Original

Association of Serum Lipid Profile Levels in Chronic Kidney Disease Patients with Cardiovascular Disease: a case control study, Khartoum State

Mohammed M.A[1*], Mohammed I.A[1], Ismail A.M[2], Ali A.M[3], Dafaalla M.H[3], Mohammed R.K[3], Edris S.M[3], Ali S.Y[3], Nourallah S.A[3], Abdalla I.A[1], Mohamed E.A[1], Mohamed A.A[1], Ali A.O[1],Alnil A.H[1]

[1.]Department of clinical chemistry, Faculty of medical laboratory sciences,Omdurman Islamic University, Omdurman, Sudan

[2.] Department of biochemistry, Faculty of science and technology, Alneelain University, Khartoum,Sudan

[3.]Department of clinical chemistry, Faculty of medical laboratory sciences,Elrazi University, Khartoum,Sudan.

***corresponding author:** Dr. Mogtaba Ahmed Mohamed, Assistant Professor, Omdurman Islamic University, Email: mogtaba1122@gmail.com

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Abstract

Background: The burden of chronic kidney disease (CKD) is increasing rapidly worldwide and has become a major health problem and most of these patients die due to cardiovascular disease (CVD) before progression to end stage renal disease (ESRD). Therefore, poor cardiovascular outcomes in CKD patients have prompted nephrologists to look for biomarkers that may improve risk stratification in this population. The objective of this study was to evaluate serum lipid profile levels in CKD patients and to determine their association with cardiovascular diseases.

Materials & Methods: This analytical case control study was conducted at Ibnsina and Military hospitals in the period from February 2016 to March 2019, (n = 150) clinically diagnosed CKD patients (age range between 22 - 76 years, 105 males and 45 females), and 150 healthy subjects were included as controls. Serum lipid profile and serum creatinine were estimated by Cobas C-311® fully automated analyzer, hemoglobin by Sysmix, glomerular filtration rate (GFR) was

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calculated by Cocroft-Gault formula and blood pressure was measured by using mercuric sphygmomanometer.

Results: The results of the current study indicated that, the means of total cholesterol, triglyceride, LDL-C, creatinine, systolic blood pressure (SBP), diastolic blood pressure (DBP) and body mass index (BMI) were significantly (*P*-value ≤0.05) higher in CKD patients when compared with that of controls, while HDL-C, hemoglobin and GFR were significantly (*P*-value ≤0.05) lower. Moreover, serum SBP and DBP were significantly (*P*-value ≤0.05) higher in CKD patients with cardiovascular disease (CVD) than CKD patients without CVD, while the means of cholesterol, TG, LDL-C, BMI and creatinine were insignificantly (*P*-value >0.05) increased, meanwhile the mean of HDL-C, GFR and hemoglobin were insignificantly (*P*-value >0.05) decreased. In addition there is insignificant increase in the means of TG, LDL-C, BMI, SBP, DBP, creatinine and hemoglobin, and insignificant decrease in the mean of cholesterol, HDL-C and GFR in male when compared with female in CKD patients.

Conclusion:dyslipidemia (high levels of cholesterol, TG, LDL-C and low levels of HDL-C) was higher in patients with CKD. Thus, the lipid profile levels were strongly associated with cardiovascular events in patients who have CKD and are on maintenance hemodialysis (HD).

Keywords

Chronic kidney disease, cardiovascular disease, lipid profile, glomerular filtration rate, systolic blood pressure, diastolic blood pressure.

Introduction

Chronic kidney disease (CKD) is a decrease in kidney function with a glomerular filtration rate (GFR) of less than 60 ml/min per 1.73 m^2 and/or kidney damage for 3 months or more (1).It is characterized by a wide variety of biochemical disturbances and numerous clinical symptoms and signs (2). The alteration includes haematological abnormalities, cardiovascular problems, gastrointestinal disturbances, neurologic disorder, osteodystrophy, skin disorder and altered sexual function (3).

