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Research Article

Serum Apolipoprotein A-I, Apolipoprotein B and Apo B/Apo A-I ratio as cardiovascular risk indicators in patients of Chronic Renal Failure

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Abstract

Aim: To study the levels of serum lipid profile, serum Apolipoprotein A-I and Apolipoprotein B in patients of Chronic Renal failure and to find out the Apo B/Apo A-I ratio as cardiovascular risk indicator in patients of Chronic Renal Failure.

Material and Methods: 45 patients of Chronic Renal failure & 45 healthy controls were studied. Blood samples were analyzed for serum Apolipoprotein A-I and B by Turbidimetric Immunoassay method on automated chemistry analyzer. Unpaired t-test was used to assess the significant difference in the means of the studied variables in the different groups.

Results: The mean level of serum apolipoprotein A-I was found to be lower (101.5 ± 13.6 and 130.7 ± 14.2, p <0.0001) and serum apolipoprotein B was higher (126.7 ± 16.6 and 102.9 ± 16.4, p <0.0001) in patients of Chronic Renal Failure when compared with the control group. The mean Apo B/Apo A-I ratio was higher in 82% patients of Chronic Renal Failure compared with the control group (1.27 ± 0.26 and 0.80 ± 0.17, p <0.0001), with normal total cholesterol level in 67% patients and normal LDL level in 64% patients with CRF and moderately correlates with S. creatinine levels.

Conclusion: Apo B/ Apo A-I ratio is high in patients of Chronic Renal failure and could be an independent risk factor for atherosclerosis and could contribute towards increasing the risk of cardiovascular diseases (CVD) in patients of Chronic Renal failure.

Keywords: Chronic Renal Failure, Serum Apo B / Apo A-I ratio

1. Introduction

Chronic kidney disease (CKD) encompasses a spectrum of different pathophysiologic processes associated with abnormal kidney function, and a progressive decline in glomerular filtration rate (GFR). The term Chronic Renal Failure (CRF) applies to the process of continuing significant irreversible reduction in nephron number, and typically corresponds to CKD stages 3–5 (GFR <30ml/min Per 1.73 m^2)[1]. CRF is associated with premature atherosclerosis which is driven by multiple risk factors, including dyslipidemia and oxidative stress[2].

Cardiovascular disease is also the leading cause of morbidity and mortality in patients at every stage of Chronic Kidney Disease. Between 30 to 45% of patients reaching stage 5 of CKD already have advanced cardiovascular complications. So focus of patient care in earlier CKD stage should be directed for prevention of cardiovascular complications[1].

The dyslipoproteinemia of renal disease has characteristic abnormalities of the apolipoprotein profile and lipoprotein composition. It develops during the asymptomatic stages of renal insufficiency and becomes more pronounced as renal failure advances[3]. The most characteristic feature of the CRF- associated dyslipidemia is the accumulation of apolipoprotein B-containing triglyceride-rich lipoprotein particles in the very low density (VLDL) and intermediate density range (IDL). This results in increased triglycerides in conjunction with low levels of high density lipoprotein (HDL) cholesterol[4].

Renal dyslipoproteinemia may contribute to the development of atherosclerotic vascular disease and progression of glomerular and tubular lesions with subsequent deterioration of renal function[3].

1.1 Pathophysiology of CRF induced dyslipidemia[5]

- Hypertriglyceridemia due to decrease in Lipoprotein lipase and hepatic lipase.
- Up regulation of HMG-Co A reductase.
- Down regulation of LDL receptors and LDL receptor related protein.
- Decrease in Lecithin Cholesterol Acyl Transferase (LCAT).
- Increase in Cholesterol Ester Transfer Protein (CETP), so increase in HDL triglyceride levels.
- Decrease in scavenger receptor- B1 (SR-B1) receptor.
- Increase in Acyl cholesterol acyltransferase (ACAT).
- Increase in Apo C-III and Apo B levels.
- Decrease in Apo A-I levels.

Initially the estimation of serum lipids like cholesterol, triglycerides, LDL and HDL were used to assess the risk of coronary heart disease. However, the inconsistency in the correlation between serum lipid profile and coronary heart disease, led to the development of better indicators. Among them the estimation of serum apolipoproteins as a risk factor in coronary heart disease and also as a marker has shown great promise[6].

