by which low-grade inflammation may increase insulin resistance, dyslipidemia, and endothelial dysfunction[7]. Markers of inflammation, such as white blood cell count and fibrinogen, have been shown to predict weight gain, a key triggering factor of the metabolic syndrome, in a 3-year follow-up of the Atherosclerosis Risk in Communities cohort [8]. Conversely, weight loss has been shown to decrease markers of inflammation in morbidly obese patients with features of the metabolic syndrome [9]. CRP concentrations have also been observed to predict the development of hypertension [10].

Although it is still unclear whether hs-CRP should be a treatment target, it is of interest to determine what types of therapeutic interventions produce changes in hs-CRP levels. Several recent studies indicate that statin treatment in patients with CAD produces significant reductions in hs-CRP—reductions that appear to be greater with regimens producing greater low-density lipoprotein cholesterol reductions. Determination of the risk level associated with the metabolic syndrome depends on precisely how the syndrome is defined.

The management approach in patients with the metabolic syndrome depends on the syndrome's perceived causes and the degree of risk attributed to its presence. Current general conceptual frameworks include (1) viewing the metabolic syndrome epidemic as being attributable to environmental causes (e.g., the basic approach of NCEP ATP III), (2) viewing the syndrome as primarily the result of insulin resistance (e.g., the WHO approach), and (3) viewing inflammation as the underlying cause of the syndrome. In the first view, the primary management approach would be lifestyle modification for reducing obesity and increasing activity. If insulin resistance is considered the underlying cause, treatment is likely to include insulin sensitizers in addition to lifestyle modifications. If inflammation is considered the underlying cause, treatment is likely to include lifestyle modification and insulin sensitizers together with other agents, such as statins, angiotensin-

converting enzyme inhibitors, or angiotens in receptor blockers, depending on the presence of specific risk factors.

CONCLUSION: Although it is clear that the presence of the syndrome is associated with increased cardiovascular risk, the levels of associated risk have not been clearly defined. Different proposed definitions would appear to result in different predictions of risk, and risk appears to differ according to which components of the proposed definitions are present. Inclusion of hs-CRP in the definition improves its predictive ability for diabetes and for CVD; in the pre diabetic state, elevated hs-CRP appears to identify individuals in whom insulin resistance is the primary defect that leads to diabetes.

Approaches to management of the metabolic syndrome should include lifestyle intervention aimed at weight loss and increased physical activity, combined with treatment of the individual component risk factors (e.g., dyslipidemia, hypertension). The management of these patients should certainly be intensified over that based on current global risk assessment (e.g., Framingham risk assessment in NCEP ATP III). At present, however, there are insufficient data to recommend that the metabolic syndrome be considered a CAD risk equivalent.

Serum hs-CRP level has a significant correlation with metabolic syndrome and might be used as future criteria of metabolic syndrome. Present study suggests that metabolic syndrome patients with high hs-CRP levels require regular screening test for prevention of complications. Elevated hs-CRP levels are a risk factor for future vascular complications in type II Diabetes mellitus and cardiovascular diseases.

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