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Research Article

The study of lipid profile, LP (a) and electrolytes with oxidative stress, total protein and albumin in nephrotic syndrome

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ABSTRACT

Nephrotic syndrome is characterized by heavy proteinuria, hypoalbuminemia, hyperlipidemia associated with peripheral edema. Recent observation revealed that serum albumin plays an important role in the host defense mechanism as it is one of the important antioxidants. Oxidative damage by free radicals has been implicated in kidney injury, especially in nephrotic syndrome (NS). Therefore, this study was carried out to investigate oxidant and lipoprotein (a) status with protein and electrolytes in nephrotic syndrome patients. The blood samples were analyzed for quantitation of malondialdehyde as index of lipid peroxide, total antioxidant capacity, lipid profile, lipoprotein (a), electrolytes, total protein and albumin. Significantly increased levels of serum lipid peroxide, lipoprotein (a) LDL, VLDL, Tcholand decreased levels of serum total antioxidant capacity and total protein and albumin were noticed in the patients with nephrotic syndrome as compared to control subjects. Electrolytes are variable Na was increased and potassium was decreased. However, significant positive correlation in lipid peroxide with lipoprotein (a),and total protein and albumin with total antioxidant capacity were observed.

Keywords: Nephrotic syndrome (NS), Total antioxidant capacity (TAC), Malondialdehyde (MDA), Total cholesterol (Tchol)

INTRODUCTION

The nephrotic syndrome is defined by heavy proteinuria due to abnormal increase of glomerular permeability and following hypoalbuminemia, hyperlipidemia and edema.[1] Hyperlipidemia is a common feature of the nephrotic syndrome. Hyperlipidemia so commonly complicates with heavy proteinuria that it has come to be regarded as an integral features of nephrotic syndrome lipid abnormalities in patients with the nephrotic syndrome have been recognized.[2] Lipoprotein abnormalities of the nephrotic syndrome are assumed to be related to the presence of proteinuria and risk for CHD.[3,4]

The nephrotic syndrome is associated with an expanded interstitial volume and edema due to the Na and water retention.[5] The pathogenesis, clinical significance, and treatment options of the disturbances in lipid metabolism in adults with persistent nephrotic syndrome are reviewed. The lipoprotein profile is characterized by elevations of total plasma cholesterol and often triglycerides, elevated very low-density lipoprotein and low-density lipoprotein cholesterol, whereas high-density lipoprotein-cholesterol levels are variable; plasma levels of the atherogenic and thrombogenic lipoprotein (a) are also elevated.[6]

Reactive oxygen species are reported to play a role in the proteinuria of nephrotic syndrome. Increase oxidant

stress may contribute to this by means of hyperlipidaemia and hypoalbuminaemia in nephrotic syndrome.[7,8]

Various biochemical parameters that are presently determined in serum/plasma total antioxidant capacity, vitamin C, lipid peroxidation, lipid profile, total protein, albumin, lipoprotein (a) and electrolytes 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 and to determine the Interrelationship of lipoprotein and antioxidant through them.

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.

Lipid profile, Total Protein and Albumin were estimated by a commercially available kit from "AGAPPE" in semiautomatic auto analyzer. LDLC and VLDLC were calculated using friedewalds formula.

Total antioxidant capacity (TAC) in serum was estimated by using spectrophotometric method (Koracevic et al. 2001).[9] MDA, one of the aldehydic by product of lipid peroxidation in serum, was estimated by its thiobarbituric acid reactivity using, spectrophotometric method (Hunter et al. 1985).[10] Plasma ascorbic acid (Vit C) was measured by colorimetric method (Roe and Kuether et al. 1943).[11] Lp(a) was estimated by 'Turbidimetric method' a commercially available kit from "Human diagnostic kit". Na^+ and K^+ were estimated by flame photometer.

The values were expressed as mean +/- SD. Student test was done for comparison of data. The laboratory investigations were performed on groups I & II. The study was approved by the ethics committee of the D.A.V.V. University.

RESULTS

Descriptive statistics of all diagnostic parameters on groups I, II presented in Table 1. There was a statistically significant decreased level of the serum TAC, vitamin C, total protein, albumin, potassium and increased serum MDA, lipoprotein (a), total cholesterol, triglyceride, very low density lipoprotein, low density lipoprotein and sodium level in group II when compared to group I. There was significant difference between group I & group II with lipoprotein (a) level ($p<0.001$).

Table 1: Comparison of all diagnosed biochemical parameters in group I and II with NS.

Parameters	Group I (control) (Mean ± SD)	Group II (Mean ± SD)
n	135	133
TGs (mg/dL)	112.09 ± 10.16	196.64 ± 23.89*
Tchol (mg/dL)	173.71 ± 15.44	297.14 ± 25.92*
VLDLc (mg/dL)	22.40 ± 1.98	39.34 ± 3.7*
HDLc (mg/dL)	49.15 ± 7.4	39.63 ± 1.28*
LDLc (mg/dL)	103.68 ± 8.24	217.38 ± 19.36*
TP (g/dL)	6.90 ± 1.6	3.26 ± 3.3*
Alb (g/dL)	4.34 ± 0.37	1.37 ± 0.70*
Na (milieq/L)	137.29 ± 1.35	170.89 ± 3.81*
K (milieq/L)	4.73 ± 0.21	3.22 ± 0.91*
Lp (a) (mg/dL)	18.15 ± 9.7	28.44 ± 2.06*
TAC (mmol/L)	2.37 ± 0.87	1.55 ± 0.28*
MDA (nmol/mL)	1.56 ± 0.96	3.58 ± 0.42*
Vit C (mg/dL)	1.48 ± 0.65	0.68 ± 0.48*
p value		*group I compare to group II *p<0.001

Table 2: Correlation coefficient and significance in the patients group II.