The high incidence of cardiovascular events in CKD warrants an accurate evaluation of risk aimed at reducing the burden of disease and its consequences (4). The most common manifestation of cardiovascular disease in CKD patients is left ventricular hypertrophy (LVH), predominantly as a result of hypertension and anaemia (4). LVH is a powerful independent predictor of cardiovascular disease (CVD) in CKD patients (5). However, identifying which patients will suffer from cardiovascular events is challenging and requires early identification and treatment. The ability to detect significant cardiovascular dysfunction at an early stage could facilitate more aggressive and focused treatment of those at increased risk (5).

Lipoprotein metabolism is altered in most patients with renal insufficiency (6). Dyslipidaemia develops early in renal failure and the imbalance between lipoprotein synthesis and degradation in prolonged renal disease results in a pronounced dyslipidemia (7). Uremic patients have elevated serum levels of triglycerides and lipoprotein and the elevated level of this lipid may contribute to increased cardiovascular risk (8). The pattern of abnormalities is due to several pathogenic mechanisms, first, urinary protein loss stimulates and increased low density lipoprotein (LDL) synthesis by liver, it is likely that proteinuria with resultant hypoalbuminemia leads to an up regulation of 3 hydroxyl-3-methylglutaryl CoA reeducates with consequent hypercholesterolemia(9). Low HDL with poor maturation of cholesterol rich HDL-2 is due to acquire lecithin-cholesterol acyltransferase deficiency secondary to abnormal urinary losses of this enzyme (10).

The present study aims to evaluate the development of cardiovascular disease

through the estimation of lipid profile among the CKD patients on dialysis.

Materials and methods

The study comprised a total of 300 individuals of whom 150 individuals withevidence of CKD were included on the basis of clinical signs and symptoms and laboratory findings of CKD. The other 150 healthy individuals served as a control group, whose age and sex was determined as healthy. Part of the CKD patients suffered from CVD in which they are diagnosed with CVD based on family histories of the patients, risk factors, physical examination,using an array of laboratory tests and imaging studies. Individuals who were diagnosed with CKD and they have other disease such as liver cirrhosis, sepsis and hyperthyroidism were excluded from this study.Informed consent was taken from the patients and subjects who participated in the present study, after agreement of general managers of Ibnsina hospital and Military hospitals.

Ethicalcommitteeapprovalhasalsobeenobtain edfrom Omdurman Islamic University and ministryofhealth.

In both groups lipid profile and serum creatinine were measured by Cobas C-311® fully automated analyzer, hemoglobin was measured by Sysmix fully automated analyzer, GFR was calculated using Cocroft-Gault formula and blood pressure was measured by using mercuric sphygmomanometer.

All results obtained were expressed as mean ± SD. Statistical analysis was performed using SPSS version 20 (Statistical Package for the Social Sciences). Difference in mean values between groups was evaluated by t-test. The person correlation test was used to find the correlation between two variables. A *P*-value ≤ 0.05 was considered of significant difference.

Results

Three hundred individuals were recruited in this study (150 CKD patients, 150 controls).

Table (1) shows the demographic and descriptive statistics of the patients with CKD. The most common cause of CKD among study subjects is HTN (36.7%), followed by DM (30.7%) then chronic glomerulonephritis (12%) and finally polycystic kidney disease (10.7%). (14.7%) of the CKD patients they have both DM and HTN. (19.3%) of the CKD patients have CVD as comorbid disease. (69%) of the CKD patients their ages (< 50 year) while (31%) their ages is (≥ 50 year), (45.3%) of the CKD patients their BMI was normal, (47.3%) were overweight and (7.4%) were

obese (>30 kg/m^2), (37.3%) of the study populations had CKD for (≤5 year) whereas (62.7%) had the CKD for (>5 years), (52%) of the CKD patients had low level of Hb (<11 g/dl) whereas (48%) had Hb level (≥11 g/dl), (20%) of the study populations were smokers.

