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Glutathione Peroxidase Activity and Its Relation with Dyslipidemia in Metabolic Syndrome Patients: A Clinical Approach

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Abstract: Oxidative stress has been found to be an important factor in the etiopathophysiology of various diseases such as diabetes, hypertension and cardiac complications. Metabolic syndrome (MS) is a major emerging problem, characterized by various sorts of cardiometabolic risk factors. In this context, the role of oxidative stress in developing components of MS has received much attention. Therefore, the present study was conducted to estimate the erythrocyte glutathione peroxidase (GSHPx) activity in MS patients and to determine the relation of GSHPx with dyslipidemia in MS subjects. In the present study, the criterion of Third Report of the National Cholesterol Education Program Adult Treatment Panel III was adopted to recruit 100 patients of MS of either sex (30-50 years age group). 100 normal healthy individuals served as control. Serum lipid profile along with erythrocyte GSHPx activity was estimated by using standard methods. The data was collected from patients and controls group subjects and statistically compared by using Student's t-test. GSHPx activity was significantly low ($p<0.001$) in MS group subjects along with abnormal lipid profile. In addition, GSHPx activity was negatively correlated with the components of lipid profile except HDL-cholesterol. Therefore, the present study suggested that incorporation of diet rich in antioxidant along with routine lipid profile monitoring and treatment of dylipidemia are important strategies to prevent the risk of cardiac complications in MS patients.
Keywords: Free radicals, antioxidant enzyme, cardiometabolic factors, hypertension.

INTRODUCTION

Metabolic syndrome (MS) is a cluster of metabolically related cardiovascular risk factors, the core components of which comprise of central obesity, insulin resistance, dyslipidemia, and hypertension. MS is also a risk factor for developing type 2 diabetes (T2D), ischemic heart disease, and arteriosclerosis associated stroke[1,2].

Interestingly, the presence of oxidative stress in MS patients, as reported in previous studies further enhances the frequency to develop CVD [3,4]. Oxidative stress is characterized by excessive production of reactive oxygen species (ROS) in combination with depleted antioxidant reserve. Oxidative stress leads to development of MS components related complications due to a series of deleterious events caused by ROS such as damage to endothelium, oxidation of LDL (lipid peroxidation), protein oxidation and DNA strand breakage [5,6]. The low levels of antioxidant vitamins and enzymes would have led to the imbalance between their protecting effects and the damaging effects of the free radicals hence the increased oxidative stress.

Glutathione peroxidase (GSHPx) is a tetrameric enzyme containing selenium. It is not only responsible for the decrease of H_2O_2, but also transforms lipoperoxide and other organic hydroperoxide into their corresponding hydroxylated compounds, which are less reactive. GSHPx is present at higher levels in peroxisomes and vesicles attached to the plasma membrane, mainly in the liver and erythrocytes [7]. Previous studies have shown that antioxidant enzyme activities alter in various diseases such as cardiovascular diseases, hypertension, obesity and diabetes etc[8-10].

Moreover, the study pertains to assessment of GSHPx activity and lipid profile in MS patients along with characteristic factors such as hypertension, hyperglycemia and increased body weight is still

obscure. Therefore, the aim of present study was to evaluate the erythrocyte GSHPx activity and lipid profile in MS patients and to determine the association of GSHPx activity with dyslipidemia in MS patients to predict the risk of MS associated complications.

MATERIALS AND METHODS

In the present study, 200 subjects belonged to age group 30 -50 years, were included. These subjects were categorized as Group I (Control group) comprised of 100 normal healthy individuals and Group II (Patient group) comprised of 100 individuals who were age and sex matched patients suffering from metabolic syndrome. A general information or pre-experimental questionnaire regarding demographic information, family history and limited physical examination including blood pressure measurement was completed from all the subjects after taking their informed consent and approval of protocol by ethics committee of college. 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).

Inclusion criteria

A total number of 100 MS patients fulfilling the National Cholesterol Education Program Adult Treatment Panel III criteria (NCEP- ATP III) and above 30 years of age were included.[11]

Exclusion criteria

Patients, aged above 50 and below 30 years, under vitamin supplements, hormone replacement therapy and those with a history of infections, abnormal renal function and malignancy were excluded from the study.

