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Original article

Study of Atherogenic Indices In Nephrotic Syndrome

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ABSTRACT

Nephrotic Syndrome (NS) describes the clinical state characterized by the presence of proteinuria, hypoalbuminemia and edema. Dyslipidemia is a contributory factor in the progression of initial glomerular injury in NS. The aim of the present study was to estimate the Atherogenic indices: Cardiac Risk Ratio (CRR), Atherogenic Coefficient (AC), Atherogenic Index of Plasma (AIP) in adult NS patients. The present study was conducted on 99 normal healthy adult subjects & 315 adult NS patients amongst which 105 controlled NS patients with primary NS, 105 managed NS patients which were on remission & 105 uncontrolled NS patients with complications. CRR AIP & AC were found to be increased in all three types of NS patients. CRR in controlled NS was increased significantly (7.16 ± 2.05), (P<0.000) when compared with normal healthy subjects (3.71 ± .95). There was significant decrease in CRR during remission (5.91±1.25), (p<0.000) when compared with controlled NS. In uncontrolled NS, further significant increase was observed in CRR (14.51±3.94), (p<0.000) when compared with controlled NS. AIP in controlled NS was increased significantly (0.96 ± .322), (P<0.000) when compared with normal healthy subjects (-0.21 ± 0.35). There was significant decrease in AIP during remission (0.291±0.205), (p<0.000) when compared with controlled NS. In uncontrolled NS, further significant increase was observed in AIP (1.511 ±0.336), (p<0.000) when compared with controlled NS. AC in controlled NS was increased significantly (6.16 ±2.05), (P<0.000) when compared with normal healthy subjects (2.71± 95). There was significant decrease in AC during remission (4.91±1.25), (p<0.000) when compared with controlled NS. In uncontrolled NS, further significant increase was observed in AC (13.51±3.945), (p<0.000) when compared with controlled NS. The study results support the hypothesis that impairment in the endothelial functions constitute a link between Nephrotic Syndrome & atherosclerosis etc. These disturbances were dependent on the degree of proteinuria and decrease in serum albumin concentration. The patients with severe clinical course of Nephrotic Syndrome were at high risk of accelerated atherogenesis.

1. Introduction

Nephrotic Syndrome (NS) describes the clinical state characterized by the presence of proteinuria, hypoalbuminemia and edema. Dyslipidemia is a contributory factor in the progression of initial glomerular injury in NS. Abnormal lipid metabolism is common in patients with renal disease [1]. This effect is most prominent in the nephrotic syndrome, where marked elevations in the plasma levels of cholesterol, LDL, triglycerides and lipoprotein (a) often occur [2]. Total HDL-cholesterol levels are usually normal or reduced in the nephrotic syndrome and there is often a pronounced decline in the cardioprotective HDL-2 fraction.[3]. Proteinuria and reduced eGFR were associated with a higher rate of thromboembolism [4].According to Dobiasova M, Frohlich J et.al., (2004)[5], the Atherogenic Index of Plasma (AIP) is defined as log (TG/HDL-C). AIP has recently been proposed as a marker of plasma atherogenicity because it is increased in people at higher risk for coronary heart disease and is inversely correlated with LDL particle size. AIP may be an important tool for analyzing the results of clinical trials. The association of TGs and HDL-C in this simple ratio theoretically reflects the balance between risk and protective

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lipoprotein forces, and both TGs and HDL-C are widely measured and available. AIP reflects the delicate metabolic interactions within the whole lipoprotein complex[1]. The aim of present study was to know the risk of atherosclerosis by determining atherogenic indices in Nephrotic Syndrome.

2.Material & Methods:

2.1.Experimental design

Present study was conducted during January 2007 to April 2010 on Nephrotic Syndrome subjects who were outdoor and Indoor patients of Nephrology Department of M.G.M. Medical College Indore and other private hospitals like Bombay hospital, CHL Apollo and clinics like Ideal pathology of Indore.The present study included 315 Nephrotic syndrome patients and 99 age and sex match healthy control subjects. They were categorized in the following four groups.

