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Original Research Article

Assessment of Glutathione peroxidase and its correlation with the components of Metabolic Syndrome

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Abstract: Metabolic syndrome (MS) is a cluster of cardio metabolic risk factors such as obesity, hyperglycemia, dyslipidemia, and hypertension and insulin resistance. However, the role of oxidative stress in developing components of MS needs further investigations. The objective of present study was to study the levels of antioxidant enzyme Glutathione peroxidase (GSHPx) and correlate them with components of MS. 300 participants were enrolled, which were divided into MS positive (n=150) and MS negative (n=150) groups as per NCEP ATP III criteria. Components of MS were assessed using standard methods and data from patients and controls were compared by using Student's t-test. Correlation of GSHPx with the components of MS was carried out using Pearson correlation coefficient. Erythrocyte GSHPx activity was decreased significantly in patient group subjects. In addition, GSHPx activity was negatively correlated with the components of MS. Oxidative stress is significantly associated with MS and its components. Furthermore, components of MS should be monitored regularly with advancing of age in order to overcome the burden of cardiovascular disease risk.
Keywords: Hyperglycemia, hypertriglyceridemia, dyslipidemia, abdominal obesity, free radical

INTRODUCTION:

The metabolic syndrome refers to the co-occurrence of cardiovascular risk factors such as insulin resistance, obesity, dyslipidemia and hypertension. The incidence of metabolic syndrome (MS), which increases the future cardiovascular disease (CVD) risk, has reached epidemic proportions worldwide. Although precise etiology of this syndrome is poorly understood, probability of MS patients to develop future CVD risk appears to be associated with chronic low level inflammation and increased oxidative stress (OS) [1-3].

OS is accepted as important mediator in development and progress of hypertension, endothelial dysfunction and atherosclerosis.(4) OS is also present in conditions of insulin resistance and inflammation [5, 6]. Oxidative stress in MS is ensued by excessive production of reactive oxygen species (ROS). Glutathione peroxidase (GSHPx) is an important antioxidant enzyme which not only neutralises H_2O_2, but also transforms lipoperoxide and other organic hydro peroxide into their less reactive hydroxylated compounds. Reduced activity of antioxidant enzymes, reflecting increased oxidative stress, has been described in patients with obesity, hypertension and other components of MS [7].

Studies related to association of GSHPx and MS are scanty. Also, there are very few reports on association of oxidative stress with components of MS. In fact, to establish the relationship between MS and oxidative stress, more concrete evidences are required in which correlations between antioxidant enzymes and the presence of triggering factors and components of the

syndrome are essential. Therefore, the aim of present study was to evaluate the erythrocyte GSHPx activity in MS patients and to determine the association of GSHPx with the components of MS.

MATERIAL AND METHODS:

A cross-sectional comparative study was carried out on a sample of 300 subjects (30-50 years old). After taking informed consent as per protocol approved by institutional ethics committee, demographic information from all participants was recorded. Patients, aged above 50 and below 30 years, on vitamin supplements, hormone replacement therapy and those with a history of infections, abnormal renal or hepatic function and malignancy were excluded from the study. Height and weight were measured with subject barefoot and light dressed. The body mass index (B.M.I.) were calculated as B.M.I. = weight (Kg) / Height (metre^2). Waist circumference was measured midway between the lowest rib and iliac crest. Blood pressure was recorded from the right arm with subject in sitting position and a mean of two successive readings was taken. After anthropometry, fasting blood samples were collected for biochemical analysis.

Fasting blood glucose was estimated by hexokinase method (Beckman coulter, USA). Serum total cholesterol, HDL and triglyceride were estimated by standard enzymatic method. Serum LDL-cholesterol and VLDL-cholesterol levels were calculated by Friedwald's formula [8].

Erythrocyte GSHPx activity was estimated by commercial kit (Ransel, Randox Laboratories). In this method, GSHPx catalyses the oxidation of Glutathione (GSH) by Cumene Hydro peroxide. In the presence of Glutathione Reductase (GR) and NADPH the oxidised Glutathione (GSSG) is immediately converted to the reduced form with a concomitant oxidation of NADPH to NADP+. The decrease in absorbance at 340 nm is measured. All colorimetric analyses were performed on fully automatic analyzer (Beckman Coulter AU 680) with 2 levels of quality control. Participants were diagnosed as with MS (n=150) or without MS (n=150), as per National Cholesterol Education Program Adult Treatment Panel III criteria (NCEP- ATP III) guidelines (Table 1). [9]

Statistical Analysis:

The data collected from patients and control were entered separately in Microsoft Excel sheet of windows 2007 and values were expressed as Mean ± SD. The significance of mean difference between patient and control groups was compared by using Student's t test. The distribution of 't'- probability was calculated depending on 'n' and significance of test was obtained. P value < 0.05 and < 0.001 were considered as significant and highly significant, respectively. P value > 0.05 was considered as insignificant. In addition, correlation analysis between aforesaid parameters was performed by using Pearson correlation test.