Fasting blood samples (4 ml) of both the study group subjects were collected in plain vial (2 ml for serum separation) and EDTA vial (2 ml for hemolysate preparation). Serum lipid profile contents (total Cholesterol, Triglycerides& HDL cholesterol) were analysed enzymatically. Serum LDL-cholesterol and VLDL-cholesterol levels were calculated by Friedwald's formula[12].

$$LDL\text{-}C = TC - [(TG/5)+HDL\text{-}C]$$

$$VLDL\ cholesterol = Total\ chol. - (HDL + LDL)$$

Erythrocyte glutathione peroxidase (GSHPx) activity was estimated by Beutler's method, after preparation of hemolysate.[13] GSHPx catalyse the oxidation of reduced glutathione (GSH) to oxidized glutathione (GSSG) by H_2O_2. The rate of formation of GSSG is measured by means of glutathione reductase reaction in which NADPH is oxidized and measured at 340 nm.

Statistical Analysis

The data obtained from the patient and control groups were expressed as Mean ± SD and compared by using Student's t-test. Correlation analysis between study group parameters was performed by using Pearson correlation test.

RESULTS

Demographic and clinical profile of the control group subjects and MS patients are depicted in Table 1. MS patients of both the sex in 1:1 ratio were taken in account to avoid the potential confounding factor i.e sex difference. Systolic blood pressure ($p< 0.05$; 11.36% high), diastolic blood pressure ($p< 0.05$, 19.6% high), BMI ($p<0.05$, 15.75% high) and waist circumference ($p<0.05$, 17.75% high) were significantly high in MS patient than healthy controls (Table 1).

Table-1: Demographic and clinical profile of controls (Group I) and MS (Group II) subjects. (Mean ± SD)

S.No.	Particulars	Group I (N= 100)	Group II (N=100)
1	Age (years)	38.40 ± 8.4	42.25 ± 7.5
2	Systolic pressure (mmHg)	112 ± 7.0	134 ± 8.4**
3	Diastolic pressure (mmHg)	74.6 ± 4.4	88.2 ± 6.5**
4	Height (meter)	1.67 ± 0.8	1.65 ± 0.6
5	Weight (kg)	64.27 ± 5.6	78.65 ± 6.4
6	BMI	23.05 ± 2.2	26.68 ± 2.3**
7	Waist Circumference (cm)	81.22 ± 8.2	95.64 ± 8.7**
8	Hip (cm)	91.12 ± 7.5	106.24 ± 7.8
9	Waist-hip ratio	0.85 ± 0.07	0.94 ± 0.06

Where, * $p < 0.1$: Non-significant; **$p<0.05$: Significant, BMI= Body mass index

Erythrocyte GSHPx activity and serum lipid profile data showed significant abnormalities in the patients group as represented in Table 2. Erythrocyte GSHPx activity was significantly low (37.21%; $p<0.001$) in MS patients as compared to healthy controls due to increased oxidative stress. Serum HDL levels were found to be reduced significantly ($p<0.05$; 19.24% low) in the MS patients, whereas serum total cholesterol, triglyceride, LDL and VLDL levels were found to be significantly high ($p<0.001$) in metabolic

syndrome patients as compared to healthy controls. Moreover, a significant correlation was observed between erythrocyte GSHPx activity and lipid profile components, as depicted in Figure 1. GSHPx activity was positively correlated with serum HDL levels in MS patients whereas GSHPx activity was negatively correlated with total cholesterol, triglycerides, LDL and VLDL levels ($p < 0.001$).

Table-2: Erythrocyte Glutathione peroxidase activity and serum lipid profile of study group subjects. (Mean ± SD)

S.No.	Particulars	Group I N= 100	Group II N=100
1	GSHPx (IU/gm Hb)	34.64 ± 2.32	21.75 ± 1.34***
2	Total cholesterol(mg/dl)	157.5 ± 25.6	198.4 ± 31.5**
3	Triglycerides(mg/dl)	84.7 ± 15.4	146.5 ± 17.2***
4	LDL (mg/dl)	97.5 ± 13.8	128.4 ± 17.4**
5	HDL(mg/dl)	44.8 ± 5.2	33.4 ± 4.7**
6	VLDL (mg/dl)	21.6 ± 3.2	32.5 ± 4.4***

where, * $p < 0.1$: Non-significant,** $p < 0.05$: Significant,*** $p < 0.001$: Highly significant