Table (2) shows the clinical and laboratory parameters of CKD patients and controls. The ratio of patients to controls was 1:1. The BMI of patients were greater than that of the controls (25.5 ± 3.5 kg/m^2 versus 23.3 ± 3.0 kg/m^2), *p* .value = 0.000. The mean of total cholesterol (168 ± 37.0 mg/dl), triglyceride (153 ± 60.1 mg/dl), LDL-C (95.9 ± 32.5) and creatinine (8.40 ± 2.80 mg/dl) were significantly higher in CKD patients when compared with that of controls (148 ± 73.7 mg/dl, 126 ± 49.2 mg/dl, 52.0 ± 31.4 and 0.80 ± 0.20 mg/dl), *p* .value = 0.003, 0.000, 0.004 and 0.000 *respectively*, while the mean GFR and hemoglobin were significantly lower in patients (14.2 ± 10.1 ml/min/1.73 m^2 and 10.5 ± 2.00 g/dl) when compared with controls (115 ± 30.1 ml/min/1.73 m^2 and 13.5 ± 1.60 g/dl), *p* .value = 0.000 and 0.005 respectively. Both the systolic (154 ± 21.0 mmHg) and diastolic (85.0 ± 12.0 mmHg) blood pressure were significantly higher in CKD patients when compared to that of the controls (117 ± 8.00 mmHg and 77.0 ± 6.00 mmHg), *p* .value = 0.003 and 0.006 *respectively*.

These results show that there is a significant increase in the mean of SBP and DBP in CKD patients with CVD when compared with CKD patients without CVD in case group, while there was an insignificant increase in the mean of cholesterol, TG, LDL-C, BMI and creatinine andan insignificant decrease in the mean of HDL-C, GFR and hemoglobin in CKD patients with CVD when compared with CKD patients without CVD in case group Table (3).

Table (4) shows that there wasan insignificant increase in the means of TG, LDL-C, BMI, SBP, DBP, creatinine and hemoglobin in male when compared with female in CKD patients, while there was an insignificant decrease in the mean of cholesterol, HDL-C and GFR in male when compared with female in CKD patients.

Figure (1) shows the results of correlation between cholesterol and age among CKD patients, in which there is negative weak correlation between cholesterol and age (r= -0.194, *p.* value= 0.017).

Figure (2) shows the results of correlation betweenHDL-Cand age among CKD patients, in which there is negative weak

correlation between HDL-C and age (r= -0.212 and *p.* value= 0.009).

Figure (3) shows the results of correlation betweenLDL-Cand age among CKD patients, in which there is positive weak correlation between LDL-C and age (r= 0.185, *p.* value= 0.024). Onthe other hand there is no correlation between triglyceride and age (*p.* value= 0.559).

Table (5) shows lipid profile levels according to the duration of CKD in patients group classified as ≤5 years and >5 years, in which there is insignificant difference in mean levels of cholesterol, HDL-C and LDL-C between the two groups (*p.* value= 0.157, 0.953 and 0.955 respectively), while there is significant increase in the mean level of triglyceride in those who have CKD for >5 years in comparison with other group with duration of CKD ≤5 years (*p.* value= 0.018).

Table (1): Demographic and descriptive statistics of the patients with chronic kidney disease:

Characteristic	**Frequency (%)**
Age	
<50 years old	103 (69%)
≥50 years old	47 (31%)
BMI (kg/m^2)	
Normal	68 (45.3%)
Overweight	71 (47.3%)
Obese	11 (7.4%)
Duration of CKD	
≤ 5 years	56 (37.3%)
> 5 years	94 (62.7%)
Cholesterol	
≤ 200 mg/dl	134 (89.3%)
> 200 mg/dl	16 (10.7%)
Triglyceride	
≤ 152 mg/dl	88 (58.7%)
> 152 mg/dl	62 (41.3%)

HDL-C	
< 35 mg/dl	73 (48.7%)
≥ 35 mg/dl	77 (51.3%)
LDL-C	
< 135.5 mg/dl	132 (88%)
≥ 135.5 mg/dl	18 (12%)
Hb	
< 11 g/dl	78 (52%)
≥ 11 g/dl	72 (48%)
SBP	
< 130 mmHg	108 (72%)
≥ 130 mmHg	42 (28%)
DBP	
< 90 mmHg	110 (73.3%)
≥ 90 mmHg	40 (26.7%)
Smoking	
Yes	30 (20%)
No	120 (80%)
CVD	
Yes	29 (19.3%)
No	121 (80.7)
Primary kidney diseases (%)	
DM	
Yes	46 (30.7%)
No	104 (69.3%)
HTN	
Yes	55 (36.7%)
No	95 (63.3%)
Both DM and HTN	
Yes	22 (14.7%)

No	128 (85.3%)
Chronic glomerulonephritis	
Yes	18 (12%)
No	132 (88%)
Polycystic kidney disease	
Yes	16 (10.7%)
No	134 (89.3%)

Table (2): Clinical and laboratory parameters of the CKD patients and controls.