RESULTS:

In the present study, 150 MS positive (MS+) and 150 MS negative (MS-) participants were included. Demographic profile of both groups is given in Table 2. Among the MS positive group, 54% were male and 46% were females. There was significant difference in BMI, waist circumference, blood pressure (systolic as well as diastolic) of MS positive and MS negative groups. While BMI of MS positive group was 25% higher than MS negative group, there was increase of 17% and 15% in waist circumference and blood pressure, respectively, of MS positive group as compared to MS negative group.

The glycemic and lipid profile data showed significant abnormalities in the patients group as represented in Table 3. Fasting blood glucose level was significantly high ($p<0.001$; 26.4%) in MS positive as compared to MS negative. Serum total cholesterol, triglyceride, LDL and VLDL levels were found to be significantly high ($p<0.001$) in MS positive participants. However, HDL levels were found to be reduced significantly ($p<0.05$; 18.35% low) in the MS positive as compared to MS negative.

Glutathione peroxidase activity in the study group subjects are also depicted in figure 1. There was a 29% reduction in erythrocyte GSHPx activity ($p< 0.001$) in the MS positive group as compared to MS- group, indicating an increased oxidative stress in MS.

In addition, we observed a significant correlation between erythrocyte GSHPx and the components of MS, as shown in Table 4. GSHPx activity was negatively correlated with waist circumference, blood pressure, fasting blood glucose, total cholesterol, triglycerides, LDL and VLDL levels ($p < 0.001$); whereas GSHPx activity was positively correlated with serum HDL levels in MS+ participants. These results clearly indicate the association of elevated oxidative stress with metabolic derangements which enhance cardiovascular disease risk.

Table 1: NCEP-ATP III criteria for Metabolic Syndrome (Any 3 of the given 5 parameters are required for a diagnosis of MS)

Parameter	Value
Waist circumference	> 40 inch (male)/ > 35 inch (female)
Blood Pressure	> 130 mmHg systolic or > 85 mmHg diastolic
Fasting Triglycerides	> 150 mg/dl
HDL	< 40 mg/dl in males
	< 50 mg/dl in females
Fasting blood sugar	> 100 mg/dl

Table 2: Demographic profile of MS negative and MS positive groups (Mean ± SD)

S.No.	Particulars	MS negative (N= 150)	MS positive (N=150)
1	Age (years)	41.66 ± 7.4	42.4 ± 8.5
2	Height (meter)	1.65 ± 0.8	1.66 ± 0.07
3	Weight (kg)	64.80 ± 5.8	72.52 ± 6.4
4	BMI	22.9 ± 2.0	28.71 ± 2.6***
5	Waist Circumference (cm)	82.54 ± 8.8	96.62 ± 9.2**
6	Hip (cm)	93.06 ± 7.2	103.53 ± 8
7	Waist-hip ratio	0.87 ± 0.08	0.94 ± 0.09
8	Systolic pressure (mmHg)	108 ± 9.5	124.8 ± 8.2**
9	Diastolic pressure (mmHg)	74.6 ± 5.2	86.4 ± 6.8**

Where,
* p < 0.1, **p<0.05, *** p < 0.001

Table 3: Glycemic and lipid profile of study group subjects (Mean ± SD)

S.No.	Particulars	MS negative N= 150	MS positive N=150	% Increase	% Decrease
1	Total cholesterol(mg/dl)	153.5 ± 28.7	186.0 ± 32.4**	21.17	-
2	Triglycerides(mg/dl)	85.7 ± 16.3	142.6 ± 20.8***	66.39	-
3	LDL (mg/dl)	97.8 ± 14.2	122.5 ± 16.7**	25.25	-
4	HDL(mg/dl)	47.4 ± 5.5	38.7 ± 6.2**	-	18.35
5	VLDL (mg/dl)	18.2 ± 4.8	31.4 ± 5.0***	72.52	-
6	Fasting blood glucose (mg/dl)	85.6 ± 12.5	112.0 ± 18.4**	26.4	-

Table 4: Correlation coefficient (r) between Glutathione peroxidase and components of MetS

Particular	SBP	DBP	TC	TG	HDL	LDL	VLDL	FBG
GSHPx	- 0.402 *	-0.378 *	- 0.563 **	-0.474 *	0.645**	-0.608**	-0.518**	- 0.670**

