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THE STUDY OF OXIDANT & ANTIOXIDANT STATUS IN NEPHROTIC SYNDROME

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ABSTRACT *Nephrotic syndrome is a clinical syndrome caused by the increased permeability of the glomerular capillary wall for macromolecules. Peroxidation of lipid membranes raises the concentration of their by product MDA and the consequent lowering of antioxidants as a result of consumption. Therefore, this study was carried out to investigate oxidant and antioxidant status in nephrotic syndrome patients. The blood samples were analyzed for quantitation of malondialdehyde as index of lipid peroxide, total antioxidant capacity, homocysteine and lipoprotein (a). Significantly increased levels of serum lipid peroxide, homocysteine and decreased levels of serum total antioxidant capacity were noticed in the patients with nephrotic syndrome as compared to control subjects. However, significant positive correlation in lipid peroxide with homocysteine and negatively correlated with total antioxidant capacity were observed.*

KEYWORDS : Nephrotic syndrome (NS), Total antioxidant capacity (TAC), Homocysteine (HCY), Malondialdehyde (MDA), Lipoprotein (a).

INTRODUCTION

In recent years it has been proposed that Nephrotic syndrome is a consequence of an imbalance between oxidant and antioxidant activity. Nephrotic syndrome is a collection of symptoms which occurs because the tiny blood vessels (The glomeruli) in the kidney become leaky. [1, 2] The present study was aimed to test that the reactive oxygen species are the mediators of excessive protein permeability and other complications of Nephrotic syndrome. [3]

The antioxidant status in NS indicates the pro-oxidant existing in this condition which may have implications in the response to treatment of these patients. [4] Hyperhomocysteinemia is independent risk factor of cardiovascular diseases. Similarly to nephrotic syndrome (NS) predisposes to vein thrombosis. [5]

The nephrotic syndrome is associated with heightened risk for arterial and venous thrombosis. [6] Hyperhomocyst (e)inemia is an independent risk factor for atherothrombosis in several clinical settings in which renal function is impaired, but its prevalence in the nephrotic syndrome has not been investigated in detail.[7] The atherogenic serum lipoprotein(a) [Lp(a)] is significantly elevated in patients with nephrotic syndrome. The nephrotic syndrome on lipoprotein(a) [Lp(a)], a plasma lipoprotein associated with atherosclerotic cardiovascular disease. [8,9]

Various biochemical parameters that are presently determined in serum/plasma homocysteine, total antioxidant capacity, lipid peroxidation, for the diagnosis of nephrotic syndrome, as well as to determine the changes that occurs in the metabolic process associated with nephrotic syndrome complications. The Purpose of this research is to establish biochemical parameters for the diagnosis of nephrotic syndrome and its complication. To determine the Interrelationship of homocysteine, oxidant and antioxidant through them.

MATERIALS AND METHODS

This study was conducted at the Department of Biochemistry S.S. Medical College Rewa (M.P.) with collaboration of Department of Biochemistry M.G.M. Medical College Indore (M.P.).

The study group: This study was conducted on 2 groups: group I comprised of 135 controls, group II comprised of 133 nephrotic syndrome patients in the age group of 30-80 years.

The patients were diagnosed on the basis of detailed clinical history, clinical examination and other relevant biochemical investigations. The patients suffering from other diseases, such as diabetes, inflammatory diseases, cardiac diseases, hepatic impairment, and respiratory diseases or other systemic diseases as well as smokers and alcoholics, were excluded from the study. Informed consent was obtained from each participant in the study. Fasting venous blood were drawn from all.

Total antioxidant capacity (TAC) in serum was estimated by using spectrophotometric method (Koracevic et al. 2001). [10] MDA, one of the aldehydic by product of lipid peroxidation in serum, was estimated by its thiobarbituric acid reactivity using, spectrophoto metric method (Hunter et al. 1985). [11] Homocysteine was estimated by commercial "Keragen diagnostic kit" using semiautoanalyser.

The values were expressed as mean +/- SD. Student T test was done for comparison of data. The laboratory investigations were performed on groups I & II.

RESULTS

Descriptive statistics of all diagnostic parameters on groups I, II is presented in Table I. There was a statistically significant decreased level of the serum TAC, and increased serum MDA, HCY level in group II when compared to group I. There was significant difference between group I & group II with HCY level ($p<0.001$).

DISCUSSION

Disturbances in oxidant and antioxidant status were observed by many other studies, which is in agreement of our study (Warwick et al. 2000). [12] The plasma ascorbate concentration was significantly lower ($p<0.001$) & decreased ratio of ascorbate: vit E ($p<0.0001$) in group of NS. Low density lipoprotein was protected from oxidation despite the severe hyperlipidemia and the low circulating Vit C. These data suggest that there may be relative deficit of oxidant/antioxidant balance in NS. This could predispose to increased oxidative stress. [12]

In the present study, mean serum MDA level was significantly higher in study group II as compared to group I. This result showed the presence of oxidative stress in adult with NS. The decreased total antioxidant status (TAS) level is related with abnormal intestine absorption of some antioxidants component in patients with NS. There is some data in the literature showing that a diet deficient in Se and Vit C may lead to renal injury characterized by proteinuria and reduced GFR (Bulucu et al. 2000). [13]

Excessive generation of reactive oxygen species is one of the incriminated mechanisms in the pathogenesis of progression renal injury. In fact, the little data is available concerning SOD in NS. Reduced activities of erythrocyte and plasma GSH-Px were reported when compared to the control. Lower Se and erythrocyte Cu-Zn-SOD activity was shown in patients of NS when compared to the control. Erythrocyte and plasma level of MDA were higher in patients with NS.These results obtained in adult NS patients support the previous data indicating abnormalities in antioxidative system of NS (Pawlak K et al. 2005). [14]

During the auto oxidation of HCY in plasma, reactive oxygen species are generated (Coppola et al. 2000). The latter initiates lipid peroxidation in cell membranes (potentially responsible for endothelial dysfunction) and in circulating lipoprotein, oxidized LDLC may trigger platelet activation as well as some of the homeostatic abnormalities reported in such patients. Thus, the oxidative stress induced by HCY may be a key process in the pathogenesis of thrombosis in HHCY. [15]The tremendously increased Lp(a) levels in nephrotic syndrome ar caused by primary genetic as well as disease-related mechanisms [16].Lp(a) and ox-Lp(a) levels were increased in NS children, which may play an important role in the processes of atherosclerosis [17,18].

CONCLUSION

We conclude that oxidative stress is enhanced in NS patients due to hyperhomocysteinemia and decreased level of TAC which may contribute to the development of NS related complication with more frequency such as cardiovascular nephropathy diseases, acute and chronic infection and many other complications. Long-term follow-up in a large number of patients would be necessary to confirm these results.

TABLE

Table I: Comparison of all diagnosed biochemical parameters in group I and II with NS

Parameters	Group I (control)(Mean ± SD)	Group II (Nephrotic Syndrome Patients)(Mean ± SD)
n	135	133
TAC (mmol/L)	2.37 ± 0.87	1.55 ± 0.28*
MDA (nmol/mL)	1.56 ± 0.96	3.58 ± 0.42*
HCY (umol/L)	10.75 ± 3.1	17.77 ± 4.15*
p value		*group I compare to group II *p<0.001

Table II: Correlation coefficient and significance in the patients group II

Parameters	Correlation coefficient (r)	Significance
HCY and MDA	+0.78	p<0.001*a
HCY and TAC	-0.25	p<0.0001*b

*a-Highly significant,*b -Significant

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