Status of Lipid Profile in Different Stages of Chronic Kidney Disease

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Abstract

Objective: To estimate and compare dyslipidemia in patients with different stages of chronic kidney disease as compared to healthy controls and to determine whether dyslipidemia is independently associated with rapid renal impairment.

Methods: This study was conducted in department of Biochemistry Basic Medical Institute (BMSI), Jinnah Postgraduate Medical Centre (JPMC) Karachi. A total of 150 participants were recruited for the study from the Nephrology department of JPMC. These were grouped as 30 stage II CKD patient, 30 stage III CKD patient, 30 stage IV CKD patient, 30 stage V CKD patient and 30 normal healthy individuals. Cholesterol, triglyceride, high density lipoprotein, low density lipoprotein, urea and creatinine were measured by commercially available kit method. Statistical analysis was done using SPSS version 11.

Results: Serum Cholesterol, Triglyceride and LDL-C among all groups were significantly increased when compared with control $p<0.05$. Serum HDL-C among all study groups was significantly decreased $p<0.05$, along with increase in LDL / HDL ratio among all study groups when compared with control $p<0.05$.

Conclusion: Dyslipidemia occurs gradually in CKD patients as disease progresses. Evaluation of dyslipidemia in early stages of CKD is useful to assess the risk for future cardiovascular disease in these patients.

Keywords: Chronic Kidney Disease (CKD), cholesterol, dyslipidemia, cardiovascular diseases (CVD). (ASH & KMDC 19(2):62;2014).

Introduction

Chronic Kidney Disease (CKD) is a worldwide public health problem, associated with a considerable increase in morbidity and mortality. CKD is recognizing as a common condition that is associated with an increased risk of cardiovascular disease[1]. Currently, CKD is the 12th highest cause of death and 17th highest cause of morbidity worldwide[2]. Estimation of CKD and End Stage Renal Disease (ESRD) in South Asia are approximately 800 and 100–200 per million people, respectively[3]. The prevalence of CKD is high in Pakistani population, since incidence of hypertension and diabetes in our inhabitants is one of the highest in the world. Kazmi et al., in a short report showed frightening increase in CKD patients in our population[4]. CKD is defined as structural and /or functional damage to the kidney with a glomerular filtration rate (GFR) of <60 mL/min for three months or more, irrespective of cause[5]. The risk factors for development and progression of CKD are age, obesity, smoking, diabetes mellitus (DM) hypertension, and dyslipidemia[6].

Dyslipidemia is a major risk factor for cardiovascular morbidity and mortality and is common among patients with CKD. The prevalence of hyperlipidemia increases as renal function declines, with the degree of hypertriglyceridemia and elevation of

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LDL cholesterol being proportional to the severity of renal impairment[7]. Some studies showing that lipid abnormalities are associated with a reduction in kidney function in the general population. Wanner et al., suggested that hyperlipidemia could cause renal injury and contribute to the progression of renal disease[8]. Lipid abnormalities were originally considered as complications of dialysis patient; these changes can be present in early stages of CKD and may actively contribute in the pathogenesis of complications such as atherosclerotic vascular disease. The present study aims to estimate and compare dyslipidemia in the patients with different stages of chronic kidney disease as compared to healthy controls and to determine whether dyslipidemia is independently associated with rapid renal impairment.

Patients and Methods

This cross-sectional study was conducted at Department of Biochemistry, Basic Medical Sciences Institute (BMSI), Jinnah Post Graduate Medical Centre (JPMC) in collaboration with the Nephrology Department of JPMC in the duration of April 2012 to May 2013. Two hundred patients were recruited for the study out of them on the basis of exclusion criteria 150 subjects of adult age were enrolled in present study. We exclude the patient with liver disease, acute or chronic inflammatory disease and patient on steroid therapy. The sample size was calculated by open Epi software and reference study was Kim et al., 2009[9]. We included chronic kidney disease patient without any known cardiovascular disease and thirty age, sex matched apparently healthy individual from paramedical staff of hospital.