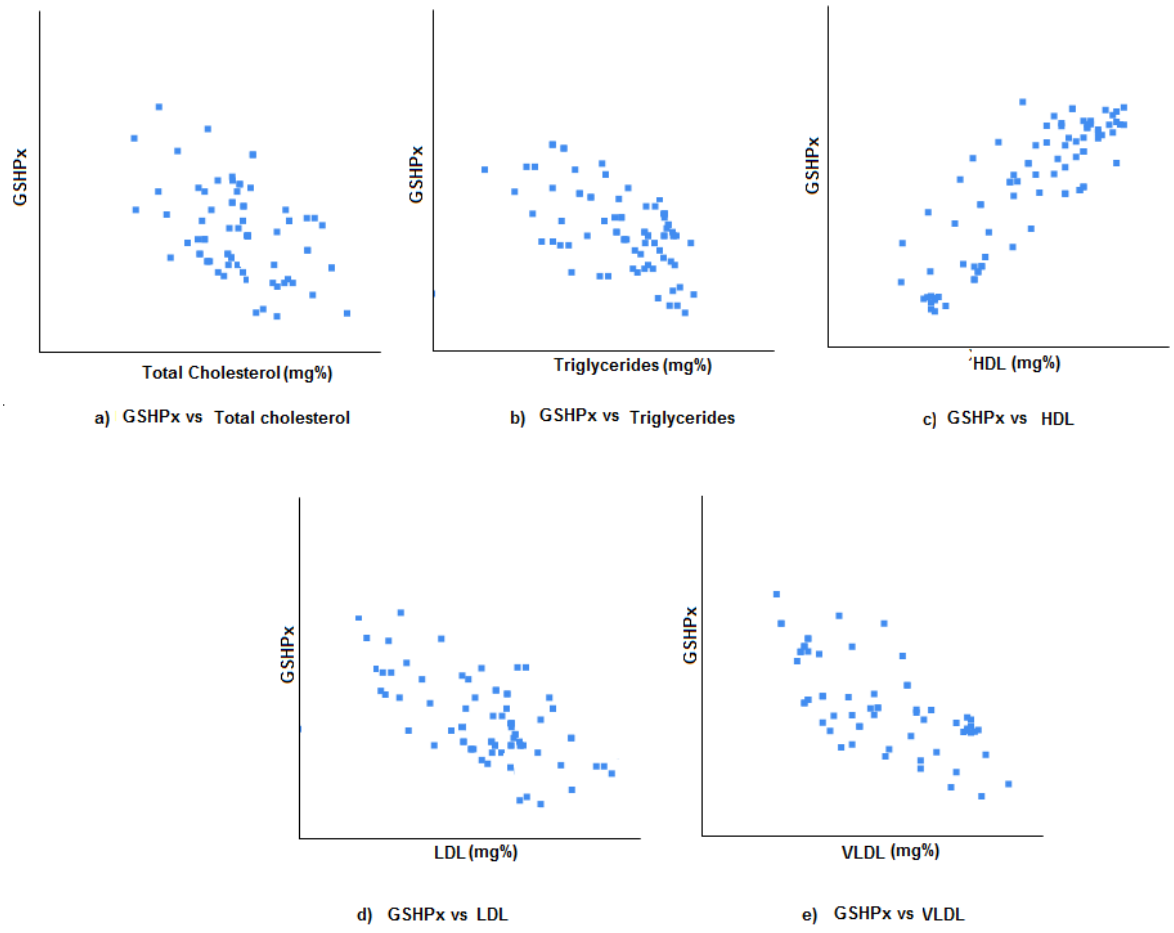

Figure 1: Correlation of Glutathione peroxidase (GSHPx) with lipid profile in MS patients

DISCUSSION

Metabolic syndrome (MetS) is considered a public health problem worldwide, both in developed as well as developing countries [7,14]. Amongst various factors, oxidative stress is known to play a crucial role in the pathophysiology of metabolic syndrome and its components. The production of free radicals and its culprit effect on biomolecules is effectively regulated by antioxidant reserves of body. In particular, increased oxidative stress has been found to be associated with decreased antioxidant enzyme activity which can lead to metabolic upsets and changes in cell signaling. In this context, H_2O_2 produced via dismutation reaction of $O_2^{-\cdot}$ is mainly removed by glutathione peroxidase.

