Research Article

Comparison of Inflammatory and Antioxidant status in lean and obese type 2 Diabetes Mellitus Patients

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Abstract

Objectives: Recent studies suggest that low grade systemic inflammation and oxidative stress is present among patients at high risk for atherothrombotic diseases. So we decided to investigate serum C reactive protein (CRP) as a marker of systemic inflammation and serum super oxide dismutase (SOD) as a marker of free radical activity in metabolic syndrome patients, obese Type II diabetes mellitus (T2DM) (BMI > 30). **Materials and Methods:** Total 102 subjects in age group 40-70 years were studied and divided as group I - (n=34) healthy controls (BMI < 25), Group II- (n= 34) diabetic patients (BMI <25), Group III – (n=34) metabolic syndrome patients, obese T2DM (BMI >30). In all these subjects BMI, CRP (latex agglutination), SOD (marklund and marklund method) were measured. **Results:** Mean CRP was 2.3+/-0.2 µg/ml and significantly raised in group III as compared to Group II (0 µg/ml) and Group I (0 µg/ml) (p< 0.001).Increased CRP was associated with high BMI (p<0.001). Mean SOD was 1.32+/-0.21 units/ml in group III as compared to group II (2.44+/- 0.09unis/ml) and group I (3.46+/-0.08 units/ml) (p<0.001). Decreased SOD was associated with high BMI (p < 0.001). **Conclusion:** We found significant association between increased CRP levels and decreased SOD with high BMI in metabolic syndrome patients, obese T2DM (BMI > 30) group III as compared to group II and group I. Thus these data further supports the hypothesis that CRP may serve as an inflammatory marker for underlying atherosclerosis and low levels of SOD suggests increased free radical activity in group III, predicting risk of coronary heart disease.

Key words: Metabolic syndrome (MS), type II diabetes mellitus (T2DM), C reactive protein (CRP), super oxide dismutase (SOD), body mass index (BMI),waist hip ratio (W/H)

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INTRODUCTION

In recent decades increase in the prevalence of type 2 diabetes mellitus (T2DM) is observed. T2DM represents the final stage of a chronic and progressive syndrome representing heterogeneous disorder caused by various combinations of insulin resistance and decreased pancreatic β cell function caused by mostly acquired abnormalities.[1] In 1988 Reaven proposed that insulin resistance is central to the etiology of T2DM, hypertension and coronary artery disease. Insulin resistance and associated abnormalities leading to increased risk of cardiovascular disease known by metabolic syndrome. Diagnostic criteria : WHO definition 1) Must present : Type II diabetes, Impaired glucose tolerance 2) Additional two out of the following a)BMI > 30 Kg/m^2 or waist hip ratio (W/H) >0.90 (men), W/H ratio >0.85 (women) b) Dyslipidemia : Triglyceride (TG) >150 mg/dl, High Density Lipoprotein (HDL) <39 mg/dl (women) c) Hypertension : on medication or untreated blood pressure > 160/90 mm of Hg d) microalbuminuria : ≥20µg/min.[2] C reactive protein (CRP) : Recently it has been found that markers of systemic inflammation predict atherosclerotic risk. Some of these factors are associated with insulin resistance or other components of metabolic syndrome. CRP has emerged as a very strong independent atherosclerotic risk factor. CRP was found to be independently associated with body mass

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index (BMI), insulin resistance and systolic blood pressure. CRP is 1, 35,000 dalton non immunoglobulin protein, having five identical subunits. The name of the CRP derived due to its reaction with capsular polysaccharide of streptococcus pneumonie. CRP specifically recognizes phosphocholine the hydrophilic part of phosphatidyl choline, other phospholipids and histone proteins. Complexion of CRP and cell wall activates complement via classical pathway, thus stimulate macrophages and other cells to undergo phagocytosis. Cytokines like interleukin-6 (IL-6) stimulate hepatocytes to produce acute phase proteins. Recent studies have proved that, quantification of CRP is superior than cytokine measurement (like Il-6, IL-1, tumour necrosis factors) for detecting presence of inflammation.[3] Superoxide Dismutase (SOD): The free radicals have a life span of micro seconds. The evidence for their existence is therefore almost entirely indirect. Reduction of oxygen by a single electron will produce super oxide anion. Two super oxide anions can react together to form hydrogen peroxide andoxygen, the reaction being catalyzed by super oxide dismutase

$$O_2^- + O_2^- \xrightarrow{SOD} H_2O_2 + O_2$$

Oxidative stress leads to decreased level of serum SOD levels in diabetes mellitus significantly correlates with glycemic status.As the glycemic status deteriorates serum SOD levels also decreases. Low levels of serum SOD signify poor metabolic control and patients are more prone to micro angiopathic complications.[4] The metabolic abnormalities that characterize diabetes particularly hyperglycemia, liberation of free fatty acids and insulin resistance may provoke vascular dysfunction and inflammation via multiple mechanism including oxidative stress.[5] As recent study suggests that low grade systemic inflammation and oxidative stress is present among patients at high risk for atherothrombotic disease. So we decided to investigate serum CRP as a marker of systemic inflammation and serum SOD as a marker of free radical activity in metabolic syndrome patients (BMI > 30).