Where,
* p < 0.1, **p<0.05, *** p < 0.001

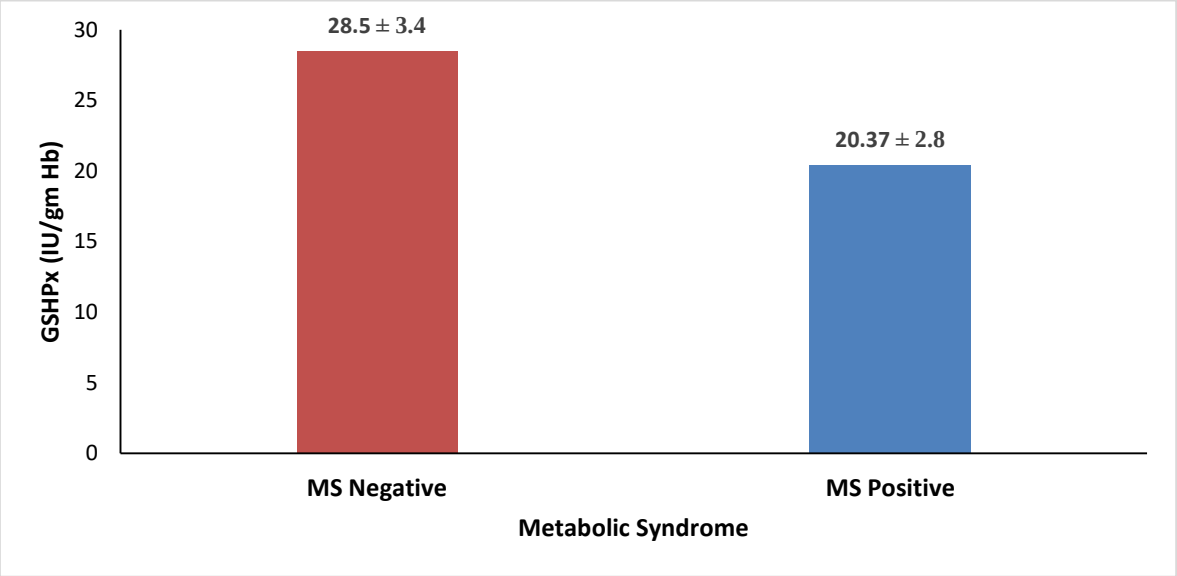

Fig-1: Erythrocyte glutathione peroxidase activity in the study population

DISCUSSION:

Metabolic syndrome is a major and escalating public-health challenge worldwide. Due to increasing urbanization, surplus energy intake, increasing obesity, and sedentary life habits, the prevalence of MS in increasing. In India, prevalence of MS varies from 20-30% [10, 11]. MS confers a 2-fold the risk of developing cardio vascular disease and 5-fold increase in the risk of type 2 diabetes mellitus over the next 5 to 10 years. Increased visceral adiposity, reflected by high BMI and waist circumference, is now known to be central to development of MS. This phenomenon is seen in our study participants also. Our findings show that there is a significant increase in BMI and blood pressure in the MS patients as compared to the participants without MS, which exposes them to increased risk of future cardiovascular disease. Here, we also show that high blood pressure is an important component of MS, as both systolic and diastolic BP were significantly elevated in MS group compared to control group. A recent study also found that high blood pressure is most important factor linked to OS in elderly [12].

Though insulin resistance is considered to be the main underlying mechanism in metabolic derangements in MS, low grade chronic inflammation and oxidative stress are also known to be associated with components of MS. Also, it has been shown that inflammation as well as oxidative stress is associated with insulin resistance [13-15]. Increased visceral adiposity is related to the establishment of insulin resistance and low-grade chronic proinflammatory state of patients, through inflammatory cytokines release. In the present study, we show that oxidative stress, as indicated by reduced erythrocyte GSHPx is significantly associated with MS. This finding is corroborated by several other studies [16, 17]. Moreover, there is a strong relationship between oxidative stress and altered metabolic profile leading to MS. Further, erythrocyte GSHPx was inversely correlated with components of MS. This could be explained either by their decreased synthesis or rapid consumption in protecting the cells from H_2O_2 mediated oxidative damage in MS patients. Such as dyslipidemia, endothelium dysfunction, hypertension and insulin resistance.

Recently, Shrestha *et al.;* on their study on metabolic syndrome patients reported the MS patients are more susceptible to develop future cardiovascular disease due to their uncontrolled metabolic profile and elevated level of oxidative stress [18]. Goyal *et al.;* also observed the low GSHPx activity in individuals with components of MS and its association with increased oxidative stress and proinflammatory state [6]. It has also been found that decrease in GSHPx activity is associated with increased body mass index (BMI) and waist circumference, as observed in our study, and thereby reinforcing the establishment of pro-oxidant condition in MS patients which may impair insulin signal pathway and lead to harmful action on the endothelium.

CONCLUSION:

On the basis of findings of the present study and consistent support of previous evidences, it is

obvious that oxidative stress plays a crucial role in MS etiopathology. Further, high blood pressure is an important derangement associated with MS. Study of oxidative stress in MS patients can help in getting better knowledge regarding pathways which contribute to complications of MS.

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