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Serum lipid profiles in patients with chronic kidney disease in a Saudi population

Abstract

Background and objective: Chronic kidney disease (CKD) is an increasing public health issue. Serum lipids might be independent risk factors for CKD. We aim to examine the association of serum lipid profiles, lipid ratios with CKD in a Saudi population.

Methods: We analyzed 3602 participants whom are between the ages 18 to 98 years. All patients were from the population of the diabetic centre and Primary health centre at King Fahad Armed Forces Hospital, Jeddah, Saudi Arabia.

Main results: A total of 3602 subjects (the mean age was 49.1 ± 14.1 years, minimum 18 years and maximum 98 years) were included in the analysis. 1358 (37.7%) subjects were men and 700 (19.4%) subjects had CKD. 391 (28.8%) cases were male and 309 (13.8%) cases were female with male to female ratio 2.1:1, P<0.0001. Patients with CKD were significantly older than patients without CKD, (57.1 ± 12.9 vs. 47.2 ± 14.1 respectively, p<0.0001). Mean BMI was significantly higher in patients with than without CKD (31.6 ± 6.4 vs. 30.8 ± 6.9 respectively, p=0.006). Moreover, Patients with CKD have significantly higher prevalence of type 2 diabetes and hypertension than patients without CKD (85.5% and 64.9% respectively, p<0.0001). Patients with CKD have significantly higher mean and percentage of TC, LDL, TG and low HDL than patients without CKD, p<0.0001. Patients with CKD had a higher TC/HDL ratio, LDL/HDL ratio and TG/HDL ratio, than patients without CKD, and all of these differences were significant (p<0.0001). Male had significant higher serum TC, lower LDL and lower HDL than female (p<0.0001). Male had also a higher significant TG/HDL ratio, a higher TC/HDL ratio and nonsignificant a higher LDL/HDL ratio than female. Percentage of TC, LDL, TG and low HDL CKD is non-statistically consistently increasing with age.

Conclusion: Dyslipidemia TC, LDL, TG and low HDL is high in patients with CKD. Moreover, TC/HDL, LDL/HDL and TG/HDL ratios were significantly high in patients with CKD. Thus, confirming presence of atherogenic lipid profile needing early intervention to prevent cardiovascular complications.

Keywords: dyslipidemia, chronic kidney disease, HDL, cardiovascular disease, diabetes

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Khalid S Aljabri,[1] Samia A Bokhari,[1] Muneera A Alshareef,[1] Patan M Khan,[1] Hesham M AbuElsaoud,[1] Mohammad M Jalal,[1] Rania F Safwat,[1] Rehab El Boraie,[1] Nawaf K Aljabri,[2] Bandari K Aljabri,[3] Arwa Y Alsuraihi,[3] Amjad I Hawsawi[3]

[1]Department of Endocrinology, King Fahad Armed Forces Hospital, Kingdom of Saudi Arabia
[2]Department of Laboratory, Northern Armed Forces Hospital, Kingdom of Saudi Arabia
[3]College of medicine, Um Al Qura University, Kingdom of Saudi Arabia

Correspondence: Khalid SJ Aljabri, MD, FRCPC, FRCPC(Endo), FACP, ABIM, ABEM, Department of Endocrinology, King Fahad Armed Forces Hospital, Jeddah, Kingdom of Saudi Arabia, PO Box 9862, Jeddah 21159, Kingdom of Saudi Arabia, Tel +966590008035, Fax +966(02)5760665, Email khalidsaljabri@yahoo.com

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Introduction

Chronic kidney disease (CKD) is defined as increased urinary albumin excretion and reduced glomerular filtration rate or both and absolutely an epidemic of increasing prevalence with worldwide prevalence estimated to be 8–16%.[1] Patients with CKD are at an increased risk for cardiovascular disease (CVD) and have a higher prevalence of hyperlipidaemia than the general population.[2] The severity of lipid abnormalities correlates with proteinuria degree and is a common complication in patients with CKD.[2,3] CKD shares some common risk factors, such as hypertension (HTN) and diabetes, with CVD.

