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Dyslipidemia correlating with reduced glomerular filtration rate in apparently healthy individuals

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Abstract

There are many studies relating the renal dysfunction with dyslipidemia. This study intended to assess the correlation of estimated glomerular filtration rate (eGFR) with the lipid levels in apparently healthy individuals. A total of 211 people with normal serum creatinine and no previous history of cardiovascular disease or renal disease were selected. Hypercholesterolemia and hypertriglyceridemia are now being reported as risk factors for progression of renal disease. Recently it has been studied that a rise in apolipoprotein B rich lipoproteins to be associated with decline in renal function. In this study there was a significant negative correlation of Low Density Lipoprotein (LDL) and total cholesterol with e GFR. There was a positive correlation with High Density Lipoprotein (HDL) and negative association with non HDL cholesterol. However larger cohort studies are required to establish dyslipidemia as a causative factor for renal dysfunction.

Keywords: eGFR, Hypercholesterolemia, Dyslipidemia.

Introduction

The age-standardized prevalence of generalized obesity in South India in women is about 47% and men about 43%.[(1)] The association between dyslipidemia and renal dysfunction is not very clear as the studies done in early stages of dyslipidemia and early stage of renal dysfunction are very few. Study done in rural population of Karnataka showed the prevalence of CKD stage 3 to be 6.3%, and in India the prevalence of CKD is about 17.2%.[(2,3)] Recent evidence shows that dyslipidemia per se is a risk factor for progressive renal disease.[(4,5)] It was found that the prevalence of low HDL was increased in subjects with an e-GFR $\leq$ 60 ml/min/1.73m^2 irrespective of obesity.[(6)] An analysis from the population-based PREVEND ("Prevention of REnal and Vascular ENd stage Disease") cohort showed an inverse relationship between HDL and creatinine clearance.[(7)] Obesity as a predictor for the development of CKD was also demonstrated in 2 larger studies.[(8,9)] Studies suggest that circulating lipoprotein play a direct role in pathogenesis of glomerulosclerosis and tubulointerstitial changes.[(10,11,12)] A prospective study of non-diabetic patients with primary CKD showed that increase in ApoB and LDL without decrease in HDL leads to faster progression of renal impairment.[(13)] A cohort study on atherosclerosis risk communities showed that increase in triglycerides and decrease in HDL but not LDL is associated with renal dysfunction.[(5)]

Objectives

To assess the correlation of eGFR with lipid profile in apparently healthy individuals.

Materials and Method

Subjects selected for our study were apparently healthy normal adults (n=211) who visited the Father Muller Medical College and hospital outpatient department for routine health check-up. They did not have any obvious symptoms or clinical manifestations of chronic kidney disease and their serum creatinine levels were within normal range. Chronic alcoholics, smokers, and individuals with chronic illness, systemic diseases (such as diabetes, hypertension, liver disorders, malignancy, and infections) were excluded from the study.

Fasting blood samples were collected after obtaining informed consent for the estimation of the parameters. All of the following biochemical parameters were assayed in Cobas c 311 chemistry autoanalyser,

1. Fasting blood sugar- by hexokinase method
2. Serum urea -by urease method
3. Serum creatinine -by kinetic Jaffe assay.
4. Serum cholesterol - enzymatic colorimetric method by cholesterol oxidase.
5. HDL cholesterol – direct enzymatic colorimetric with cholesterol esterase and cholesterol oxidase coupled with polyethylene glycol.
6. Triglcerides (TG) - enzymatic colorimetric assay using lipoprotein lipase.
7. LDL cholesterol –direct enzymatic by selective micellary solubilisation of LDL cholesterol by a non-ionic detergent and the interaction of a sugar compound and lipoproteins.
8. Calculated VLDL= TG/5
9. The variables used in this study for estimation of GFR is

Modification of Diet in Renal Disease study (MDRD Study equation)

MDRD=186 ×(SCr) $^{1.154}$ × [age (years)] $^{0.203}$ × (0.742 if female)×(1.210 if African–American)
Where SCr is serum creatinine in mg/dL

The data was tabulated and statistically analysed using student t test (p value < 0.05 is considered to be significant). The correlation study was done using the Karl Pearsons Correlation Coefficient. The significant relationship was determined at 95% confidence interval (CI).