Erythrocyte GSHPx activity was found to be significantly low along with altered lipid profile ($P< 0.001$; Table 2) as compared to controls which 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. Our findings were quite similar to the recent findings of Sabir *et al*. who have also reported the marked oxidative damage and altered antioxidant defense system in metabolic syndrome patients having characteristic high blood pressure [15]. Similarly, altered antioxidant protection as well as increased oxidative damage has been observed in different studies related to MS patients [16-18]. However, some researchers did not find any difference in the level in the antioxidant vitamins between the subjects with metabolic syndrome and those without metabolic syndrome [19].

Moreover, dyslipidemia has been known to be associated with several clinical conditions such as cardiovascular disease, hypertension, diabetes and vascular diseases [20, 21]. Dyslipidemia seen in patients with metabolic syndrome further leads to increased production of free fatty acids that are substrates for ROS[22]. The oxidized form of LDL and TGs are known to play important roles in the pathogenesis of atherosclerosis and increased predisposition to oxidative stress. On the contrary, HDL has antioxidant properties and has a protective role against oxidation. The oxidative changes of lipoprotein metabolism, therefore, plays an important role in the development of cardiovascular diseases [23].

In the present study, abnormal lipid profile was observed in MS patients along with oxidative stress as characterized by low GSHPx activity and its inverse correlation with components of lipid profile except HDL cholesterol. These results clarify the role of oxidative stress in enhancing the CVD risk in MS patients most probably by its relation with abnormal lipid profile. Furukawa *et al.* found a correlation between fat accumulation and systemic oxidative stress in humans and mice[24]. Thus, it is obvious that occurrence of dyslipidemia in MS patients and its association with oxidative stress play a crucial role in solving the anonymity of future CVD incident in MS patients.

CONCLUSION

On the basis of present study and consistent findings of previous studies we can conclude that dyslipidemia plays an etiopathological role in the development of MS and erythrocyte glutathione peroxidase activity is inversely related to components of lipid profile in metabolic syndrome. Thus, erythrocyte GSHPx activity may be an excellent marker of oxidative stress in MS. Furthermore, it is obvious that oxidative stress is emerging as a major underlying mechanism in the metabolic syndrome. As the oxidative stress in MS increases, erythrocyte GSHPx activity decreases continuously not only due to its free radical scavenging action but also in maintaining body's antioxidant reserve. Therefore, our study suggests that the diet rich in antioxidants is essential for MS patients and consumption of fruit, vegetables and grains should be increased with the appearance of MS related factors. In addition, there is a need to educate the community and adoption of healthy life style with regular physical exercise should be recommended in the management of MS.

REFERENCES

1. Doelle GC. The clinical picture of metabolic syndrome: an update on this complex of conditions and risk factors. Postgraduate Medicine. 2004; 116(1): 30–38.
2. Shrestha S, Saxena R, Srivastava S, Thakur RK. Evaluation of cardio metabolic profile, endothelial dysfunction and oxidative stress in Metabolic Syndrome: A comparative perspective. Medical Science. 2016; 4(3): 334-340.
3. Isomaa B, Almgren P, Tuomi T, Forsen B, Lahti K, Nissen M. Cardiovascular morbidity and mortality associated with the metabolic syndrome. Diabetes Care 2001; 24:683–689.
4. Butler J, Rodondi N, Zhu Y, Figaro K, Fazio S, Vaughan DE. Metabolic syndrome and the risk of cardiovascular disease in older adults. J Am Coll Cardiol 2006; 47:1595–602.
5. Skalicky J, Muzakova V, Kandar R, Meloun M, Rousar T, Palicka V. Evaluation of oxidative stress and inflammation in obese adults with metabolic syndrome. Clin Chem Lab Med. 2008;46(4):499–505.
6. Goyal R, Nandkeoliar MK, Saxena V, Payal P, Saxena R. Assessment of Glutathione peroxidase and its correlation with the components of Metabolic syndrome: A biochemical approach. SJAMS. 2017; 5(5A): 1770-1774.
7. Roberts CK, Sindhu KK. Oxidative stress and metabolic syndrome. Life Sci. 2009;84 (21-22):705-12.
8. Sharma D, Gupta N, Saxena R. Glutathione peroxidase and its correlation with the marker of lipid peroxidation in essential hypertension patients. Sch J App Med Sci. 2018; 6(7): 2782-2785.
9. Vávrová L, Kodydková J, Zeman M. Altered activities of antioxidant enzymes in patients with metabolic syndrome. Obes Facts. 2013; 6(1): 39-47.
10. Faldesai N, Shareef MA, Saxena R, Bhattacharya I. Association of vitamin C with erythrocyte malondialdehyde levels in Type 2 Diabetic patients- A clinical approach. Sch. J. App. Med. Sci., 2017; 5(11D):4606-4610.
11. Grundy SM, Cleeman JI, Merz CN, et al. Implications of recent clinical trials for the National Cholesterol Education Program Adult