Serum lipids might be independent risk factors for CKD. Previous studies were inconsistent.[4–8] Dyslipidemia might be associated with renal dysfunction development and progression.[9,10] One study found that higher total cholesterol (TC), higher non-HDL-cholesterol and lower HDL (HDL) were significantly associated with an increased risk of developing renal dysfunction.[9]

The recent Kidney Disease Outcomes Quality Initiative guidelines suggest that lipid abnormalities (TC, low density lipoprotein (LDL) and HDL, and triglyceride (TG) should be evaluated in patients with CKD.[11] The National Cholesterol Education Program's Adult Treatment Panel criteria 2003 (NCEP ATPIII) suggests that anyone with hyperlipidaemia should undergo laboratory evaluation for secondary dyslipidaemias.[12] There are limited data on the association of serum lipids with CKD in Saudi populations. The aim of the current study is to examine the association of serum lipid profiles, lipid ratios with CKD in a Saudi population.

Methods

We analyzed 3602 cases that are between the ages 18 to 98 years. All patients were from the population of the diabetic centre and Primary health centre at King Fahad Armed Forces Hospital, Jeddah, Saudi Arabia. All data were collected on the basis of a review of electronic medical data. All patients in the present study fulfilled the revised National Kidney Foundation criteria for the diagnosis of CKD.[11] Weight (kg) and height (cm) were measured were recorded. Body mass index (BMI) was expressed as kg/m^2.[13] Participants were defined as having type 2 diabetes mellitus (T2DM) according to self-report, clinical reports, use of antidiabetic agents and HbA1c (≥ 6.5).[14] HTN was defined when the systolic blood pressure was ≥ 130 mm Hg and/or diastolic blood pressure was ≥ 85 mm Hg in addition to

receiving any medication for hypertension. 15 The method used for determining the cholesterol and TG levels in the laboratory was the Enzmatic method. Dyslipidemia was defined according to the NCEP ATPIII, if one or more of the following are found: serum total TC level ≥ 5.18 mmol/L, TG level ≥ 1.7 mmol/L, LDL-C level ≥ 3.37 mmol/L, and HDL-C- cholesterol level < 1.04 mmol/L, and/or having received treatment for dyslipidemia during the previous 2 weeks.[15,16] The total number of cohort were separated on basis of age values into five groups: <30 years, 30-39 years, 40-49 years, 50-59 years and ≥60 years.

Statistical analysis

Unpaired t-test analysis and Chi square (X2) test (categorical data comparison) were used between variables to estimate the significance of different between groups for demographic and clinical laboratory. All statistical analyses were performed using SPSS Version 23.0. The difference between groups was considered significant when P<0.05.

Results

A total of 3602 subjects (the mean age was 49.1 ± 14.1 years, minimum 18 years and maximum 98 years) were included in the analysis. 1358 (37.7%) subjects were men and 700 (19.4%) subjects had CKD, Table 1. 391 (28.8%) cases were male and 309 (13.8%) cases were female with male to female ratio 2.1:1, P<0.0001. Patients with CKD were significantly older than patients without CKD, (57.1 ± 12.9 vs. 47.2 ± 14.1 respectively, p<0.0001). Mean BMI was significantly higher in patients with than without CKD (31.6 ± 6.4 vs. 30.8 ± 6.9 respectively, p=0.006). Moreover, Patients with CKD have significantly higher prevalence of T2DM, HTN than patients without CKD (85.5% and 64.9% respectively, p<0.0001). Patients with CKD have significantly higher mean and percentage of TC, LDL, TG and low HDL than patients without CKD, p<0.0001. Patients with CKD had a higher TC/HDL ratio, a higher LDL/HDL ratio and TG/HDL ratio, than patients without CKD, and all of these differences were significant (p<0.0001).

Male had significant higher serum TC, lower LDL and lower HDL than female (p<0.0001), Table 2. Male had also a higher significant TG/HDL ratio, a higher TC/HDL ratio and nonsignificant a higher LDL/HDL ratio than female.

Percentage of TC, LDL, TG and low HDL CKD is consistently non-statistically increasing with age, Figure A-D.