Characteristic	**CKD (N= 150)**	**Control (N= 150)**	***P*. value**
Cholesterol(mg/dl)	168 ± 37.0	148 ± 73.7	0.003*
Triglyceride (mg/dl)	153 ± 60.1	126 ± 49.2	0.000**
HDL-C (mg/dl)	36.3 ± 22.1	75.1 ± 36.8	0.000**
LDL-C (mg/dl)	95.9 ± 32.5	52.0 ± 31.4	0.004*
Creatinine (mg/dl)	8.40 ± 2.80	0.80 ± 0.20	0.000**
GFR (ml/min/1.73 m^2)	14.2 ± 10.1	115 ± 30.1	0.000**
Hemoglobin (g/dl)	10.5 ± 2.00	13.5 ± 1.60	0.005*
BMI (kg/m^2)	25.5 ± 3.50	23.3 ± 3.00	0.000**
SBP mmHg	154 ± 21.0	117 ± 8.00	0.003*
DBP mmHg	85.0 ± 12.0	77.0 ± 6.00	0.006*

** Highly significant difference at 0.01

* Significant difference at ≤ 0.05

Table (3): Clinical and laboratory parameters of the CKD patients with and without CDV.

Characteristic	**CKD with CVD (N= 29)**	**CKD without CVD (N= 121)**	***P*. value**
Cholesterol (mg/dl)	170 ± 36.8	163 ± 38.2	0.357^{NS}
TG (mg/dl)	155 ± 70.2	153 ± 57.7	0.880^{NS}
HDL-C (mg/dl)	36.0 ± 25.1	36.3 ± 21.4	0.944^{NS}
LDL-C (mg/dl)	103 ± 30.8	94.2 ± 32.7	0.176^{NS}
BMI (kg/m^2)	26.1 ± 3.50	25.4 ± 3.4	0.315^{NS}
SBP mmHg	157 ±16.0	134 ± 18.0	0.032*
DBP mmHg	94.0 ± 10.0	85.0 ± 12.0	0.022*
Creatinine (mg/dl)	9.04 ± 3.10	8.30 ± 2.70	0.252^{NS}
GFR (ml/min/1.73 m^2)	13.5 ± 9.40	14.4 ± 10.3	0.668^{NS}
Hemoglobin (g/dl)	10.0 ± 2.20	10.6 ± 2.00	0.136^{NS}