2.1.1.A. Control Group: In this group 99 normal healthy subjects were included, which were free from any illness by clinical examination and taking balance diet with no history of NS and CVD.

2.1.2.B. Controlled (Pre treated) NS: In this group 105 Nephrotic syndrome patients with PNS, with no active medical complication were included.

2.1.3.C. Managed (Post treated) NS group: In this group 105 adult Nephrotic syndrome patients who are on remission after receiving standard oral corticosteroid induction therapy for one month were included.

2.1.4.D. Uncontrolled NS: In these groups 105 patients with complicated nephrotic syndrome were included.

2.2.Biochemical investigation

The patients were diagnosed on the basis of detailed clinical history; clinical examination and other relevant biochemical investigations.After 12 hours overnight fasting 10 ml venous blood were drawn from all subjects. The blood was allowed to clot at room temperature and centrifuged at 5000 rpm for 10 minutes and then the serum was kept frozen at -70°C in aliquots until the time of assay of the parameters. Biochemical parameters selected for present study were determined by using commercially available kit from Lab Kit diagnostics from Span in semi automated auto analyzer. LDL-Cholesterol level was calculated by using Friedewald's equation. Serum TAC was measured by the method described by Koracevic et al [6].Serum MDA was measured by colorimetric method described by Ohkawa et al [7].Lp a) was estimated by a commercially available kit from human diagnostic kit method. Homocysteine was estimated by a commercially available kit from Keragen diagnostic kit method.

The atherogenic indices were calculated as follows:

Cardiac Risk Ratio (CRR) =TC/HDLC [8]
Atherogenic Coefficient (AC) = (TC HDLC)/HDLC)[9]
Atherogenic Index of Plasma (AIP) = log (TG/HDLC) [5]
(Note: for calculation of atherogenic indices we have converted mg/dl values of TC, HDL-C, and TG into mmol/L).

3.Result

Table shows Comparisons of all diagnosed biochemical parameters between control and patients (pre-treatment & post-treatment NS)

4.Discussion:

Epidemiological studies have shown that an elevated concentration of total cholesterol in the blood is a powerful risk factor for coronary disease [10].An increased plasma level of LDL-cholesterol were found in Nephrotic Syndrome, and is a risk factor for cardiovascular disease. A high plasma triglyceride level is both an independent and synergistic risk factor for cardiovascular diseases [11]. Low plasma HDL-C is a risk factor for cardiovascular diseases[12]. High HDL exerts a protective effect by enhancing reverse cholesterol transport by scavenging excess cholesterol from peripheral tissues, which it esterifies with the aid of lecithin: cholesterol acyltransferase (LCAT), then delivers to the liver and steroidogenic organs for subsequent synthesis of bile acids and lipoproteins , eventually eliminated from the body inhibiting the oxidation of LDL as well as the atherogenic effects of oxidized LDL by virtue of its antioxidant property [13] and anti-inflammatory property [10]. The increase oxidative stress and high atherogenic index in CKD may accelerate the process of cardiovascular complications in adult SCD patients. Atherogenic index of plasma was negatively correlated with antioxidant enzymes and positively with MDA [14].

Atherogenic indices are powerful indicators of the risk of heart disease: the higher the value, the higher the risk of developing cardiovascular disease and vice versa.[15].Universally, atherogenic index of plasma (AIP) calculated as log (TG/HDL-C) has been used by some practitioners as a significant predictor of atherosclerosis [16],[17]. Dobiasova M (2006)[18] suggested that AIP was a highly sensitive marker of differences of lipoprotein profile in patients. AIP values of -0.3 to 0.1 are associated with low, 0.1 to 0.24 with medium and above 0.24 with high cardiovascular risk. In this study we observed that AIP values is highest in Uncontrolled NS (1.51±0.34) and significantly high in controlled NS (0.96±0.32) as compared to control. Thus the result of present study indicates that NS patienrs have high risk of CV. Treatment with ciprofibrate, and combination of statin and niacin dramatically decreased AIP as was observed in managed NS (29±0.21).Universally, atherogenic index of plasma (AIP) calculated as log (TG/HDL-C) has been used by some practitioners as a significant predictor of atherosclerosis[16][17].