MATERIALS AND METHODS

The study was conducted at the department of Biochemistry, Government Medical College, Aurangabad. Total 102 subjects in age group of 40 to 70 years were studied. Informed consent was taken from the subjects included in the study. Study was conducted as per guidelines of ethics committee. The subjects were divided in three groups, Group I – (n=34) healthy controls (BMI <25) not suffering from any major illness comprised control group. Group II – (n=34) non obese diabetic patients (BMI < 25) without any recent infection comprised non obese diabetic group. Group III – (n =34) metabolic syndrome patients, obese type II diabetes mellitus (T2DM),(BMI > 30) patients were non smokers, non-estrogen using, without any history of major illness.

In all these subjects BMI, W/H ratio, serum CRP, serum SOD estimations were done. BMI calculated as Wt (Kg)/ height (m^2), W/H ratio calculated as waist circumference/ hip circumference, fasting blood sugar was estimated by using commercial kit. The serum CRP estimation was done by using commercial kit for in vitro detection of CRP in human serum by semi quantitative rapid latex slide test by span diagnostic Ltd. was used. CRP level can be calculated in terms of µg/ml by multiplying the highest dilution giving clear cut agglutination with a factor of 6 (sensitivity of antigen 6 µg/ml). Normal values in healthy persons = 0 to 5 µg/ml. Estimation of serum SOD was done by method of Marklund S, Marklund G :1974, modified by Nandi *et al.* (1988).[6] Normal range of SOD in serum = 2.93 – 3.71 units/ml.

Statistical analysis

All the values calculated represent the mean $\pm$S.D. The two groups were analysed by comparing parameters by applying unpaired t test.

RESULTS

The study group was composed of 50 females and 52 males in the age group of 40 to 70 years. The mean serum CRP values in metabolic patients, obese Type II diabetes mellitus T2DM (group III) were significantly high as compared to mean serum CRP values in group I (p = 0.001) and group II (P = 0.001). As mean values are 0.00(nil) for both the groups (I and II), t value was not calculated, so not compared statistically.(Table 1 and 2)

The mean serum SOD values were significantly lower in metabolic syndrome patients, obese type II diabetes mellitusT2DM (group III) as compared to mean serum SOD values in group I (p < 0.0001) and group II (p < 0.0001). The mean serum SOD values in group II were significantly lower as compared to mean serum SOD values in group I. (Table 1and 2)

High levels of serum CRP were statistically significantly associated with high BMI and W/H ratio in all the study subjects. Low levels of serum SOD values were statistically significantly associated with high BMI and W/H ratio in all the study subjects. (Table 3)

BMI was statistically significant when group I and group II compared with group III. W/H ratio was also statistically significant when group I and group II compared with group III. (Table 4)

Table 1: Clinical data with mean values of serum c reactive protein and super oxide dismutase in all the three groups

Parameter	Group I (non obese adult control)	Group II (non obese diabetic patients)	Group III (metabolic Syndrome patients)
BMI (kg/m^2)	22.65+/- 0.92	21.58+/-1.7	32.08+/-1.58
W/H ratio (male)	0.86+/-0.01	0.87+/-0.01	0.95+/-0.01
W/H ratio (female)	0.81+/-0.02	0.82+/-0.01	0.90+/-0.02
Serum CRP (µg/ml)	0.00(nil)	0.00(nil)	2.3+/-2.3
Serum SOD (units/ml)	3.46+/-0.08	2.44+/-0.09	1.32+/-0.21

Table 2: t values and p values of CRP and SOD comparison in between the groups

		t value	p value
CRP	Controls (group I) Vs metabolic syndrome patients (group III)	4.52	0.001
	Non obese diabetic patients (group II) Vs metabolic syndrome patients (group III)	4.52	0.001
SOD	Control (group I) Vs metabolic syndrome patients (group III)	53.26	<0.0001
	Non obese diabetic patients (group II) Vs metabolic syndrome patients (group III)	27.31	<0.0001
	Control (group I) Vs non obese diabetic patients (group II)	45.95	<0.0001

Table 3: Association between high levels of serum CRP and low levels of serum SOD with high BMI and W/H ratio in all study subjects

	χ^2 value	P value
CRP and BMI	29.82	<0.001
CRP and W/H ratio (female)	7.06	<0.01
CRP and W/H ratio (male)	18.21	<0.001
SOD and BMI	73.44	<0.001
SOD and W/H ratio (female)	41.81	<0.001
SOD and W/H ratio (male)	31.43	<0.001

Table 4: comparison of BMI, W/H ratio (male and female) in Group III with Group I and Group II

		t value	p value
Body mass Index	Group I and Group III	21.47	<0.001
	Group II and Group III	36.45	<0.001
W/H ratio (male)	Group I and Group III	4.84	<0.001
	Group II and Group III	11.25	<0.001
W/H ratio (female)	Group I and Group III	16.0	<0.001
	Group II and Group III	18.0	<0.001