Table 1 Baseline demographic and clinical characteristics of all subjects and patients with and without chronic kidney disease [mean±standard deviation or number (%)]

Parameters		All subjects 3602	Chronic kidney disease		P value
			Present 700 (19.4)	**Absent 2902 (80.6)**	
Gender	**Male**	1358 (37.7)	391 (28.8)	967 (71.2)	<0.0001
	Female	2244 (62.3)	309 (13.8)	1935 (86.2)	
Age (years)		49.1 ± 14.1	57.1 ± 12.9	47.2 ± 14.1	<0.0001
Body mass index (kg/m²)		31.0 ± 6.8	31.6 ± 6.4	30.8 ± 6.9	0.006
Type 2 diabetes mellitus		1791 (49.7)	598 (85.4)	1193 (41.1)	<0.0001
Hypertension		1256 (34.9)	454 (64.9)	802 (27.6)	<0.0001
Total cholesterol (mmol/l)	Mean ± SD	4.8 ± 1.0	4.9 ± 1.2	4.8 ± 1.0	0.001
	≥5.18	1150 (31.9)	264 (37.7)	886 (30.5)	<0.0001
Low density lipoprotein (mmol/l)	Mean ± SD	3.0 ± 0.9	3.1 ± 1.0	3.0 ± 0.9	0.001
	≥3.37	864 (31.2)	230 (37.2)	634 (29.4)	<0.0001
Triglyceride (mmol/l)	Mean ± SD	1.6 ± 1.0	1.8 ± 0.9	1.5 ± 1.0	<0.0001
	≥1.7	1130 (32.5)	328 (47.3)	802 (28.8)	<0.0001
High density lipoprotein (mmol/l)	Mean ± SD	1.2 ± 0.3	1.1 ± 0.3	1.2 ± 0.3	<0.0001
	<1.04	916 (32.7)	285 (45.5)	631 (29.0)	<0.0001
Total cholesterol/ High density lipoprotein		4.3 ± 1.4	4.7 ± 1.5	4.2 ± 1.3	<0.0001
Low density lipoprotein / High density lipoprotein		2.6 ± 1.1	2.9 ± 1.1	2.6 ± 1.0	<0.0001
Triglyceride / High density lipoprotein		1.5 ± 1.2	1.9 ± 1.3	1.4 ± 1.1	<0.0001
Serum creatinine (μmol/L)		72.3 ± 30.1	95.3 ± 53.8	66.8 ± 16.3	<0.0001

Table 2 Lipid Abnormalities by Target gender in subjects with chronic kidney disease