lipoprotein forces, and both TGs and HDL-C are widely measured and available. AIP reflects the delicate metabolic interactions within the whole lipoprotein complex[1]. The aim of present study was to know the risk of atherosclerosis by determining atherogenic indices in Nephrotic Syndrome.

Table shows Comparisons of all diagnosed biochemical parameters between control and patients (pre-treatment & post-treatment NS)

Parameter	Control	Controlled NS (Pre-treatment)	Uncontrolled NS (Pre-treatment	Managed NS (Post-treatment)	p-value
Albumin (gms/dl)	4.33±0.33	2.47±0.57	1.90±0.29	3.44±0.48	a<0.0001,b<0.0001, c<0.0001,d<0.0001
tHcy (µmol/l)	7.58±2.47	10.11±2.85	14.68±6.40	10.08±3.08	a<0.0001,b<0.0001, c<0.0001,d<0.942
Lp(a) (mg/dl)	8.89±4.84	44.74±28.24	63.05±52.87	28.00±27.30	a<0.0001,b<0.0001, c<0.0001,d<0.0001
MDA (nmol/ml)	2.91±0.67	5.12±1.98	8.40±2.18		a<0.001,b<0.0001, c <0.001,d<0.0001
TAC (mmol/L	1.94±0.16	1.30±0.20	1.24±0.35	1.76±0.24	a<0.001,b<0.0001, c<0.0001, d<0.0001
Zinc (µg/dl)	118.11±29.43	92.75±20.14	93.80±19.97	117.25±20.94	a<0.001, b<0.0001, c<0.243,d<0.0001
Copper (µg/dl)	106.19±18.35	88.01±20.92	87.65±18.98	102.37±17.43	a<0.001, b<0.0001, c<0.055, d<0.0001
TC (mg/dl)	170.68±23.87	305.90±63.00	402.31±28.39	270.37±44.62	a<0.001,b<0.0001, c<0.000 ,d<0.0001
TG (mg/dl)	90.69±28.89	267.68±69.63	301.55±55.51	142.80±23.26	a<0.0001,b<0.0001, c<0.0001,d<.006
HDL-C (mg/dl)	48.35±11.16	44.00±7.00	29.65±8.01	46.61±6.5	a<0.001,b<0.0001, c<0.175,d<.006
LDL-C (mg/dl)	104.19±26.52	208.36±61.42	312.35±31.41	195.19±44.41	a<0.0001,b<0.0001, c<0.0001,d<0.077
Atherogenic Index of plasma(AIP)	-0.22±0.36	0.96±0.32	1.51±0.34	.29±0.21	a<0.001,b<0.0001, c<0.0001, d<0.0001
Cardiac risk ratio	3.71±0.96	7.17±2.06	14.51±3.95	5.91±1.26	a<0.001,b<0.0001, c<0.0001, d<0.0001
Atherogenic coefficient	2.71±0.96	6.17±2.06	13.51±3.95	4.91±1.26	a<0.001,b<0.0001, c<0.0001, d<0.0001

Note: a - Control versus Controlled NS. b- Control versus Uncontrolled NS, c-Control versus Managed NS, d- Managed NS versus Controlled NS.P value indicates, <0.05 significant, <0.001 highly significant, <0.000 extremely significant

5.Conclusion:

Until this is rectified, AIP which can easily be calculated from standard lipid profile can act as an adjunct that significantly adds predictive value beyond that of the individual lipids, and/or TC/HDL-C, LDL/HDL-C ratios. Dietary interventions and increased physical activity should also be encouraged in Nephrotic Syndrome patients, especially when there are other associated risk factors.

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