** Highly significant difference at 0.01

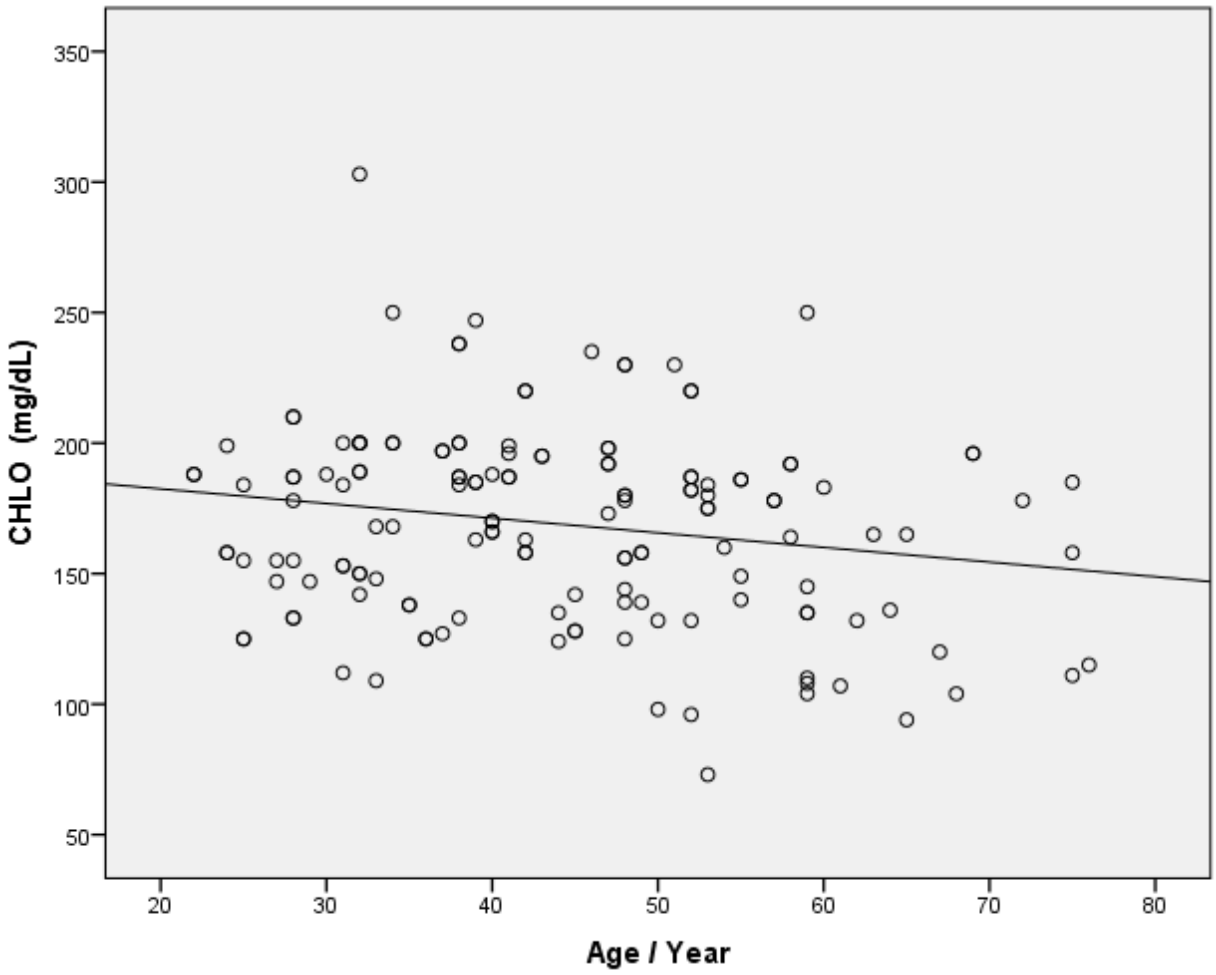
* Significant difference at ≤ 0.05

NS: Not significantly different

Table (4): Clinical and laboratory parameters of the CKD patients according to gender.