Apo A-I and B are structural and functional protein components of lipoprotein particles that serve as transporters of cholesterol[7]. Apo A-I and HDL are protective; Apo B and LDL are atherogenic. Increased Apo B /Apo A-I ratio was seen in CHD patients[8]. The ratio reflects two powerful components of risk and provides a tool to express the balance between the proatherogenic and the antiatherogenic lipoproteins. More recent work however provides growing evidence that apo B and apo A-I are more effective indicators of Cardiovascular risk[9].

Purpose of the study was to estimate the levels of serum Apolipoprotein A-I, Apolipoprotein B and serum lipid profile and to find out Apo B/Apo A-I ratio and its role as cardiovascular risk indicator in patients of Chronic Renal Failure.

2. Material and Methods

2.1 Study Design

The study was undertaken at the Clinical Chemistry Laboratory of Biochemistry Department at Medical College and S.S.G.Hospital, Baroda. The study parameters were analyzed on fully automated biochemistry analyzer. Ethical Clearance was obtained from the Institutional Ethics Committee for Human Research, Medical College and S.S.G. Hospital, Baroda. Period of data collection was July 2013 to November 2013.

After taking informed consent, blood samples were collected in fluoride vacutainer for sugar estimation, in plain vacutainer for biochemical parameters and in EDTA vacutainer for hemoglobin, ESR and Peripheral smear examination. Urine sample was collected in universal container for urine albumin and urine sugar estimation.

The subjects selected for the study were grouped as follows:

2.2 Inclusion criteria

Group I – Control group (n=45)

This group consisted of age and sex matched healthy subjects from medical or paramedical staff and persons coming to hospital for fitness purpose & for routine health check up.

Group II – Patients with Chronic Renal Failure (n=45)

Clinically diagnosed patients of Chronic renal failure with age group of 30-65 years with altered renal function test.

2.3 Exclusion criteria

The following patients were excluded from the study:

1. Patients on lipid lowering agents e.g. Statins.
2. Patients with coronary artery disease with atrial fibrillation or pacemaker.
3. Patients with history of stroke, intermittent claudication, peripheral vascular disease, carotid surgery, coronary artery bypasses graft surgery or PTCA.
4. History of hemodialysis or/and peritoneal dialysis.
5. Patient having H/O chronic alcohol consumption, hepatobiliary disorders or any other acute liver diseases and diabetes mellitus.

Estimation of serum Apo A-I and Apo B were done by Turbidimetric Immunoassay Method on fully automated biochemistry analyzer Miura-300.[10] Serum lipid profile, renal function test, liver function test and plasma glucose were measured on fully automated biochemistry analyzer and Apo B/Apo A-I ratio was calculated.

2.4 Statistical method

Data analysis was done by MedCalc version 11.5.0.0. Unpaired t-test was used to assess the significant difference in the means of the studied variables in the different groups. Interpretation is done according to p-value as follows:

$p < 0.05$ is considered significant

$p \geq 0.05$ is considered not significant

$p < 0.0001$ is considered highly significant

3. Results

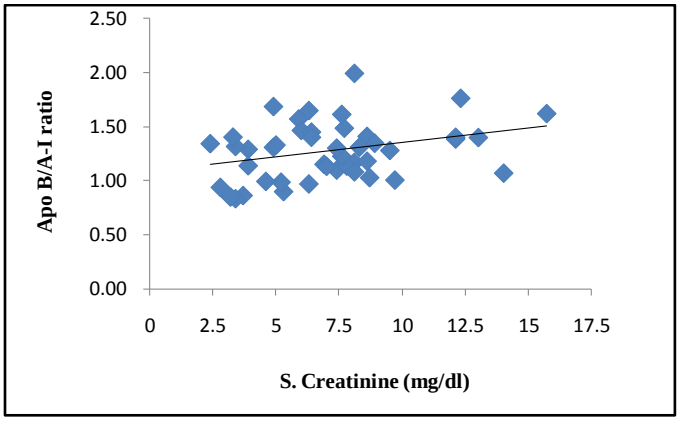
Table 1: Results of the control group and patients with chronic renal failure