The study protocol was approved by the Institutional Review Board of the Basic Medical Science Institute, Jinnah Postgraduate Medical Centre (NO.F.1-2/2013/BMSI-E.COMT/003/JPMC). Informed consents were obtained in written form from patients and all clinical investigation was conducted according to the principles expressed in the Declaration of Helsinki. The patients gave consent for the publication of the clinical details.

Baseline demographic and clinical data were obtained from medical records and interviews with patients at enrollment. All study participants were requested to come with 10-12 hours of fasting for sample collection. The analysis of Biochemical parameter including Cholesterol, Triglycerides, HDL-C, Urea and Creatinine were measured by spectrophotometry using commercially available Merck kits. Low density lipoprotein (LDL-c) was measure by Friedwal's formula[10]. Glomerular filtration rate (GFR) was estimated by Cockcroft & Gault equation[11].

A descriptive statistical analysis of continuous variables was performed using SPSS (version 11; SPSS Inc., Chicago, IL, USA). Data on continuous variables i.e. biophysical (age, height, weight, BMI and blood pressure etc.) and biochemical (Serum Cholesterol, Triglycerides, HDL-C, Urea and Creatinine etc.) parameters were calculated as mean ± standard deviation (SD). Statistical comparisons were computed using a student t-test and a one-way analysis of variance (ANOVA) for continuous/ quantitative variables. Pearson's or Spearman's coefficient of correlation (r) was used to determine the correlation between GFR levels and lipid profile. In all statistical analysis performed p-values<0.05 were considered significant.

Results

Group A consist of 30 healthy individuals (GFR >90ml/min/1.73m^2), group B include 30 stage 2 CKD patients (GFR 60-89 ml/min/1.73m^2), group C include 30 stage 3 CKD patients (GFR 30-59 ml/min/1.73m^2), group D include 30 stage 4 CKD patients (GFR 15-29 ml/min/1.73m^2), group E include 30, stage 5 CKD patients (GFR <15 ml/min/1.73m^2). The demographic, biophysical and biochemical variables were outlined in (Table 1). Significant changes were observed in weight, systolic BP and diastolic BP among study group. (Table 2) shows the values of cholesterol, Triglycerides, HDL-C, LDL-C, VLDL-C, LDL-C /HDL-C ratio among 5 study groups with the mean ± SD values. The Correlation coefficient (r) of Lipid Profile with GFR is shown in Fig. 1.

Table 1. Comparison of baseline characteristics and some laboratory variables between the five GFR groups

Variable	Group - A Mean ± SD	Group - B Mean ± SD	Group - C Mean ± SD	Group - D Mean ± SD	Group - E Mean ± SD
Age (Years)	55.27 ± 6.59	55.6 ± 4.20	55.23 ± 5.93	57.10 ± 5.91	57.43 ± 5.25
Weight (Kg)	65.85 ± 9.88	74.45± 6.19*	75.17 ± 10.47*	76.83±9.89*	74.48± 8.98*
Height (Cm)	162.53 ± 10.01	162.83 ± 7.83	164.4 ± 9.88	166.97 ± 8.17	163.17± 11.23
Systolic BP (mmHg)	116.67 ± 12.69	125.00 ±15.92	127.33 ± 16.80	131.33 ± 20.13*	131.33± 23.87*
Diastolic BP (mmHg)	77.17 ± 7.15	80.67 ± 7.40	83.0 ± 9.52	88.00 ± 11.86*	85.17 ± 14.53*
Urea (mg/dl)	27.03 ± 5.63	64.23 ± 18.24*	107.87 ± 32.07*□	114.63 ± 36.69*	134.30 ± 32.24*□△
Creatinine (mg/dl)	0.74 ± 0.19	1.24 ± 0.14	2.21 ± 0.57*□	3.27 ± 0.62*□△	8.43 ± 1.81*□△⌓
GFR (ml/min/ 1.73m^2)	108.38 ± 9.78	68.11± 7.59*	38.45±7.35*□	26.06 ± 2.79*□△	9.95 ± 2.34*□△⌓

