

Original article

Evaluation of alteration of various lipid parameters including Apolipoprotein A1 and Apolipoprotein B in chronic kidney disease (CKD) patients in a tertiary care centre in Eastern India

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Abstract:

Aim and Objective: -To study the alteration of various lipid parameters including Apolipoprotein A1 and Apolipoprotein B in chronic kidney disease (CKD) patients.

Materials and Methods: -Observational, cross-sectional, hospital-based, single centre study included 100 patients diagnosed with CKD on conservative management or hemodialysis. Blood investigations like complete hemogram, blood urea, creatinine, total cholesterol, LDL, HDL, VLDL, triglycerides, serum apolipoprotein A1 and serum apolipoprotein B and other relevant investigations were done.

Results: -The mean values of Se Total Cholesterol was 245.58(245.58±38.34) , Se LDL 163.75 (163.75±35.06), Se Triglyceride 242.25 (242.25±96.79) and TC/HDL ratio 5.7 (5.7±1.3) were higher than the normal range. In those receiving hemodialysis the Se LDL, Apo B/Apo A1 ratio was found to be significantly higher and Apo A1 was significantly lower when compared to those not on hemodialysis (P<0.05).

Conclusion:-This study showed that there was significant increase in the risk factors resulting in increased cardiovascular disease related mortality amongst all CKD patients. The patients on hemodialysis were probably at more risk than those managed conservatively.

Keywords: -Chronic Kidney Disease (CKD), Low Density Lipoprotein (LDL), Very Low Density Lipoprotein (VLDL), High Density Lipoprotein (HDL), Apolipoprotein A1 (Apo A1), Apolipoprotein B (Apo B), Hemodialysis (HD), Serum (Se).

Introduction:

Chronic kidney disease (CKD) encompasses a spectrum of different pathophysiological processes associated with abnormal kidney function and a progressive decline in glomerular filtration rate (GFR)⁽¹⁾. CKD is a worldwide public health problem, both for the number of patients and cost of treatment involved. Globally, CKD is the 12th leading cause of death and the 17th cause of disability. This is an underestimate as patients with CKD are more likely to die of cardiovascular disease (CVD) than to reach end-stage renal disease (ESRD)⁽²⁾. It is well documented that cardiovascular disease (CVD) is a major cause of morbidity and mortality in patients with CKD⁽³⁻⁷⁾. Thus, although some patients with CKD will ultimately develop end stage renal disease (ESRD), most patients with CKD will die of CVD before dialysis becomes necessary⁽⁸⁾. Several observational studies

have shown that total and LDL- cholesterol values are two of the most important independent predictors of cardiovascular morbidity and mortality⁽⁹⁾. Some recent studies have also shown that apo B/apoAI ratio is a better discriminator of coronary artery disease(CAD) risk in the atherosclerosis-prone Indian population, than any of the conventional lipid ratios. The reduction of value of the apo-B/apo-AI ratio may drastically decrease the risk for CAD. Hence, the apo B/apoAI ratio may be suggested as an alternative to other lipid ratios for risk assessment in patients with CAD^(10,11). Hence noting the prevalence of dyslipidemia and the pattern of rise in various plasma lipoproteins and apolipoprotein in patients of CKD with various clinical profiles would be important. It would help to establish the relevance of doing a routine lipid profile in every newly diagnosed CKD patient and predicting the risk of cardiovascular disease related morbidity and mortality.

Materials and Methods:

The observational, cross-sectional, hospital-based, single centre study was conducted at Nilratan Sircar Medical College & Hospital, A.J.C. Bose Road, Kolkata on diagnosed cases of CKD patients including patients on hemodialysis after informed consent was obtained from them.

The total number of patients under study was 100 with study period from January 2015- December 2016. A detailed history of onset, progression and duration of symptoms of CKD was taken along with other relevant history. A thorough clinical examination as well as blood tests for hyperlipidemia was performed.

The blood samples were collected for investigations like complete hemogram, blood urea, creatinine, total cholesterol, LDL, HDL, VLDL, triglycerides, serum apolipoprotein A1 and serum apolipoprotein B and other relevant investigations were done. Ultrasonogram was done for noting sizes and echotextures of both the kidneys of all patients.

Data Analysis:

For statistical analysis, data were entered into a Microsoft excel spreadsheet and then analysed by SPSS 20.0.1 and GraphPad Prism version 5. Data have been summarized as mean and standard deviation for numerical variables and count and percentages for categorical variables. Student's independent sample's t-test was applied to compare normally distributed numerical variables between groups. Unpaired proportions were compared by Chi-square test or Fischer's exact test, as appropriate. Correlation was calculated by Pearson correlation analysis.

P value \leq 0.05 was considered for statistically significant.

Results:

An observational study was taken to determine lipid profile along with apoA1 and apoB changes in patients with CKD. Among the 100 patients of CKD included in the study, the mean age was 57.85, male to female ratio was 1.4:1, 89% were hypertensive and 84% were on hemodialysis.

The mean Se urea, Se creatinine and eGFR value found were 197mg/dL(197 \pm 57.79), 7.149mg/dL(7.149 \pm 2.47) and 8.614mL/min/1.73m² respectively.

The mean values of Se Total Cholesterol 245.58(245.58 \pm 38.34), Se LDL 163.75 (163.75 \pm 35.06), Se Triglyceride 242.25 (242.25 \pm 96.79) and TC/HDL ratio 5.7 (5.7 \pm 1.3) were higher than the normal range. Se HDL was 44.39 (44.39 \pm 8.62). There was no statistically significant variation in the lipid profile on the basis of gender. Patients receiving hemodialysis(HD) and those not receiving hemodialysis were categorized in different lipid parameters and shown in Table 1. In those receiving HD the Se LDL, Apo B/Apo A1 ratio was found to be significantly higher and Apo A1 was significantly lower when compared to those not on hemodialysis.