Parameters	Correlation coefficient (r)	Significance
Lp (a) and MDA	+0.86	p<0.001*a
LDLc and Lp(a)	+0.82	p<0.001*a
Lp (a) and TAC	-0.22	P<0.0001*b
TP and LP(a)	- 0.37	P<0.0001*b
TP and TAC	+ 0.50	P<0.001*a
TP and MDA	-0.55	P<0.001*a

*a-Highly significant, *b-Significant

DISCUSSION

Lipid abnormalities in patients with the nephrotic syndrome have long been recognized. However, the significance of these lipid abnormalities, the mechanisms producing them, and their potential treatment has all been a cause of debate. Recent data have helped clarify each of these areas of controversy. Studies of the lipoprotein abnormalities of patients with the uncomplicated nephrotic syndrome have shown that many will have elevated levels of total and low-density lipoprotein cholesterol, whereas only a few will have elevated levels of high-density lipoprotein cholesterol. If these lipid abnormalities have the same significance in this population as in other populations studied, then some patients with unremitting nephrotic syndrome will be at high risk for cardiovascular disease. The elevated cholesterol levels noted in the nephrotic syndrome are caused primarily by enhanced hepatic synthesis, with lesser contributions by decreased clearance and altered enzyme activities. The signal for enhanced hepatic lipogenesis may relate to changes in plasma albumin concentration, plasma oncotic pressure, a local effect of viscosity at the hepatic sinusoidal level, or a loss of urinary proteins or other liporegulatory substances.[12]

Although hyperlipidemia is a common feature of the nephrotic syndrome, the distribution of cholesterol among the plasma lipoproteins and the mechanism of the enhanced hepatic synthesis of lipoprotein lipids. Enhanced hepatic synthesis of lipoprotein lipids may be stimulated by a decreased plasma albumin concentration or oncotic pressure but does not appear to be due to changes in plasma viscosity.[13]

Hyperlipidemia is a hallmark of nephrotic syndrome that has been associated with increased risk for ischemic heart disease as well as a loss of renal function in these patients.[14] Triglyceride (TG)-rich lipoproteins are primarily increased in the nephrotic syndrome (NS) as a result of decreased catabolism. Lipoprotein lipase (LpL) is the rate limiting enzyme for lipolysis of TG. The biologically active endothelial bound LpL pool is reduced in NS providing one mechanism for decreased clearance of very low density lipoprotein (VLDL).[15]

In the nephrotic syndrome abnormal sodium and water retention occurs at the kidney level that ultimately causes expansion of interstitial volume and edema.[16,17] Sodium retention and edema are common features of nephrotic syndrome that are classically attributed to hypovolemia and activation of the renin-angiotensin-aldosterone system.[16]

Recent literature data suggest that the roles of albumin, intravascular volume, and neurohormones on edema formation and highlight the evolving literature on the role of primary sodium absorption in edema formation. Mechanisms in addition to sodium retention are likely operant in the formation of nephrotic edema.[18]

Literature data suggest that a primary impairment in sodium excretion is the basic abnormality in the pathogenesis of edema formation in the nephrotic syndrome, there is evidence that functional hypovolemia contributes to stimulation of renal sodium and fluid retention. Vasoactive hormones such as renin and aldosterone are involved in this process. Discrimination between both mechanisms would be possible by assessment of aldosterone bioactivity and will have therapeutical consequences by indicating the need for administration of i.v. albumin or diuretics.[19]

The tremendously increased Lp (a) levels in nephrotic syndrome are caused by primary genetic as well as disease-related mechanisms.[20] Lp (a), ox-Lp (a) and Lp (a)-IC levels were increased in NS, which may play an important role in the processes of atherosclerosis.[21] Nephrotic syndrome, the increased Lp (a) levels are mainly related to hypoalbuminemia, probably through a mechanism involving Apo B overproduction, which leads to an increased number of LDL particles to be converted into Lp (a).[22]

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 connected 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). Excessive generation of reactive oxygen species is one of the incriminated mechanisms in the pathogenesis of progression renal injury.[23]

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.[24]

EI Melegy et al. recently reported significantly higher serum level of malondialdehyde, oxidized LDL, Tchol, LDLc, TGs apolipoprotein A-I and apolipoprotein B. The serum level of albumin, glutathione peroxidase activity, Vitamin C, Vitamin E and HDLc were significantly lower, a significant strong relationship between the oxidant/antioxidant status and dyslipidemia was documented in patients with steroid sensitive nephrotic syndrome, especially among relapsers.[25]

Scrzep-Polozek B et al. showed that higher amounts of electro negatively charged (oxidized) LDL particles as well as different oxysterol in patients have also been reported, significant disturbances in oxidant/antioxidant status during NS leading to plasma accumulation of oxidized LDLc and cholesterol oxidation products that exert cytotoxicity and were known to induce atherosclerosis.[26]

Recent observation revealed that serum albumin plays an important role in the host defence mechanism as it is one of the important antioxidants. Our results suggest that decreased antioxidant potentials caused by hypoalbuminemia in NS may contribute to an aberrant immunity.[27]

Changes in the concentrations of malondialdehyde, lipoproteinemia (a), TAC, electrolytes, total protein and albuminare compatible with increased amounts of oxidation in nephrotic syndrome.

CONCLUSION

We conclude that oxidative stress is enhanced in NS patients due to hypoalbuminemia, hypoproteinuria, hyperlipoproteinemia (a) and decreased level of TAC and increased MDA which may contribute to the development of NS related complication with more frequency such as cardiovascular nephropathy disease, 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.

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