DISCUSSION

There has been considerable interest in the concept that a state of systemic inflammation and increased oxidative stress is present in the metabolic syndrome. In present study we included the metabolic syndrome patients on the basis of WHO criteria. The difference in mean BMI in group III and both the other groups (I and II) was statistically significant ($p < 0.001$) for both groups. The difference in mean W/H ratio (male and female) in group III in comparison with the other groups (I and II) was statistically significant ($p < 0.001$) for both groups. Wildman *et al.* (2005)[7] suggested the waist circumference adds additional risk information to the BMI in Chinese adults. Metabolic syndrome increases with successive waist circumference tertiles (p for trend < 0.001 for all). Waist circumference and waist to hip ratio remain strong predictors of cardiovascular disease incidence and mortality after adjustment for BMI. In present study serum CRP levels in metabolic syndrome patient, obese type II diabetes mellitus T2DM(group III) were significantly high than other two groups (group I and group II). Also higher values of BMI and W/H ratio in (male and female) were significantly correlates with high levels of CRP in all study subjects. Pai *et al.* (2004)[8] reported that the elevated levels of inflammatory markers particularly CRP indicate an increased risk of coronary heart disease. The relative risk was 1.79 higher with CRP levels at least 3 mg/l as compared with those having the levels less 1 mg/l ($p < 0.001$). Tomiyama *et al.* (2005)[9] showed that in linear regression analysis all metabolic disorders and logarithms of CRP significantly correlated with pulse wave velocity as a marker of arterial stiffness. Thus in metabolic syndrome patients elevated CRP aggravates cardio vascular risk. In present study SOD

levels in metabolic syndrome patients, obese type II diabetes mellitus (T2DM) were significantly lower than other two groups (group I and group II).Also high values of BMI and W/H ratio (male and female) were significantly correlates with low levels of SOD in all study subjects. Shigetada *et al.* (2004)[10] demonstrated that production of reactive oxygen species (ROS) increased selectively in adipose tissue of obese mice. Total SOD activities were significantly lower in study group than in control. Christian *et al.* (2006)[11] showed that protein expressions of key reactive oxygen species producing enzyme NADPH oxidase gp 91 (phox) subunit was significantly up regulated and of main antioxidant enzyme SOD was down regulated in aorta of fischer rats fed on high fat and high refined sugar leading to metabolic syndrome. The data in present study show that high BMI and W/H ratio adds additional cardio vascular risk information to that increased levels of CRP and decreased levels of SOD in patients of metabolic syndrome i.e. obese T2DM patients. A state of low grade systemic inflammation and oxidative stress leads to cardiovascular disease in these patients. We observed a statistically significant link between inflammatory marker and anti oxidant in lean and obese T2DM patients. Subjects with high inflammatory status had imbalance in oxidant/ antioxidant mechanism. In summary obesity with T2DM is oxidative burden with reduced antioxidant and a state of systemic inflammation.

REFERENCES

1. Jayram BM, Jayanthi CR, Insulin Resistance – Glitazones and beyond Newer horizons in type II diabetes : 2003 First edition Micro Labs Ltd Banglore : 241-256
2. Miranda PJ, Defzonzo RA, Califf RM, Guyton JR, Metabolic syndrome : definition, pathophysiology and mechanisms, Am Heart J 2005;149 (1);33-45.
3. Mitra B, Panja M,high sensitive C reactive protein; a novel biochemical marker and it's role in coronary artery disease. JAPI 2005; 53; 25 – 32.
4. Nischal HK, Sharma MP, Goyal RK, Kaushi CG, serum super oxide dismutase with or without microangiopathic complications; JAPI 1998; 46;853 – 55.
5. Tiog AG and Breiger D, Inflammation and coronary artery disease; Am Heart J 2005; 366;11 – 8.
6. Marklund S, Marklund G (modified by Nandi *et al.* 1998) serum super oxide dismutase levels in diabetes mellitus with or without micro angiopathic complications : JAPI 1998; 46 (10);853 – 5.
7. Wildman RP, Dongfeng G, Reynolds K, Duan Y, Jiang H, Are waist circumference and body mass index independently associated with cardio vascular disease risk in Chinese adults ? Am J Clin Nutr 2005; 82;1195 – 202.
8. Pai JK, Pischon T,Jing M, Manson PH, Hankinson SE, Joshipura G, Cannuscio CC, Rimm EB, Inflammatory markers and the risk of coronary heart disease in men and women. N- ENG J MED 2004; 351;2599 – 2610.
9. Tomiyama H, Koji G, Yambe M, Motobe K, Yammato Y, Yamashina A, Elevated C reactive protein augments increased arterial stiffness in subjects with the metabolic syndrome, Hypertension 2005; 45; 997.
10. Shigetada F, Fujita J, Shimabukuro M, Iwaki M, Gamada G, Nakajima G, Nakayama O, Makishima M, Mastuda M, Shimomuza L, Increased oxidative stress in obesity and its impact on metabolic syndrome, J Clin. Invest 2004; 114; 1752 – 1761.
11. Christian KR, Beznard RJ, Sindhu RK, Juczak M, Ehdie A, Vazizi ND, Oxidative stress and dysregulation of NADPH oxidase and anti oxidant enzymes in diet included metabolic syndrome, Metabolism 2006; 55; 928 – 34.

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