		Group I (Controls)	Group II (CRF)	p value
Number of patients		45	45	-
Sex (M/F)		33/12	24/21	-
	Reference range	**Mean ± SD**	**Mean ± SD**	**-**
Average age (years)	-	43 ± 8	45 ± 8	-
S. Urea (mg/dl)	13-45	28 ± 11	151 ± 55	< 0.0001
S. Creatinine (mg/dl)	M:0.7-1.4 F:0.6-1.2	0.9 ± 0.1	7.2 ± 3.1	< 0.0001
S. Total Cholesterol (mg/dl)	< 200	166 ± 20	192 ± 34	< 0.0001
S. HDL Cholesterol (mg/dl)	M: 35-50 F: 45-60	47 ± 6	38 ± 7	< 0.0001
S. LDL Cholesterol (mg/dl)	< 130	98 ± 16	126 ± 26	< 0.0001
S. VLDL Cholesterol (mg/dl)	5-35	20 ± 8	27 ± 8	<0.001
S. Triglyceride (mg/dl)	<150	116 ± 51	151 ± 46	0.001
S. Apolipoprotein A-I (mg/dl)	M:107-177 F:107-205	130.7 ± 14.2	101.5 ± 13.6	< 0.0001
S. Apolipoprotein B (mg/dl)	M:60-138 F:52-129	102.9 ± 16.4	126.7 ± 16.6	< 0.0001
Apo B/Apo A-I ratio	< 1.00	0.80 ± 0.17	1.27 ± 0.26	< 0.0001

Table 2: Distribution of controls and cases according to Apo B/ Apo A-I ratio

Apo B/ Apo A-I ratio	Controls (n=45)	Cases (n=45)
> 1.00 (high)	2 (4%)	37 (82%)
< 1.00 (normal)	43 (96%)	8 (18%)
Inference	Percentage of patients with Apo B/Apo A-I ratio > 1.0 is significantly larger in cases when compared to controls (P < 0.001)	

Figure 1: Graph showing Correlation of S. Creatinine and S. Apo B/A-I ratio in cases (n=45, r=0.3175)



4. Discussion

The study was undertaken to assess the level of serum apolipoprotein A-I and B, Apo B/Apo A-I ratio, serum lipid profile and serum renal function test in patients of Chronic Renal Failure. It is evident from the values across groups that the patients having CRF have raised concentration of Apo B and decreased concentration of Apo A-I compared to the controls. These values also showed large inter-individual variations (SD for Apo A-I is 13.6, Apo B is 16.6) Although normal total cholesterol level in 67% patients and normal LDL level in 64% patients with CRF, Apo B/Apo A-I ratio is significantly high in 82% of CRF cases and moderately correlates with S. creatinine levels.

The occurrence of hyperlipidemia contributes to the high incidence of CHD and increased cardiovascular mortality in patients of chronic renal failure. For over three decades it has been recognized that a high level of total cholesterol and low density lipoprotein cholesterol is a major risk factor for developing CHD but a considerable proportion of patients with CHD have normal levels of LDL and total cholesterol. Prospective and retrospective studies have suggested an independent association between high level of Apo B/ Apo A-I ratio (>1.00) and presence and extent of coronary artery disease and cardiovascular risk. More recently two studies, the AMORIS[11] (17553 cases) study and the INTERHEART study[12] (case control study of acute MI in 52 countries, 15152 cases and 14820 controls), have reported findings that the Apo B/Apo A-I ratio is a significantly better predictor of cardiovascular and stroke risk than any of the conventional cholesterol indices.

In chronic renal failure, lipid profiles are altered and also affect the apolipoproteins. Hence dyslipidemia is present which is commonly associated with atherogenesis. So they are at risk of cardiovascular disease. Apolipoproteins A-I and B can be helpful in early prediction of the cardiovascular risk in CRF patients. By treating such patients with hypolipidemic drugs and diet modification, the morbidity and mortality related to cardiovascular risk can be decreased.

5. Conclusion

The findings shows that increased serum Apo B/ Apo A-I ratio could be an independent risk factor for atherosclerosis and could contribute towards increasing the risk for cardiovascular diseases in patients with Chronic Renal Failure.

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