Table .1

Parameters	HD (No)	HD (Yes)	P Value
Se Total Cholesterol			
Desirable (<200)	3	9	0.6230
Borderline High (200-239)	4	27	
High (\geq 240)	9	48	
Se Triglycerides			
Normal (<150)	3	19	0.6538
Borderline High (150-199)	3	9	
High (200-499)	10	56	
Se LDL			
Near Optimal (100-129)	3	21	0.0454
Borderline High (130-159)	3	14	
High (160-189)	1	28	
Very High (\geq 190)	9	21	
Se HDL			
<40	7	21	0.1257
\geq 40	9	63	
Apo A1			
Low	5	83	0.01
Normal	11	1	
Apo B			
Normal	15	75	0.5853
High	1	9	

P value <0.05 is considered as significant.

The mean values of Apo A1, ApoB and Apo B/Apo A1 ratio were found 0.9132 ± 0.1364 , 0.943 ± 0.169 and 1.0574 ± 0.0645 respectively. A majority of patients (88%) had their Apo A1 levels lower than the laboratory reference.

The Apo B/Apo A1 ratio mean was compared in hypertensives(1.0814 ± 0.2532) and non hypertensives(0.8629 ± 0.1673). It was found that the mean of Apo B/Apo A1 ratio was higher in the hypertensives than the non hypertensives.

The eGFR showed a significantly strong positive correlation with Apo A1($P < 0.001$) and a negative correlation with Apo B/Apo A1 ratio ($P < 0.001$).

The mean Apo B/ApoA1 ratio was compared in those receiving HD(1.1020 ± 0.246) and those on conservative management (0.8230 ± 0.1454).It was found to be more in those receiving haemodialysis ($P < 0.01$)

Discussion:

The results of this study show that total serum cholesterol, Se LDL, triglyceride and TC/HDL ratio levels were higher than normal range in CKD patients on conservative management or hemodialysis. In addition, those

receiving hemodialysis, the Se LDL, Apo B/Apo A1 ratio was found to be significantly higher and Apo A1 was significantly lower when compared to those not on hemodialysis.

In a study by Vaziri N D⁽¹²⁾ it was found that the patients had elevated serum triglycerides level, with high levels of VLDL and pre β HDL. However, the levels of HDL and ApoA were reduced.

Another study was conducted by Vaziri ND et al⁽¹³⁾ in patients with focal glomerulosclerosis. He found that the level of LDL was increased in this group of patients.

In a study by Abrass⁽¹⁴⁾ he found that the patients with CKD had an elevated serum triglyceride level and decreased clearance of chylomicrons and VLDL. In a study by Attman PO and colleagues⁽¹⁵⁾, it was found that all the patients with moderate to advanced renal failure had elevated triglycerides. They also found that the cholesterol was elevated and HDL reduced. No change was seen in the LDL level. GoekON et al⁽¹⁶⁾ found that higher serum apolipoprotein A1 was associated with lower prevalence of CKD and higher eGFR estimated by the CKD-EPI equation in two large multiethnic population-based samples. While apolipoprotein B showed no consistent associations, a higher apolipoprotein B/A1 ratio was significantly associated with lower eGFR in both studies.

In this study also the mean eGFR was compared in patients with different levels of Se TC, TG, LDL and HDL and no statistically significant difference was found with P values (of >0.05). The eGFR was also plotted against ApoA1, ApoB and ApoB/Apo A1 ratio and it was found that the eGFR had a strong positive correlation with ApoA1 and a strong negative correlation with ApoB/Apo A1 ratio, with P values <0.05 , thus suggesting that as the eGFR worsens in a patient with CKD, the cardiovascular mortality risk increases. However Apo B when plotted against eGFR did not show any significant correlation. In a study by Ravichandran et al⁽¹⁷⁾ and Shah and colleagues⁽¹⁸⁾ with 48 patients managed with hemodialysis and those on conservative management, they found that the patients had marginally elevated levels of triglycerides and the level of dyslipidemia had no statistical correlation to the caloric intake in both these groups.

In a study by KimakEand Solski J⁽¹⁹⁾, on ApoA- and ApoB-containing lipoproteins and Lp(a) concentration in non-dialysed patients with chronic renal failure, they found that the reduced levels of apoA-containing lipoproteins and increased TG-rich apoB-containing lipoproteins and Lp(a) indicated a clear atherogenic pattern in early renal disease. Increased Lp(a) concentration may result in nonspecific synthesis or catabolism disturbances. Measurement and monitoring of lipoprotein family profiles offers a new means for selecting appropriate therapies targeted for normalizing dyslipidemia in non-dialysed patients.

Limitations:-

This study did not include a detailed dietary history. It did not compare the caloric intake and the triglyceride levels. The duration of CKD has not been taken into account. The study group consisted only of End Stage Renal Disease patients. The study group was small and heterogeneous.

Conclusion:

This study thus showed that there is significant increase in the cardiovascular disease related mortality amongst all Chronic Kidney Disease patients and the risk increases with worsening of eGFR. Also the patients on hemodialysis are probably at more risk than those managed conservatively. Thus it is important to measure lipid profile in all patients with CKD and initiate therapy for the same when deemed necessary.

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