

# **Albuminuria does not Affect the Level of Low-density Lipoprotein Cholesterol in Patients with Stage 5 Chronic Kidney Disease**

**AdiL O. Bahathiq<sup>1</sup> and Bahaeldin E. Elawad<sup>1</sup>**

## **Abstract**

Chronic kidney disease is a major public health problem. Patients with stage 5 chronic kidney disease on dialysis have 3- to 30-fold increase in mortality. The risk of cardiovascular disease varies depending on the type of lipid abnormalities, the target population, the cause of renal disease, and the degree of reduction in glomerular filtration rate. In patients with pre-existing cardiovascular disease, the presence of chronic kidney disease is associated with an increased risk of cardiovascular events. Plasma total cholesterol is usually normal and only occasionally elevated in end stage renal disease patients. This study was carried out at renal clinic of King Abdulaziz hospital and AL-Noor specialist hospital in holy Makkah district. Thirty adult male patients with stage 5 chronic kidney disease were randomly selected. Low-density lipoprotein cholesterol concentration was measured using automated spectrophotometer machine. Urinary dipsticks (Multistix) were used to test the presence of albumin in urine. The data were recorded and SPSS test was used to analyze the results.

Patients with stage 5 chronic kidney disease with albuminuria have normal concentration of low-density lipoprotein cholesterol. This study concludes that, the presence of albuminuria in patients with stage 5 chronic kidney disease, does not elevate the concentration of low-density lipoprotein cholesterol.

**Keywords:** Patients with stage 5 chronic kidney disease, on dialysis, cholesterol concentration, the presence of albuminuria in urine.

---

<sup>1</sup> Department of Physiology, Faculty of Medicine, Umm AL-Qura University.

## 1 Introduction

Chronic kidney disease is a major public health problem. Adverse outcomes of chronic kidney disease is defined as either kidney damage or glomerular filtration rate less than 60 ml/min/1.73 m<sup>2</sup> of surface area for three months or more irrespective of the particular diagnosis of kidney disease. Kidney damage is defined as pathological abnormalities or markers of damage, including abnormalities in blood or urine test or imaging studies. The national kidney foundation has divided chronic kidney disease into five stages to create a guideline to identify and treat each level of kidney disease. stage is defined by the level of glomerular filtration rate: stage 1: kidney damage with normal or increased glomerular filtration rate (equals or more than 90 ml/min/1.73 m<sup>2</sup>); stage 2: kidney damage with mild decrease in glomerular filtration rate (60-89 ml/min/1.73m<sup>2</sup>); stage 3: moderate decrease in glomerular filtration rate (30-59 ml/min/1.73m<sup>2</sup>); stage4: severe reduction in glomerular filtration rate (15-29 ml/min/1.73m<sup>2</sup>); stage 5: kidney failure or end stage renal disease in which the life of the patient cannot be preserved without dialysis or transplantation (glomerular filtration rate is less than 15 ml/min/1.73 m<sup>2</sup>). In chronic kidney disease the kidneys don't usually fail at once. Instead, kidney disease often progresses over a period of years (1)

Cardiovascular disease is the leading cause of mortality in patients with chronic kidney disease (2). Patients with stage 5 chronic kidney disease on dialysis, in combination with the general population, have 3- to 30- fold increase in mortality, and cardiovascular disease accounts for more than half of all deaths, with myocardial infarction, ischemic cardiomyopathy, stroke and peripheral vascular disease making up the bulk of death (3). The risk of cardiovascular disease varies depending on the type of lipid abnormalities, the target population, the cause of renal disease, and the degree of reduction in glomerular filtration rate. In patients with pre-existing cardiovascular disease, the presence of chronic kidney disease is associated with an increased risk of cardiovascular events (4).

The upper limit of normal for total cholesterol is 240 mg/dl (6.21 mmol/L), low-density lipoprotein cholesterol is 130 mg/dl (3.36 mmol/L), triglycerides is 200 mg/dl (2.26 mmol/L), and the lower limit of high-density lipoprotein is 35 mg/dl (0.91 mmol/L) (5).

Patients with stage 5 chronic kidney disease are characterized by a number of biochemical abnormalities including hyperlipidemia. Hypertriglyceridemia is the most common plasma lipid abnormality in patients with stage 5 chronic kidney disease, co-existing with cholesterol levels within normal range(6).

Plasma cholesterol is usually normal, even reduced, and only occasionally elevated in patients with stage 5 chronic kidney disease. Low-density lipoprotein cholesterol is usually normal and only occasionally elevated in end stage renal disease patients (7).