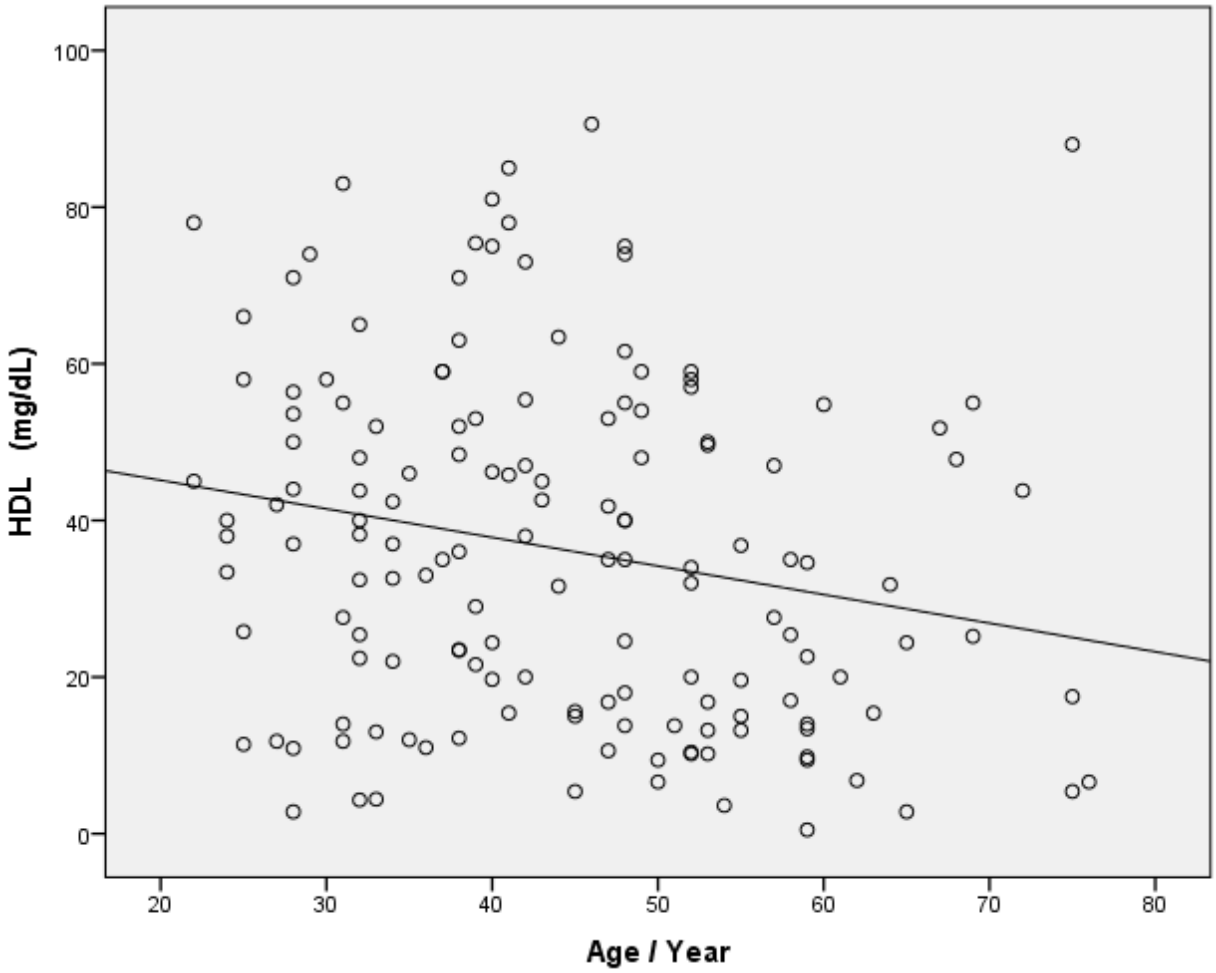
Characteristic	**Male**	**Female**	***P*. value**
Cholesterol (mg/dl)	170 ± 36.8	163 ± 38.2	0.357^{NS}
TG (mg/dl)	155 ± 70.2	153 ± 57.7	0.880^{NS}
HDL-C (mg/dl)	36.0 ± 25.1	36.3 ± 21.4	0.944^{NS}
LDL-C (mg/dl)	103 ± 30.8	94.2 ± 32.7	0.176^{NS}
BMI (kg/m^2)	25.7 ± 3.05	25.0 ± 4.37	0.237^{NS}
SBP mmHg	138 ± 14.5	136 ± 15.0	0.332^{NS}
DBP mmHg	89.3 ± 10.0	88.0 ± 12.0	0.512^{NS}
Creatinine (mg/dl)	8.67 ± 2.71	8.13 ± 2.96	0.285^{NS}
GFR (ml/min/1.73 m^2)	13.8 ± 10.1	15.1 ± 10.2	0.481^{NS}
Hemoglobin (g/dl)	10.5 ± 2.11	10.3 ± 1.97	0.577^{NS}

