Comparative Evaluation of Carotid Intima-Media Thickness (CIMT) in Children with Early-Stage Chronic Kidney Disease and Healthy Individuals

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Abstract

Background and Aim: The prevalence of Chronic Kidney Disease (CKD) in children is 18 per million. The first stage of atherosclerosis in children at risk begins with vascular endothelial dysfunction and thickening of the intima-media of the arteries. The aim of this study was to evaluate the thickness of the carotid artery intima-media in children with early-stage chronic kidney disease.

Methods: The cases were selected from patients with chronic renal failure presenting to the pediatric nephrology clinic whose CKD was confirmed by ultrasound, kidney scan or laboratory tests. Ultrasound of all patients was performed by a sonographer and an ultrasound machine. The control group was also selected from subjects who presented to a kidney clinic for routine examination and testing without a history of any diseases and did not have kidney or cardiovascular disease. Chi-square and t tests, one-way analysis of variance, and Pearson's correlation coefficient were applied to compare and describe the results.

Results: One-way analysis of variance showed no significant difference in the mean carotid intima-media thickness (CIMT) between patients with early-stage CKD and control subjects. Moreover, according to the results of the Pearson's correlation coefficient, there was no significant relationship between CIMT and laboratory variables in the patient group.

Conclusion: No significant relationship was observed in the carotid artery intima-media thickness between patients with early-stage CKD and control group. Thus, CIMT is not a reliable method in selection of high risk patients in early stages CKD but it can be very useful in high stages CKD.

Keywords: Children; Chronic Kidney Disease; Intima Media Thickness.

Introduction

The prognosis of chronic kidney disease (CKD) has improved dramatically since 1970 due to improved medical procedures (1).
One of the problems in CKD is the increased risk of cardiovascular disease, which increases mortality in the patients.

Compared to the general population of the same age and sex, patients with CKD are more likely to develop atherosclerosis (hardening of the arterial wall) (2). Hypertension is a major risk factor for atherosclerosis. Since patients with CKD also suffer from hypertension, they are at a higher risk for

developing atherosclerosis (3). The first stage of atherosclerosis in at-risk children begins with vascular endothelial dysfunction and thickening of the arterial wall (1).

Increased intima-media thickness of the common carotid artery is used as a criterion for the onset of atherosclerosis (4). One method to find people who are at a higher risk for coronary artery disease is direct imaging of the arteries, which can be identified before the onset of clinical symptoms (pre-clinical phase). The best method is to measure the thickness of the common carotid artery using ultrasound and to perform a CT scan to observe coronary artery calcification. Both methods can identify high-risk individuals for cardiovascular disease. In a single meta-analysis of 14 population-based cohort studies, every 0.1 mm increase in the carotid intima-media thickness (CIMT) increased the risk of cardiovascular disease by 9% (5). One autopsy study found a significant increase in coronary artery intima-media thickness in patients with CKD compared to other non-CKD patients with coronary artery disease (although these patients were age- and sex-adjusted) (6).

Many recent studies have shown an increase in the intima-media thickness even in patients with early stages of CKD. This indicates that the glomerular filtration rate (GFR) independently predicts the carotid artery diameter.

Arterial wall thickness can be obtained non-invasively by measuring the CIMT using ultrasound (6). CIMT is also independent to other risk factors of cardiovascular death in CKD patients. It is used as a useful method in epidemiological studies. In adults, increased intima-media thickness (IMT) has been found to be associated with the prevalence of myocardial infarction (7).

A study of 32 children with high blood pressure by Sorof and et al found a significant relationship between carotid media thickness and left ventricular muscle mass (after adaptation in terms of age and sex) (7).

CIMT has also been shown to be a useful predictor of pre-clinical (pre-symptomatic) atherosclerosis in children and adults (7).

This study was conducted to measure the CIMT in children with early-stage chronic renal failure in Kurdistan Province and to compare the results with similar studies.

Methods
This descriptive-analytical cross-sectional study was performed on patients with chronic renal failure that presented to a nephrology clinic. The study population was 31 patients with chronic renal failure (stags 1 to 3) that with normal cardiac echo findings and without hypertension or cardiovascular disease. After obtaining informed consent, they were introduced to a radiologist (sinologist) and a laboratory using predesigned forms. The control group comprised 30 normal children selected from subjects who presented to the kidney clinic for routine check-ups and routine tests without a history of any diseases and did not have kidney or cardiovascular disease. After obtaining informed consent and checking their blood pressure, they were also referred for an ultrasound examination. Ultrasound examination was performed by a sonographer and an ultrasound machine and the measurement was done from the left common carotid artery 2 cm below the carotid bifurcation in the supine position with the head elevated at 30˚. Blood samples were also collected and tested by a technician in one laboratory. Calcium, phosphorus, blood urea, creatinine, total cholesterol, triglyceride, blood glucose and uric acid levels were measured for both groups (patients and controls). The Body Mass Index (BMI) and GFR were calculated for both groups.

The data were analyzed with SPSS version 22 using chi-square and t tests, one-way analysis of variance, and Pearson's correlation coefficient. P values less than 0.05 were considered significant.