Results

The study group consisted of 211 individuals of whom 82 were females and 129 were males. Biochemical parameters like FBS and lipid profile were analysed [Table 1]. According to the Karl Pearsons correlation coefficient there is a negative correlation of eGFR with urea (r = -.377, p=0.001). The independent variables LDL and cholesterol had a significant negative correlation (r = -0.143 and r = -0.211 respectively, p=0.001). Triglycerides and VLDL were found to be negatively correlating, whereas HDL cholesterol was positively correlating with eGFR. [Table 2]

Table 1: Range and mean of biochemical parameters

Parameter	Mean ± SD
Age(yrs)	50.78± 14.84
Fasting Blood Sugar (mg/dL)	105.97±16.11
Serum urea(mg/dL)	24.24±8.49
Serum creatinine(mg/dL)	0.885± 0.183
eGFR(mL/min/1.73m^2)	90.89± 18.92
HDL(mg/dL)	44.52±11.031
LDL(mg/dL)	133.44±36.79
Cholesterol (mg/dL)	210.62±45.71
Triglycerides (mg/dL)	144.97±73.64
VLDL(mg/dL)	28.93±13.67
Cholesterol/HDL ratio	4.95±1.47

Table 2: Association of eGFR with the biochemical parameters

Parameter	Karl Pearsons correlation coefficient (r value)	p value
Age	- 0.413	0.00*
Fasting Blood Sugar	- 0.204	0.003*
Serum urea	- 0.377	0.00*
Serum creatinine	- 0.738	0.00*
HDL	0.013	0.852
TG	- 0.076	0.273
LDL	- 0.143	0.039*
Cholesterol	- 0.211	0.002*
VLDL	- 0.069	0.317
Cholesterol/HDL ratio	- 0.171	0.013*

* indicates significant correlation

Discussion

It is already known that renal dysfunction causes hyperlipoproteinemia but there are very few studies on dyslipidemia as a causative factor for renal dysfunction.[14,15] Hypercholesterolemia and hypertriglyceridemia, recognized as contributing to atherosclerosis, are also emerging as risk factors for progression of renal disease.[16,4] This study has shown a significant inverse relation of non-HDL cholesterol and a positive correlation of HDL with eGFR. Schaeffner et al.[17] have suggested that elevated total cholesterol, high non-HDL cholesterol, a high ratio of total cholesterol/HDL, and low HDL in particular were significantly associated with an increased risk of developing renal dysfunction in men with an initial creatinine ≤ 1.5 mg/dl. Study of relationship of lipids and renal function indicated that the patients with impaired renal function (eGFR<60 ml min^{-1} 1.73 m^{-2}) had significantly higher levels of total cholesterol, triacylglycerol and apolipoprotein B, and lower HDL cholesterol concentrations than patients with normal renal function or mildly impaired renal function.[18] A study by Tozowa et al.[19] has shown that TG levels predicted the development of CKD. Samuelsson et al[4] showed that triglyceride-rich, but not cholesterol-rich, apolipoprotein B-containing lipoproteins are associated with a rapid loss of renal function in chronic renal insufficiency. Another study[20] done to evaluate the prevalence of CKD among people with and without metabolic syndrome (MS) showed 2.9% existence of CKD in Non-MS category. Hypercholesterolemia and hypertriglyceridemia are also associated with podocyte injury, which secondarily leads to mesangial sclerosis.[21] This study showed hypertriglyceridemia which was not in significant correlation with eGFR. Recently Penn Diabetes Heart Study[22] conducted on type 2 diabetics without cardiovascular or renal complications showed that there could be a possibility of circulating lipoprotein - Lp(a) may play a role in renal impairment. It was shown that two fold increase in Lp(a) resulted in decline in eGFR by 0.50 ml/min/year and Lp(a) levels greater than atherogenic cut off was associated with a reduction in eGFR by 2.75ml/min/year. Higher apolipoprotein C III (apoC-III) was also associated with decline in eGFR. The limitations in this study are that it's a cross sectional study and the information on baseline proteinuria is missing. If the study population with reduced GFR already had proteinuria it would have indicated presence of renal injury. Larger prospective cohort studies with measurements of apolipoproteins and lipoproteins along with better markers of kidney function is required to declare dyslipidemia as a causative factor for renal injury.

Conclusion

This study was intended to find the association of dyslipidemia with renal function. Though the study consisted of apparently healthy individuals with mild

dyslipidemia there was a significant population having renal dysfunction. Thus this study shows that increase in non HDL cholesterol can lead to decrease in glomerular filtration rate. In our study there was a significant negative association of eGFR with LDL and total serum cholesterol. However, further studies with large sample size, and taking into account all the predisposing factors for CKD are required. Studies are also required to determine the levels of the various cholesterols beyond which there could be renal injury. Large cohort studies are needed to describe lipids as predictive and progressive factors for renal injury.

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