## 2 Methodology

This is a cross-sectional study, among patients attending renal clinic at King Abdul-Aziz hospital and AL-Noor specialist hospital in holy Makkah district. Thirty patients with stage 5 chronic kidney disease were randomly selected. All of them are male adult patients. Apparently healthy adult male volunteers were also randomly selected as control groups. An informed consent of the patients and volunteers was obtained. The hospitals' authority was informed and asked for permission and ethical approval was provided. Venous blood was collected. Blood samples were subjected to measurement of

concentration of low-density lipoprotein cholesterol concentration using fully automated spectrophotometer machine (Dimension). It is a direct method using selective detergents without specimen pre-treatment. Blood samples collected after overnight fasting in containers containing EDTA. Blood is centrifuged and plasma is removed immediately. Low density lipoprotein cholesterol is stable in the specimen for 1-3 days at 2-8 C and for 1 month at -20 C. With addition of reagent enzymes (First phase), only non-low density lipoproteins are solubilized. Such generated cholesterol, subjected to cholesterol oxidase and cholesterol esterase actions, produces a colorless compound. During the second phase, specific detergent solubilizes the low-density lipoprotein cholesterol with the development of N,N-bis (4-sulphobutyl)-m-toluidine-disodium (BSBm). The chromogenic coupler allows for color formation that is proportional to the concentration of low density lipoprotein-cholesterol. The absorbance is measured at 546 nm (520-580) ( 8 ). Urinary dipsticks were used to test the presence of albumin in urine. Untimed (spot) urine samples were collected in a clean sterile container. Multiple combination strips (Multistix) immersed completely in the fresh urine and withdrawn immediately, drawing edge along rim of container to remove excess. The reagent pad contains a colorimetric P<sup>H</sup> indicator dye which changes color when bound by negatively charged serum proteins, including albumin (9). The data were recorded. The statistical package for social science (SPSS) version 17 was used to analyze the results.

### **3 Results**

In all patients with stage 5 chronic kidney disease the concentration of low-density lipoprotein cholesterol lies within the normal range with a mean concentration of 2.12 mmol/L ( 82 mg/dl) (Table 1).

#### **3.1 Discussion**

Patients with chronic kidney disease, in general, are at higher risk for cardiovascular disease than patients in the general population. One of the most important potentially modifiable risk factor for cardiovascular disease in patients with chronic kidney disease is dyslipidemia. Patients with chronic kidney disease showed significantly decreased total cholesterol and low-density lipoprotein cholesterol with increased triglyceride concentration. The latter is consistently associated with a great risk of increased creatinine levels, and thus a decrease in kidney function. Similarly low levels of high-density lipoproteins are associated with great risk for cardiovascular disease. In contrast, total cholesterol and low-density lipoprotein cholesterol concentration showed no association with the risk of chronic kidney disease. Patients with chronic kidney disease have normal concentration of low-density lipoprotein cholesterol (10). Therefore, the assessment of the risk of cardiovascular disease in patients with chronic kidney disease should base on other measurement instead of low-density lipoprotein cholesterol. Recent studies have confirmed that albuminuria is another strong factor for cardiovascular disease (11). Albuminuria increases the likelihood of high level of low-density lipoprotein cholesterol in patients with chronic kidney disease (12).

In this study, all patients with stage 5 chronic kidney disease have albuminuria. However, the concentration of low-density lipoprotein cholesterol for all of them remain within the

normal range. The mean concentration of low-density lipoprotein in these patients is 2.12 mmol/L (82 mg/dl). It is lower than that of control group. Thus, the presence of albuminuria in patients with stage 5 chronic kidney disease is not supposed to be responsible for the elevation of the concentration of low-density lipoprotein cholesterol in these patients. We infer that, the impairment of renal function has got a positive impact on the metabolism of low-density lipoprotein cholesterol. Although, such impact remains to be elucidated. Albuminuria, is regarded as a sensitive measure of progression of glomerular disease. Glomerular injury (damage of glomerular capillaries, basement membrane, and/or podocytes), usually induces an increase in glomerular permeability to macromolecules, resulting in increased urinary excretion of plasma proteins. Under conditions of severe glomerular injury, albumin (molecular weight is approximately 69 KD) is the most abundant protein excreted in the urine, generally accounting for more than 50% of the urinary proteins. Thus albumin is the hallmark of glomerular proteinuria. It seems that, albuminuria is associated with release of certain endothelial factors which are likely to lower the level of low-density lipoprotein cholesterol. It is not clear whether the impairment of renal function in patients with stage 5 chronic kidney disease is responsible for dyslipidemia or the dyslipidemia is responsible for the deterioration of renal function in patients with stage 5 chronic kidney disease. Therefore, experimental and interventional studies are needed to prove that albuminuria is established before the elevation of low-density lipoprotein cholesterol in order to conclude that albuminuria induces elevation of low-density lipoprotein cholesterol in patients with stage 5 chronic kidney disease. Although our study is small, it calls for further magnified studies to support the fact that albuminuria does not affect the concentration of low-density lipoprotein cholesterol in patients with stage 5 chronic kidney disease. The measurement of urinary albumin creatinine ratio is recommended as a marker of proteinuria rather than albuminuria. The involvement of both sexes is necessary to see whether the gonadal hormones have something to do with the level of low-density lipoprotein cholesterol in patients with stage 5 chronic kidney disease.

