Correlation between LDL, HDL, Total Cholesterol, and Triglyceride with the Degree of Chronic Kidney Disease in Children

Ahmedz Widiasta1,*, Sudung O Pardede2, Dedi Rachmadi1

1Department of Child Health, Universitas Padjadjaran, Bandung, Indonesia
2Department of Child Health, Universitas Indonesia, Jakarta, Indonesia
*Corresponding author: ahmedzwidiasta@gmail.com

Abstract Chronic kidney disease (CKD) is a noncommunicable harmful disease that might decrease child quality of life. The mortality is mostly caused by cardiovascular disease and dyslipidemia as the major risk factor. At present there is lack of study about the correlation between lipid profile and degree of CKD in children. Underlying causes in adults and children are quite different, so it is very important to find out the lipid profile in various degrees of CKD in children. This cross-sectional study was carried out during January–June 2016 in Hasan Sadikin Hospital Bandung and M Djamil General Hospital Padang, Indonesia. Samples were collected consecutively, calculated from coefficient determinant. The power samples gained with G*Power software were 41 children. The study was permitted by the Ethical Committee Hasan Sadikin and M Djamil General Hospital. The correlation was analyzed using multiple linear regression with SPSS 24.0. From the samples we performed ureum, creatinine, LDL, HDL, triglyceride, and total cholesterol. The degree of CKD based on glomerular filtration rate (GFR) was determined by Schwartz formula. The sample consisted of 87 children with CKD stage 1–5 respectively (43, 11, 8, 8, 17).

Correlation between GFR with LDL, HDL, triglyceride, and total cholesterol level were: rs=0.29, IK 95% (0.08; 0.49), p=0.007; rs=0.16, IK 95% (-0.07; 0.37), p=0.150; rs=-0.05, IK 95% (-0.26; 0.15), p=0.625; and rs=0.25; IK 95% (0.04; 0.45), p=0.022, respectively. There were significant correlation between various degrees of CKD with LDL and total cholesterol. No significant correlation between various degree of CKD with HDL and triglyceride.

Keywords: chronic kidney disease, HDL, LDL, triglyceride, total cholesterol


1. Introduction

Chronic Kidney Disease (CKD) is a childhood noncommunicable disease in all over the world. The disease contributed 30–150 times to children mortality, irreversible, and potentially decrease children quality of life. [1,2] The best effort to prevent CKD is early screening in primary, or early treatment of diseases that might progress to be a CKD, and early treatment of pediatric CKD patients to inhibit the progression of CKD.

Like an iceberg-phenomenon, the real prevalence is more than reported, because the early stage of CKD might be without symptom. The diagnosis of CKD is made according to National Kidney Foundation-Kidney Disease Outcome Quality Initiative (NKF-K/DOQI). [3] The prevalence of this disease is 18.5–58.3 cases in 1,000,000 population. The prevalence in America 2–16 cases every 1,000,000 children; in New Zealand 13.6 cases every 1,000,000 children; in Asia 11–12% from all of pediatric admission; in Europe 7.5–21 cases a year; and in Africa 3.0 cases a year. The prevalence in Hasan Sadikin General Hospital Bandung were 52 cases in a year. The late stage of the disease in adults is often caused by metabolic abnormality, including dyslipidemia that can contribute to cardiovascular disease. [1,4,5]

Mostly the disease is associated with glomerulopathy and congenital anomaly of the kidney and urinary tract (CAKUT) 10–15% and 3–25%, respectively. [1] In animal model, dyslipidemia occurs as the degree of CKD increase. The prevalence of cardiovascular disease in CKD is 24.3% in under 5 years, and 36.9% in 15–19 years old. [1] The increased level of total cholesterol, LDL, and triglyceride in CKD might increase the risk of cardiovascular disease, so NKF recommended the protocol of dyslipidemia treatment for CKD patients. [12,4,5,6,7]

Previous studies on lipid profile in CKD were mostly on adult patients, only a few were about triglyceride, LDL, and total cholesterol in CKD children. [5,6,7,8]