^{NS}: Not significantly different



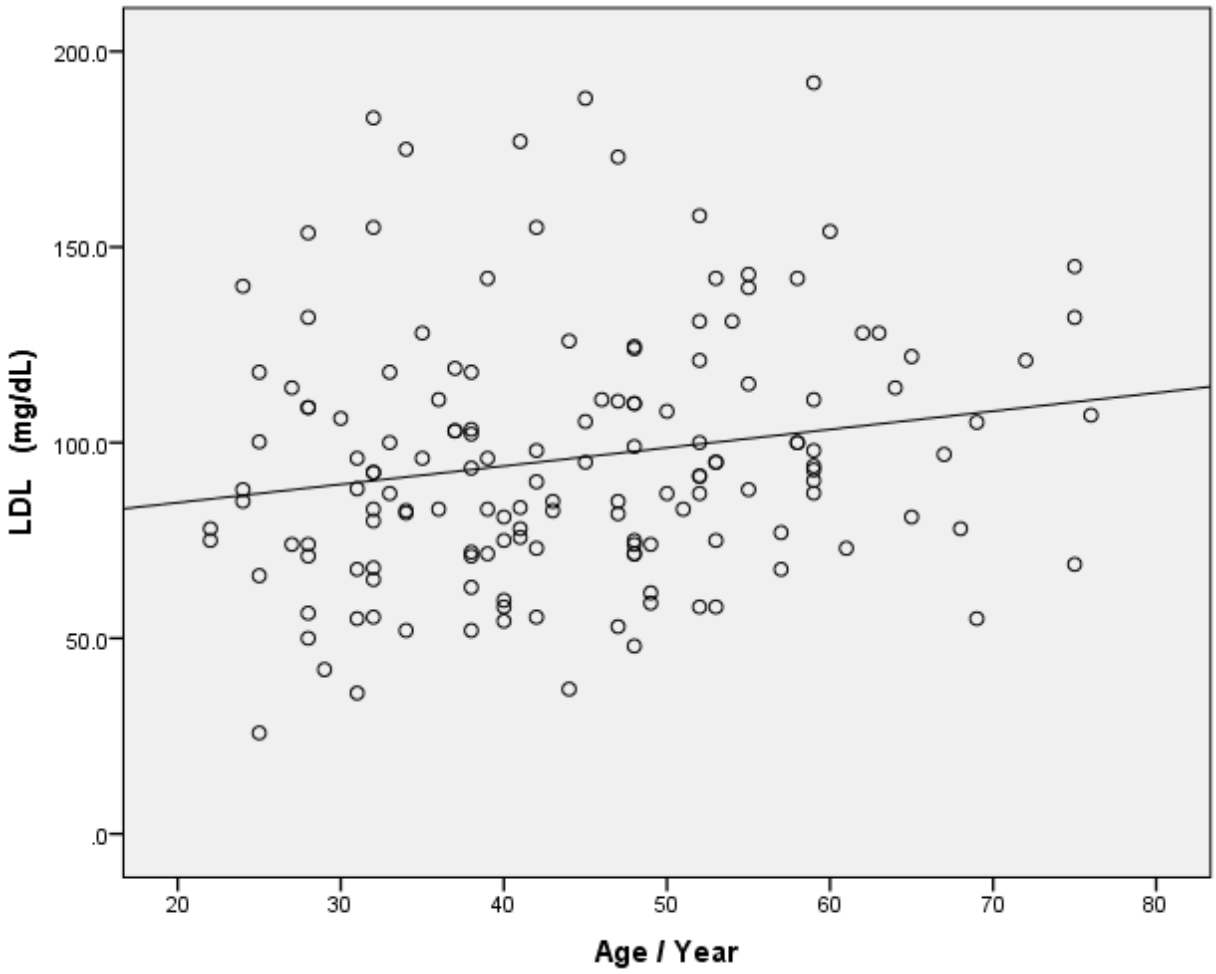
R = -0.194, *p.* value= 0.017

Figure (1): Correlation between cholesterol level and age among CKD patients.



R = -0.212, *p.* value= 0.009

Figure (2): Correlation between HDL-C level and age among CKD patients.



R = 0.185, *p*. value= 0.024

Figure (3): Correlation between LDL-C level and age among CKD patients.

Table (5): Lipid profile levels according to the duration of CKD in ≤5 years and >5 year's patientgroups.