#### 4 Labels of Figures and Tables

Table 1: Concentration of low-density lipoprotein (LDL) cholesterol in mg/dl in patients with stage 5 chronic kidney disease (CKD) and control group. SD (standard deviation); SE (standard error of the mean)

	Control	Stage 5 CKD
Total Number	30	30
Mean	96	82
SD	17	19
SE	3.5	3.6

Albuminuria is recorded in all patients with stage 5 chronic kidney disease and summarized in (Table 2).

Table 2: Albuminuria in patients with stage 5 chronic kidney disease (CKD) and control group.

	Albuminuria				Total Number
	+3	+2	+1	nil	
Control	0%	0%	0%	100%	30
Stage 5 CKD	20%	57%	23%	0%	30

## 5 Conclusion

The presence of albuminuria, in patients with end stage renal disease, does not lead to elevation of the concentration of low-density lipoprotein cholesterol.

## References

- [1] Guideline for Chronic Kidney Disease: Evaluation, Classification, and Stratification .National Kidney Foundation. K/DOOJ Clinical Practice. *Am J Kidney Di* 39: (1), (2002),1-266.
- [2] Block GA, Klassen PS, Lazarus JM, Ofsthun N, Lowrie EG, Chertow GM: Mineral Metabolism, Mortality, and Morbidity in Maintenance Hemodialysis.*J Am SocNephrol* 15:(2208), (2004),2218.
- [3] Foley RN, Parfrey PS, Sarnak MJ. Clinical Epidemiology of Cardiovascular Disease in Chronic Renal Disease.*Am. J. Kidney Dis.* 32: (5 suppl 3), (1998), S112–19.
- [4] Weiner DE, Tighiouart H, Stark PC, Amin MG, MacLeod B, Griffith JL, et al. Kidney Disease as a Risk factor for Recurrent Cardiovascular Disease and Mortality. *Am J K Dis*44:(2), (2004), 198-206.
- [5] Executive Summary of the Third Report of The National Cholesterol Education Program (NCEP) Expert Panel and Detection Evaluation And Treatment of High Blood Cholesterol In Adults (Adult Treatment Panel III). *JAMA* 285: (19), ( 2001) ,2486-97.
- [6] Castelli D, Stone NJ, Krumlowsky A. Putative Atherogenic Factors in Patients with Chronic Renal Failure. *ProgCardiovasc Dis*; 26: (2), ( 1983) ,133-144.
- [7] AMajumdar, DC Wheeler.Lipid Abnormality in Renal Disease. *J R Soc Med* 93 (4), (2000 ), 178-182.
- [8] Biolabo Reagents. WWW.Biolabo.fr LDLCholesterol. Direct Method Reagent for Quantitative Determination of Low Density Lipoprotein Cholesterol in Human Serum or Plasma 2011
- [9] Landry DW, Bazari H. *Approach to the Patient with Renal Disease. In: Goldman L, Ausiello D, eds. Cecil Medicine.* 24<sup>th</sup> ed. Philadelphia, Pa: Saunders Elsevier; 2011: chapter 116
- [10] Weiner DE, Tighiouart H, Stark PC, Amin MG, Macledo B, Griffith JL, et al. Kidney Disease as a Risk factor for Recurrent Cardiovascular Disease and Mortality. *Am J Kidney Dis*44 :(2), (2004), 198-206.
- [11] Wang Z, Hay WE: Albuminuria and Incident Coronary Heart Disease in Australian Aboriginal People. *Kidney Int*, 68 , (2005) , 1289-1293.
- [12] Shankar A, Klein R, Moss SE, Klein BE, Wong TY: The Relationship Between Albuminuria and Hypercholesterolemia. *J Nephrol*17: (5), (2004), 658-665.