The underlying disease of CKD in adults is quite different than in children. The most frequent causes of CKD in adults are diabetes mellitus and uncontrolled hypertension, while in children it is represented as glomerulopathy and congenital anomaly of the kidney and urinary tract (CAKUT), so it is probable that the lipid profile in CKD of adult is totally different than in children. [1,5]
Chronic kidney disease is a kidney damage for 3 months or longer, defined by structural or functional abnormalities of the kidney, with or without decreased glomerular filtration rate (GFR), manifested by either pathologic abnormalities or markers of kidney damage, including abnormalities in the composition of the blood, urine, or abnormalities in imaging studies. [3] The disease is associated with a lot of metabolic disorders, including hypertension and dyslipidemia. [1,2,4,5,6,7] In CKD there is a progressive decrease of lean body mass (LBM), and higher risk of malnutrition with increased stage of CKD, caused by uremia, acidosis, inhibition of insulin like growth factor-1 (IGF-1), and proteolytic enzyme activation. [8,9,10,11] Loss of LBM and malnutrition is also contributing to atherosclerosis, caused by hypertension, oxidative stress, insulin resistance, inhibition of nitric oxide synthesis, adiposokin dysfunction, and inhibition of HDL maturation. [12,13] Hormonal metabolism is also impacted by CKD, growth hormone-insulin like growth factor (GF-IGF) resistance, thyroid dysfunction, hypogonadism, also cause catabolic state. [12,13,14] Specific cytokines like interleukin-1β (IL-1β), IL-6, TNF-α and interferon-α increase as an inflammation stress and result in appetite regulation, lipid, and protein metabolism. [8,15,16,17,18] Specific characteristics of late stage of CKD are cachexia and lipid composition abnormality, that are caused by lipolysis hormone activation and cytokine. [8,19,20,21] Proinflammatory cytokines increase reactive oxygen species (ROS) and regulate positive feedback through nuclear kappa-β (NFKβ). [8,11] In CKD cellular distruction is caused by proinflammatory response in ROS production and cytokine effect. [8]

2. Method

This was a cross sectional study in CKD children, got ethical approval from the ethical committee of Dr. Hasan Sadikin Bandung and M. Djamil General Hospital Padang, Indonesia, and every participant had completed the informed consent. The subject included all CKD pediatric patients in both hospitals during the period of January–August 2016 who met the inclusion criteria and were not excluded based on the exclusion criteria. The inclusion criteria included 1 –18 years old children with CKD. The exclusion criteria included acute exacerbation of CKD.

Sample size was determined by determination coefficient, α-value, β-value, and number of predictor in a model. Determination coefficient got by a pilot study in 15 CKD children, then processed by SPSS version 24.0 to get the sample size. Determination coefficient (R²) was decided by linear regression curve, y = mx + c, 0 < R² < 1. Sample size was estimated by formulation for linear multiple regression, assisted by G* Power version 3.1.9.2 for windows operation. [22]

Based on the pilot study of 15 subjects, determination coefficient was 0.2139. Parameter amount in linear regression = 3, type I error (α) = 0.05, probability of type II error (β) = 0.2, determined sample size was 41.

All of the subjects were identified by age and gender. Chronic kidney disease was diagnosed by pediatric nephrologist in both hospitals based on kidney disease outcome quality initiative (KDOQI) criteria, the subject was then determined staging of CKD by Schwartz formula and performed low density lipoprotein (LDL), high density lipoprotein (HDL), trygliceride, and total cholesterol level from blood.

3. Results

During the study there were 87 children with CKD consisted of 54 males and 33 females, none of them had obesity. Stage I to V CKD were 43, 11, 8, 7, 17, respectively. Children with CKD stage I 45.6% had high LDL level, 89% were nephrotic syndrome. Of 43 children with stage I CKD, 32 had low HDL level, 87.5% with nephrotic syndrome. Of 43 children with stage I CKD (51.2%), 22 had high triglyceride level, 19 (86.4%) with nephrotic syndrome. Of 43 (65.1%) children with stage I CKD, 28 had high total cholesterol level, and 25 children (89.3%) with nephrotic syndrome.

![Figure 1. Correlation between GFR and LDL level](image)

Table 1. Characteristics of CKD

<table>
<thead>
<tr>
<th>Degree of CKD</th>
<th>Male</th>
<th>Female</th>
<th>Nephrotic syndrome</th>
<th>Non nephrotic syndrome</th>
<th>CAKUT and Urinary Tract Infection</th>
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Of 11 children with stage II CKD, 6 (54.5%) had high LDL level and 4 children (66.7%) were diagnosed as nephrotic syndrome. Of 11 children, 8 (72.7%) had low HDL level, and 5 of 8 (62.5%) were with nephrotic syndrome. Of 11 children with stage II CKD (27.3%), 3 had high triglyceride level and 2 children (66.7%) were with nephrotic syndrome. Of 11 (45.5%) children with stage II CKD, 5 had high total cholesterol level and 4 children (80%) with nephrotic syndrome.

In 3 of 8 (37.5%) children with stage III CKD the level of LDL were high, all of them were with nephrotic syndrome. Eight children (100%) had low HDL level, 5 of which (62.5%) were with nephrotic syndrome. Four of 8 (50%) children had high triglyceride level, and 1 (25%) was with nephrotic syndrome. Of 8 children with stage III CKD, 4 (50%) had high total cholesterol level, and 3 (75%) were with nephrotic syndrome.

Of 8 children with stage IV CKD, 3 (37.5%) had high level of LDL. None of them had nephrotic syndrome. Of 8 children with stage IV CKD, 5 (62.5%) had low HDL level. None of them had nephrotic syndrome. Of 8 children with stage IV CKD, 4 (50%) had high triglyceride level. None of them had nephrotic syndrome. Of 8 children with stage IV CKD, 4 (50%) had high total cholesterol level. None of them had nephrotic syndrome.