Parameters	**duration of CKD (years)**	**No.**	**Mean ± SD**	***P.* value**
Cholesterol (mg/dl)	≤5years	56	170.65 ± 37.09	0.157
	>5years	94	158.29 ± 35.97	
Triglyceride (mg/dl)	≤5years	56	148.89 ± 50.11	0.018
	>5years	94	182.17 ± 99.30	
HDL(mg/dl)	≤5years	56	36.26 ± 21.94	0.953
	>5years	94	36.57 ± 23.68	
LDL(mg/dl)	≤5years	56	96.005 ± 33.18	0.955
	>5years	94	95.952 ± 28.34	

Discussion

The present study indicated that, the percentages of HTN, DM, chronic glomerulonephritis and polycystic kidney disease among CKD patients were, (36.7%), (30.7%), (12%) and (10.7%) respectively. Meanwhile the CKD is common in elderly than young adult which accounts for 2.2 fold, this finding is in accord with other study conducted by Alebiosuet al (11),who stated that, the third and fourth decades of life account for the high incidence of CKD. Other studies in developed countries found that, the prevalence of CKD increases with advancing age and the peak incidence is found in 7th and 8th decades (11, 12). In contrast, the early onset of CKD in undeveloped countries attributed to the socioeconomic status, risk factors and miss-diagnosis which lead to late intervention and thus CKD (13).Moreover, the current study revealed that, the CKD is most frequent among overweight patients followed by normal weight and obese, these findings have been shown previously by Morales et al (14),who reported that, the frequency of

overweight and obese were higher in CKD patients, therefore considered as risk factor.

The current study indicated that, the total cholesterol, triglyceride and LDL-C levels in the CKD patients were significantly elevated than the control group, while HDL-C level was significantly decreased. This finding agree with the findings of Kennedy et al (15),who reported that, lipoprotein metabolism is altered in most patients with renal insufficiency, and the elevation of plasma LDL-C is associated with atherosclerosis in accelerating.

The current study also revealed that, there is an insignificant decrease in the mean of cholesterol and HDL-C in male group compared with that of female in CKD patients. This finding is in an agreement with the previous studies conducted by Liying et al (16), and Pornpen et al (17).

Meanwhile, the mean of TG and LDL-C levels were insignificantly increased in male group compared with female in CKD patients.This finding disagrees with the previous study conducted in China by Liying and his colleagues and this may be due to differences in ethnicity and social habits (16).

The magnitude of CKD and the scarcity of existing treatmentmodalities for such patients in our environment which theycan hardly afford, means that effort should be geared toward preventive measures and early treatment in order to curtail future ESRD epidemic. An aggressive proactive approach is required in the management of CKD and this will include the control of dyslipidemia, hypertension, infections, diabetes mellitus, smoking and alcohol consumption. The need to intensify effort on health education and screening of general public for CKD and dyslipidemia cannot be overlyemphasized.

Thisstudy indicated that,there is a negative weak correlation between cholesterol and HDL-C with age, while there is a positive weak correlation between LDL-C with age.On the other hand no correlation between triglyceride and age was found.

Concurrent with previous finding, both systolic and diastolic blood pressure were significantly increased in CKD patients in comparison with control group.This finding is in an agreement with previous study conducted by Eric and David (18), who reported that, sustained elevations in blood pressure worsen the progression of kidney disease; in contrast, the declines in kidney function could lead to rises in blood pressure. In fact, hypertension is the second leading cause of CKD (19).

The results of creatinine and GFR level showed that, most CKD patients are in advanced stages of the disease.This finding is in an agreement with the pervious study conducted by Khmer (20), who found that, the prognosis of advanced CKD in most Sub-Saharan Africa is still very poor due to late presentation/referral and inability to pay for treatment.

Moreover the present study showed that, there is an insignificant decrease in the mean of GFRin CKD patients with CVD when compared with CKD patients without CVD.This findingis in an accord with the study conducted by Tarek et al (21), who reported that, the reduction of GFR lead to worsen of the CVD outcomes in CKD patients.

Furthermore, both SBP and DBP were significantly increased in CKD patients with CVD compared to that without CVD, which is in an agreement with previous work conducted by Lancet (22) who found that, each 20-mm Hg increase in SBP or 10-mm Hg increase in DBP doubles the death rates from CVD in adult patients who have CKD.

Conclusion: dyslipidemia (high levels of cholesterol, TG, LDL-C and low levels of HDL-C) was higher in patients with CKD. Thus, the lipid profile levels were strongly associated with cardiovascular events in patients who have CKD and are on maintenance hemodialysis (HD).

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