Lipids parameters (mmol/l)		All subjects 700	Gender		P value
			Male 391 (55.9)	Female 309 (44.1)	
Total cholesterol	Mean ± SD	4.9 ± 1.2	4.8 ± 1.2	5.2 ± 1.2	<0.0001
	≥5.18	264 (37.7)	139 (35.5)	125 (40.5)	0.2
Low density lipoprotein	Mean ± SD	3.1 ± 1.0	2.9 ± 0.9	3.3 ± 1.0	<0.0001
	≥3.37	230 (37.2)	103 (30.7)	127 (44.9)	<0.0001
Triglyceride	Mean ± SD	1.8 ± 0.9	1.9 ± 1.0	1.2 ± 0.3	0.2
	≥1.7	328 (47.3)	190 (49.0)	138 (45.1)	0.3
High density lipoprotein	Mean ± SD	1.1 ± 0.3	1.0 ± 0.3	1.2 ± 0.3	<0.0001
	<1.04	285 (45.5)	199 (58.7)	86 (29.9)	<0.0001
Total cholesterol/ High density lipoprotein		4.8 ± 1.6	5.1 ± 1.6	4.7 ± 1.6	0.03
Low density lipoprotein / High density lipoprotein		2.9 ± 1.1	3.0 ± 1.1	2.9 ± 1.1	0.2
Triglyceride / High density lipoprotein		1.9 ± 1.3	2.0 ± 1.4	1.6 ± 1.2	<0.0001
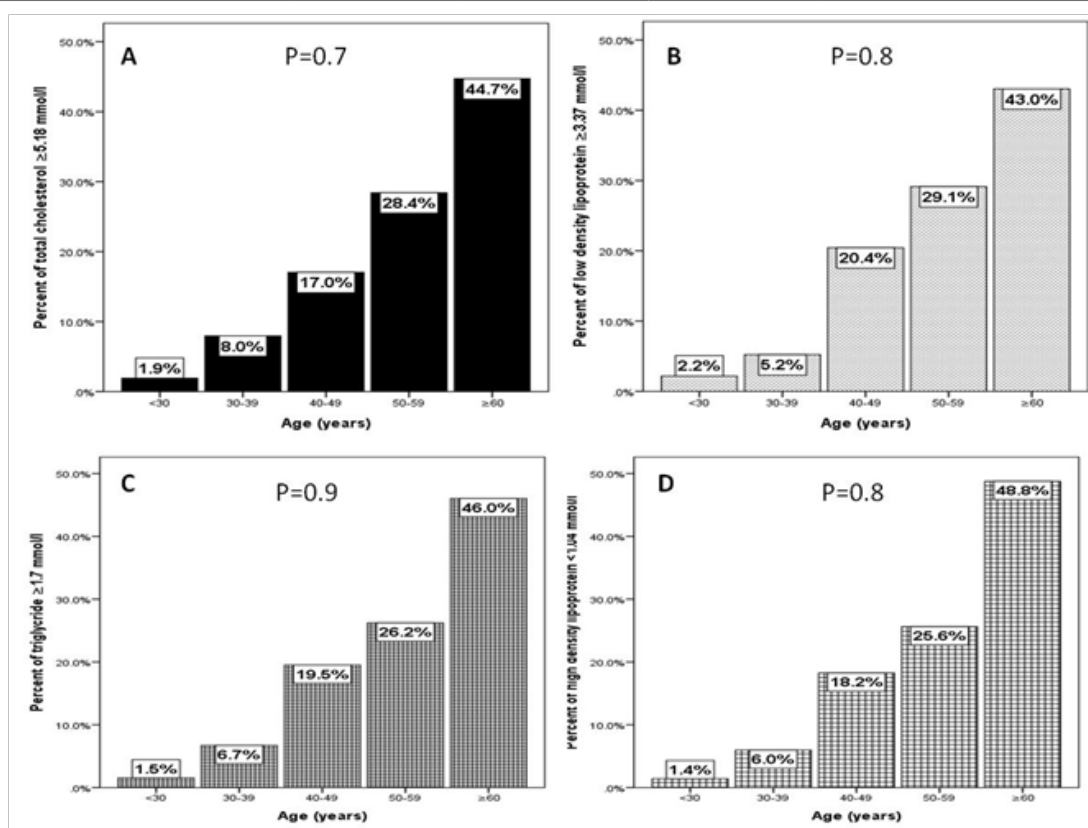
Figure A–D: Percent of lipids profiles in subjects with chronic kidney disease among age groups.

Discussion

We found that dyslipidemia, either higher TC, higher LDL, higher TG or lower HDL were associated with CKD. Moreover, in female, higher TC and higher LDL were associated with CKD.

Globally, increasing trend of CKD has put the health care facilities around the world under tremendous strain. Increase CVD morbidity and mortality in CKD is caused by dyslipidemia. Dyslipidemia seen in CKD is characterized by high TG and low HDL levels, accumulation of remnant particles, predominance of LDL particles.[17] Dyslipidemia might cause kidney damage and to play an important role in the progression of renal failure.[18] Mesangial cells express receptors for LDL and oxidized LDL, which upon activation induce mesangial cell proliferation. Macrophages infiltration release cytokines causing damage to the endothelial cells, mesangial cells and podocytes leading to progressive renal damage.