Results
Present study was carried out on clinical and para-clinical data of 31 patients (13 (42%) female and 18 (58%) male) and 30 controls (17 (56.7%) female and 13 (43.3%) male). The mean age of the CKD and control group was 7.7 (SD=3.4) and 7.3 (SD=3) years, respectively. The age range of the subjects was 4-16 years in both groups. The mean BMI was 16.9 (SD=4.1) in the CKD and 16.8 (SD=3.4) in the control group. Of 31 CKD patients, 22 were in stage 1, 8 were in stage 2, and 1 was in stage 3. The mean CIMT was 0.55 mm in the CKD and 0.50 mm in the control group. The results Pearson's correlation test in CKD and control groups are summarized in Table 1.

Table 1. Baseline characteristics of study groups based on Pearson correlation coefficient

Uric acid	TG	Chol	Ph	Ca	Cr	BUN	BS	GFR	CIMT	Groups
-.128	-.251	-.219	-.286	.083	.057	.059	-.164	.112	1	CKD
.165	.251	-.176	.324	-.005	.107	-.449*	-.277	.127	1	control
-.070	.082	.220	.135	-.311	-.688*	-.141	-.180	1	.112	CKD
.011	.056	.096	.239	-.111	-.440*	.201	.051	1	.127	control
.286	-.412*	-.111	.237	.104	.246	.205	1	-.180	-.164	CKD
.341	.246	-.231	-.003	.015	.399*	.130	1	.051	-.277	control
-.092	-.426*	.114	-.227	-.014	.014	1	.205	-.141	.059	CKD
-.123	-.401*	.083	-.012	-.180	-.065	1	.130	.201	-.449*	control
.394*	-.146	-.374*	-.239	.066	1	.014	.246	-.688*	.057	CKD
.325	.218	-.280	-.049	-.108	1	-.065	.399*	-.440*	.107	control
-.123	.015	.100	-.126	1	.066	-.014	.104	-.311	.083	CKD
-.124	.289	-.036	-.082	1	-.108	-.180	.015	-.111	-.005	control
.049	.144	.231	1	-.126	-.239	-.227	.237	.135	-.286	CKD
.351	.048	.040	1	-.082	-.049	-.012	-.003	.239	.324	control
-.304	.495*	1	.231	.100	-.374*	.114	-.111	.220	-.219	CKD
.053	-.291	1	.040	-.036	-.280	.083	-.231	.096	-.176	control
-.172	1	.495*	.144	.015	-.146	-.426*	-.412*	.082	-.251	CKD
.104	1	-.291	.048	.289	.218	-.401*	.246	.056	.251	control
1	-.172	-.304	.049	-.123	.394*	-.092	.286	-.070	-.128	CKD
1	.104	.053	.351	-.124	.325	-.123	.341	.011	.165	Control

*Significant 0.05

According to the results of one-way analysis of variance (as seen in above tables), there was no significant difference in the mean CIMT between children with early-stage CKD and control group. Moreover, Pearson's correlation test showed no significant relationship between CIMT and laboratory variables in the patient group. Finally, the results of the Pearson's correlation test revealed a significant relationship between CIMT and BUN in the control group but no significant correlation was observed for other variables.

Discussion

The study showed no significant relationship between the CIMT and paraclinical variables in patients with early-stage CKD. However, a 0.05 mm difference was found in CIMT between the two groups, which was not significant. It seems that no changes occur in the intima-media thickness of the arterial wall in the early stages of CKD. In the laboratory data, the mean calcium level was 9.25 mg/dl in the CKD and 9.04 mg/dl in the control group, which was significantly higher in the CKD group (P=0.036). The mean total cholesterol was 154.84 mg/dl in the CKD and 137.34 mg/dl in the control groups, which was significantly higher in the CKD group (P=0.01).

There was no significant difference in other laboratory data between the two groups. Similar results were obtained in a study by Adibi A et al in Isfahan (11). However, in some other studies such as a study by Ali M. Elshafie et al (2014), CIMT had a significant positive correlation with systolic and diastolic blood pressure and a negative correlation with BMI and GFR. Moreover, there was a significant increase in CIMT in patients on dialysis (end-stage renal disease) compared to the control group (8). The present study was conducted on normotensive patients with early-stage CKD. In a study by Tammy Mcloughlinbrady (2012) on 101 CKD patients, CIMT was 0.02 mm thicker in the CKD group versus the control group (9). Renalta L. et al studied 55 CKD (43 patients on maintenance treatment and 12 on dialysis) and found ITM

thickening in 74.5% of the CKD patients. Sorof et al conducted a study on 32 hypertensive children and found a significant relationship between CIMT and left ventricle muscle mass (7).

Conclusion
The results of the present study on early-stage CKD and other studies on higher stages of CKD suggest that the CIMT does not change significantly in early stages of CKD and it becomes thicker in higher stages. As a result, CIMT is not a reliable method for identification of high-risk patients in early stages of CKD while it can be very useful in higher stages.

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Conflict of Interest
The authors declare no conflicts of interest.

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Not declared.

Ethics
This study was approved by ethics committee of Kordestan University of Medical Sciences.

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