Treatment Panel III Guidelines. J Am Coll Cardiol. 2004; 44(3): 720-32.
12. Friedewald WT, Levy RI, Friedrickson DS. Estimation of the concentration of LDL – cholesterol in plasma, without use of the preparative ultracentrifugation. Clin. Chem. 1972; 18 : 499 – 502.
13. Beutler E. Red cell metabolism. A manual of Biochemical methods. New York. Grune & Stratlon Inc.1971; 3rd ed. p 112-114.
14. Prasad DS, Kabir Z, Dash AK, Das BC. Prevalence and risk factors for metabolic syndrome in Asian Indians: A community study from urban Eastern India**.** J Cardiovasc Dis Res. 2012; 3(3): 204–211.
15. Sabir AA, Bilbis LS, Saidu Y, Jimoh A, Iwuala SO, Isezuo SA. Oxidative stress among subjects with metabolic syndrome in Sokoto, North-Western Nigeria. Niger J Clin Pract. 2016; 19:128-32.
16. Beydoun MA, Shroff MR, Chen X, et al. Serum antioxidant status is associated with metabolic syndrome among U.S. adults in recent national surveys. J Nutr. 2011; 141: 903-913.
17. Ford ES, Mokdad AH, Giles WH, Brown DW. The metabolic syndrome and antioxidant concentrations: findings from the Third National Health and Nutrition Examination Survey. Diabetes. 2003 Sep 1;52(9):2346-52.
18. Palmieri VO, Grattagliano I, Portincasa P, Palasciano G. Systemic oxidative alterations are associated with visceral adiposity and liver steatosis in patients with metabolic syndrome. The Journal of nutrition. 2006 Dec 1;136(12):3022-6.
19. Veigas NM, Dharmalingam M, Marcus SR. Oxidative stress in obesity and metabolic syndrome in Asian Indians. J Med Biochem. 2011; 30: 115-120.
20. Shanmugasundaram M, Rough SJ, Alpert JS. Dyslipidemia in the elderly: should it be treated? Clin Cardiol. 2010; 33(1): 4-9.
21. Ferrieres J, Amber V, Crisan O, Chazelle F, Junger C, Wood D. Total lipid management and cardiovascular disease in the dyslipidemia international study. Cardiology. 2013; 125(3):154–63.
22. de Oliveira J, Hort MA, Moreira EL, Glaser V, Ribeiro-do-Valle RM, Prediger RD. Positive correlation between elevated plasma cholesterol levels and cognitive impairments in LDL receptor knockout mice: Relevance of cortico-cerebral mitochondrial dysfunction and oxidative stress. Neuroscience. 2011; 197: 99-106.
23. Demircan N, Gurel A, Armutcu F, Unalacak M, Aktunc E, Atmaca H. The evaluation of serum cystatin C, malondialdehyde, and total antioxidant status in patients with metabolic syndrome. Med Sci Monit 2008;14:CR97-101.
24. Furukawa S, Fujita T, Shimabukuro M, Iwaki M, YamadaY, Nakajima Y. Increased oxidative stress in obesity and its impact on metabolic syndrome. J Clin Invest. 2004; 114: 1752–61.