Of 8 children with stage V CKD, 7 (46.7%) had high LDL level, and 2 children (28.6%) had nephrotic syndrome. Of 17 children with stage V CKD, 12 (70.6%) had low HDL level, 3 (25%) children had nephrotic syndrome. Three of 17 (17.6%) children had high triglyceride level. Of 17 children with high total cholesterol level, 7 (41.2%) and 1 (14.3%) had nephrotic syndrome.

Most of the CKD were caused by glomerulopathy, and most of glomerulopathy in our study were caused by nephrotic syndrome. None of the children had obesity, most of them had good nutritional state and mild–moderate malnutrition. Glomerulopathy that were found in stage I to V CKD were 86.1%, 81.8%, 62.5%, 75%, and 76.5%, respectively.

4. Discussion

The study was performed during January–August 2016 in Hasan Sadikin General Hospital, Bandung and M. Djamil General Hospital, Padang. There were 87 children with CKD, aged 1–16 years. Mostly the CKD were caused by glomerulopathy. The incidence of glomerulopathy in stage I to V CKD were 86.1%, 81.8%, 62.5%, 75%, and 76.5%, respectively. This was similar with previous studies which revealed that most of the etiologies of CKD was resulted from glomerulopathy and CAKUT. [2,4,6-21]

The children with stage I CKD in this study 45.6% had high LDL level, 74.4% had low HDL level, 51.2% had high triglyceride level, and 65.11% had high total cholesterol level. Children with stage II CKD 54.5% had high LDL level, 72.7% had low HDL level, 27.3% had high triglyceride level, and 45.5% had high total cholesterol level. Children with stage III CKD 37.5% had high LDL level, 100% had low HDL level, 50% had high triglyceride level, and 50% had high total cholesterol level. Most of stage I, II, and stage III children with CKD had
nephrotic syndrome as underlying disease, so that dyslipidemia can be due to nephrotic syndrome. Probably dyslipidemia caused by lack of lipoprotein due to hipoalbuminemic state in nephrotic syndrome.

The children with stage IV CKD in this study 37.5% had high level of LDL, 62.5% had low level of HDL, 50% had high triglyceride level, and 50% had high total cholesterol level. The condition was very different with stage I, II, or III, which in stage IV CKD no one had nephrotic syndrome as underlying disease. Most of them caused by congenital anomaly of the kidney and urinary tract (CACUT) and complicated urinary tract infection. Children with stage V CKD in this study 46.7% had high LDL level, 70.6% had low HDL level, 17.6% had high triglyceride level, and 41.2% had high total cholesterol level, most of their underlying disease were CACUT.

There was significant correlation between glomerular filtration rate (GFR) with LDL and total cholesterol level. The lower GFR the lower LDL and total cholesterol level. From this study there was no significant correlation between degree of CKD with triglyceride and HDL level.

This result is different with previous studies in adult patients, the higher stage of CKD, the higher LDL, total cholesterol, triglyceride, and the lower HDL level. [22,23,24,25,26,27] The difference is probably due to hyperleptinemia, inflammation response, and loss of lean body mass (LBM). [8-13] The response of inflammation also increased Reactive Oxidative Stress (ROS) that role in anorexia and metabolic dysfunction. [8-13] Anorexia-cachexia syndrome make LDL, total cholesterol, and triglyceride level decrease. Late stage CKD is usually accompanied by Protein Energy Malnutrition (PEM). Children body need adenosine triphosphate (ATP) to maintain daily requirements. If the energy from carbohydrate and protein is not adequate, lipid will be used, then lipolysis will occur.

The difference with previous studies was that HDL level decreased with higher stage of CKD. There is an impairment on HDL maturation in CKD children, because of lechitin colin acyl transferase (LCAT) and cholesteryl ester transfer protein (CETP) deficiency. [28-35] Maturation of HDL is very determined by LCAT, apo A-I, apo A-II, apo-B, apo-E, and apo C-III. In our study we didn’t perform LCAT, apo A-I, apo A-II, apo-B, apo-E, and apo C-III, and CETP examinations.

5. Conclusion

Dyslipidemia is relatively frequent in children with CKD (about 20% of pediatric CKD cases). [36] Unsimmilar with previous studies in adult, there was no correlation between the degree of CKD with triglyceride level in this study, in which the higher the degree of CKD, the higher the triglyceride level was, as an impact of lipase deficiency. This might be caused by the underlying cause of CKD in adults were quite different than in children. CKD in adults were mostly caused by Diabetes Mellitus (DM), uncontrolled hypertension, and metabolic syndrome due to obesity, while in children it was mostly caused by glomerulopathy and CACUT.

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References