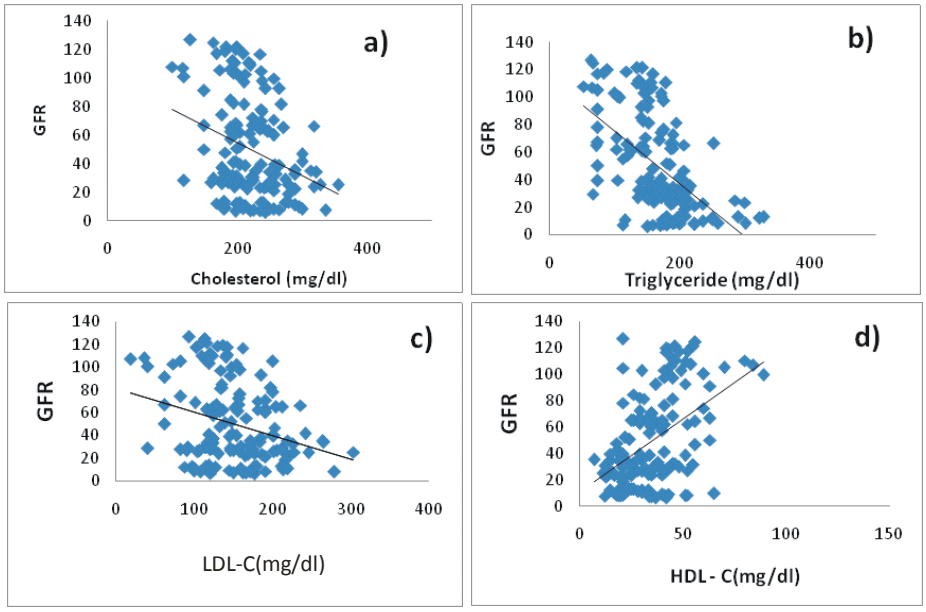
Values are expressed as mean ± SD, Statistically significant as compared to group A p<0.01, Statistically significant as compared to group B p<0.01, △ Statistically significant as compared to group C p<0.01, Statistically significant as compared to group D p<0.01.*

Table 2. Comparison of lipid profile among five GFR groups

Variable	Group – A Mean ± SD	Group - B Mean ± SD	Group – C Mean ± SD	Group - D Mean ± SD	Group - E Mean ± SD
Cholesterol (mg/dl)	194.00 ± 41.25	221.77 ± 35.25*	225.63 ± 46.38*	229.23 ± 54.70*	230.30 ± 43.40*
Triglyceride (mg/dl)	121.90 ± 39.28	148.00 ± 41.93	165.33 ± 38.00*	185.77 ± 42.72*□	207.70 ± 53.12*□△
HDL-C (mg/dl)	49.83 ± 15.65	37.23 ± 1.23*	29.73 ± 14.15*	29.93 ± 12.10*	25.13 ± 12.16*
LDL-c (mg/dl)	119.90 ± 42.18	154.07 ± 40.59	166.17 ± 47.45*	159.49 ± 57.88*	154.93 ± 45.75
VLDL-c (mg/dl)	25.27 ± 8.23	29.73 ± 8.31	33.49 ± 7.41*	37.15 ± 8.49*□	41.54 ± 10.62*□△
LDL-c / HDL-c Ratio	2.77 ± 1.72	4.62 ± 2.09	7.72 ± 6.87*	7.29 ± 5.85*	6.02 ± 4.08*

Values are expressed as mean ± SD, Statistically significant as compared to group A p<0.01, Statistically significant as compared to group B p<0.01,△ Statistically significant as compared to group C p<0.01,⌓ Statistically significant as compared to group D p<0.01.*

Fig. 1 : a,b,c and d. **Correlation (r) Of Lipid Profile With GFR**



Discussion

In the present study, we evaluated the association of dyslipidemia in different stages of chronic kidney disease patients. We found that dyslipidemia occur gradually as disease progress in CKD patients. Higher total cholesterol, Triglyceride and LDL-C were significantly associated with rapid renal impairment.