Various studies have shown that the prevalence of hyperlipidaemia in patients with CKD is higher than in the general population.[2] The severity of lipid abnormalities is a common complication in patients with CKD. There have been few studies reporting the prevalence of dyslipidaemias in patients with CKD.[2] Generally, the prevalence of hyperlipidaemia increases with deteriorating renal function and being proportional to the severity of renal impairment. However, diabetic CKD patients have higher TG and lower HDL suggesting that diabetes itself exacerbates lipid abnormalities in patients with renal impairment.[19]

Although, hyperlipidemia is independent risk factors for progression of CKD, no conclusive evidences demonstrate that isolated hyperlipidemia can lead to CKD in healthy individuals.[20] Recently, studies have demonstrated that statin therapy can halt the progression of kidney failure in patients with CKD.[21–25] The small, dense LDL phenotype is more commonly accompanied by the presence of hypertriglyceridemia, low HDL cholesterol levels, centrally obesity, and insulin resistance. An elevated level of TG and a low level of HDL are also components of metabolic syndrome.[26] a Chinese study showed an increased number of metabolic syndrome components is associated with CKD.[27] Several studies have been performed to assess the role of lipids in the development and progression of CKD. There was an independent association between high LDL levels and decline of renal function.[28] They also reported an elevated LDL/HDL ratio (>4.4) which was associated with a worse loss of renal function. Similar conclusions were achieved by Muntner et al.,[29] evaluating over 2000 subjects.[29] In particular, high TG and low HDL levels were independent risk factors for renal dysfunction. Conversely, cholesterol-LDL values were not predictive for increased risk of kidney injury.

Increased TC/HDL ratio and TG/HDL ratio indicative of atherogenic risk in CKD patients. We found to be high and was statistically significant (p<0.0001) concordant with studies of Cheung et al.,[30] and Avram et al.[31] The mean value of LDL/HDL ratio was statistically significant (p<0.0001) also high which is concordant to the studies of Cheung et al.,[30] and Avram et al.[31] TG/HDL ratio can be used as a surrogate of insulin resistance and can be used to predict coronary heart disease independently.[33–35] Kim et al.,[36] used lipid ratios to predict CKD in Korean populations. The results indicated that TG/HDL-C ratio is the only lipid ratio associated with CKD.[36] However, in the current study, found significant association of lipid ratios with CKD.

Saudi Arabia is ranked among the top 10 countries in the world for the prevalence of diabetes.[37] The prevalence of T2DM is high among Saudi population and is estimated to be 34.1% in males and 27.6% in females.[38] Diabetes mellitus is the leading cause of CKD in both developed and developing countries.[39] The results of our study showed that the frequency of T2DM among patients with CKD was 85.4%, which support that diabetes is the most common cause of CKD which was higher than previously reported (33-69%).[40–42] The difference in the prevalence estimated from this hospital based study and the previous community based study might be attributed to underdiagnoses of CKD in patients with T2DM. The difference could also due to an increase in the prevalence of diabetes and CKD as a complication of diabetes. A similar increase in the prevalence of diabetic kidney disease has been reported in a study carried in Tabuk, Saudi Arabia in the period 2009 to 2012.[43] Mechanisms that lead to kidney disease in diabetes included hyperfiltration injury, advanced glycosylation end products and reactive oxygen species.[44]

HTN is well known to be a risk factor for CKD worldwide.[45] The results of our study showed that the prevalence of HTN among patients with CKD was 64.9%. A retrospective study of 540 Chinese patients with CKD found that 39.6% had HTN.[46] In HTN, glomerular infiltration rate has been reported to decline faster compared to those without HTN.[47] Furthermore, some studies have found a close relation between the rate of decline of glomerular infiltration rate and the development of new onset CKD after a while in patients with HTN.[48]

Strengths and limitations

This study was a retrospective and not longitudinal, preventing determination of whether any risk factors were the cause or result of CKD. Finally, this study was based on a primary care population; thus, the correct sampling weights were not used for insufficient data, thus limiting the generalization of our results to the general population of Saudi Arabia.

Conclusion

It can be concluded from this study that dyslipidemia TC, LDL, TG and low HDL is high in patients with CKD. Moreover, TC/HDL, LDL/HDL and TG/HDL ratios were significantly high in patients with CKD. Thus, confirming presence of atherogenic lipid profile needing early intervention to prevent cardiovascular complications.

Acknowledgments

Conflict of interest

The authors have no conflict of interest to disclose.

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