Dyslipidemia has been established as a well-known traditional risk factor for CVD in the general population and large-scale observational studies have shown that total and low-density lipoprotein (LDL) cholesterol values are two of the most important independent predictors of cardiovascular morbidity and mortality[12,13]. The mortality rate due to CVD for patients with CKD is 10 to 30 times higher than for those who have normal kidney function. The cardiovascular risk is increased very early on in the progression of CKD (at a GFR of about 75 ml/min) and increases continuously with decreased renal function[14,15].

Our results depict increase level of cholesterol, triglyceride and LDL-C in CKD patients. The most common quantitative lipid abnormalities in predialysis CKD patients are hypertriglyceridemia, increased concentrations of triglyceride-rich lipoprotein remnants, reduced high density lipoprotein (HDL) levels as well as increased concentrations of lipoprotein(a)[16].This study showed that dyslipidemia in these patients may actively participate in the pathogenesis of CVD as well as in the deterioration of renal function. The End Stage Renal Disease (ESRD), is often seen with the low levels of cardioprotective high density lipoprotein, high levels of atherogenic triglycerides and low density lipoprotein[17]. Our result also showed significant decrease level of HDL-C in different stages of CKD patients which are similar to Muntner et al., who demonstrated that low HDL-C levels predicted cardiovascular complication in patient with increased serum creatinine[18].

Hypertriglyceridemia is partially due to a down regulation of lipoprotein lipase (LPL), hepatic lipase, very low density lipoprotein (VLDL-C) and low-density lipoprotein receptor (LDL-r) expression[19]. We also found increase level of VLDL-C in our study population. It may imply that low HDL levels are the profound inflammatory state of these patients[19]. The trial studies naked that the accumulation of triglyceride-rich lipoprotein[20] such as VLDL, Chylomicrons, and their remnants in individuals with CKD is mainly due to their decreased catabolism. Lacquaniti[20] et al., have reported that the down regulation of several genes, along with the changes in the composition of lipoprotein particles and the direct inhibitory effect of various uremic 'toxins' on the enzymes involved in lipid metabolism, represents the most important pathophysiological mechanisms underlying the development of hypertriglyceridemia in renal failure[21]. We found significant increase in LDL-C/HDL-C ratio but no previous study reported these finding to best of our knowledge. We also found strong negative correlation of GFR with triglyceride and VLDL-C, while positive correlation was found with HDL-C. In our results serum Cholesterol, Triglyceride and LDL-C levels were significantly increased in stage three CKD patients and gradual increase with the decrease in GFR was observed. Thus our result may indicate that dyslipidemia may have a role in the etiology of cardiovascular complications in patients with CKD. Our result suggested that early detection and treatment of dyslipidemia in CKD patient will reduce adverse consequence of CVD and motility rate in these patients.

Our study has a number of potential limitations include small sample size and effect of drug was not investigated. Longitudinal studies are required on these aspects.

Conclusions

CKD Patients are at high risk of developing cardiovascular disease. They have a higher prevalence of dyslipidemia as compared to the general population. The majority of patients do not develop kidney failure but die as a result of CVD. It is recognized that dyslipidemia begins in the early

stages of CKD. Therefore, it is important not only to identify these patients early but also to treat intensively before they develop end stage renal disease. Most patients will require lifestyle modification and lipid-lowering therapy. CKD patients should be considered as patients at very high risk for CVD and treated accordingly.

Conflicts of Interest

The authors declare no conflict of interest.

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