CAROTID INTIMA-MEDIA THICKNESS IN CHILDREN WITH CHRONIC KIDNEY DISEASE

By
Ali raga abdel Aal*, Gehan Lotfy Abdel Hakeem*, Khaled salah**,
and Hany Taha Askalany***
Departments of *Pediatric, **Clinical Pathology, ***Cardiology,
El-Minia Faculty of Medicine.

ABSTRACT:

Introduction and objectives: Cardiovascular complications are the main cause of morbidity and mortality among patients with ESRD, mainly in adults, but also in children. Carotid intima-media thickness (CIMT) is the noninvasive technique most frequently used in clinical trials to determine atherosclerosis. Clinical guidelines and medical societies recommend it to obtain a more precise evaluation of cardiovascular health in selected populations, and in cardiovascular disease prevention programs.

Methods: the study involved 80 children divided into 2 groups: 40 had chronic kidney disease which subdivided into, 20 children on conservative therapy (predialysis) and 20 children on hemodialysis, and 40 children were control group. All patients and control were subjected to detailed history taking, clinical examination and investigations as follows:Laboratory investigations included serum creatinine, blood urea, albumin, calcium (Ca), phosphorus (PO_4), alkaline phosphatase, total cholesterol, triglyceride and serum Fetuin-A. $CaXPO_4$ product was calculated. Glomerular filtration rate (GFR) was calculated from serum creatinine from Schwartz formula. All subjects underwent measurements of carotid artery intima-media thickness.

Results: CIMT had a significant positive correlation with duration of illness and CaXPo4 product in both group Ia and Ib. There was a significant increase of carotid artery intima media thickness (CIMT) in group Ia and group Ib when each group was compared to group II, p=0.0001*, and in group Ib compared to group Ia, p=0.0001*. GFR had a significant negative correlation with CIMT.

Conclusions: CKD is associated with significant arterial wall abnormalities in children. This suggests that even in young children, uremia and/or metabolic alterations have a profound impact on arterial structure and function leading to cardiovascular morbidity and mortality. Functional change in the cardiovascular system may start when kidney function is mildly impaired. Duration of illness has an impact on increased aortic stiffness and CIMT.

KEY WORDS:

INTRODUCTION:

Cardiovascular diseases are the leading cause of mortality and morbidity in patients with chronic kidney disease (CKD) including predialysis, dialysis and post renal transplantation subjects[1], and has been established as the leading cause of death in adults with childhood onset end stage renal disease ESRD[2]**.** Vascular ultrasound has a number of potential advantages for the clinical diagnosis of vascular diseases. The most obvious is its non invasiveness and the negligible degree of patient discomfort and morbidity it causes. Ultrasound has some less obvious, but important advantages over more standard imaging technologies

such as angiography. Vascular ultrasound provides multiple longitudinal viewing angles for analysis of arterial lesions, as well as transverse views. It also visualizes the arterial wall and its components, whereas angiography visualizes the arterial lumen[3]. High-resolution carotid ultrasound is a recognized method of evaluating changes in blood vessel walls both in adults and children[4]. Carotid intima-media thickness (CIMT) is the noninvasive technique most frequently used in clinical trials to determine atherosclerosis. Clinical guidelines and medical societies recommend it to obtain a more precise evaluation of cardiovascular health in selected populations, and in cardiovascular disease prevention programs[5].

AIM OF THE STUDY:

The aim of the study is to investigate CIMT in children with CKD.

SUBJECTS AND METHOD:

The study was conducted at El-Minia University Hospital, Faculty of Medicine, El-Minia University and Pediatric Hemodialysis Unit El-Minia General Hospital during the period from August 2010 to June 2011 .

Eighty children were included in this study and were classified as follows:

Group I: included 40 children with chronic kidney disease from stage 1 to stage 5. They were further subdivided into 2 groups:

- **Group IA:** included 20 children with chronic kidney disease on conservative therapy (12 (60%) males and 8 (40%) females with mean age of 9.5±4.1 years.
- **Group IB:** included 20 children with chronic kidney disease on regular hemodialysis therapy (11 (55%) males and 9 (45%) females with mean age of 10.7±2.5 years.

Group II: Included 40 ages and sex matched healthy children enrolled as a control group (20 (50%) males and 20 (50%) females with mean age of 9.7±4.2 years).

All patients and control were subjected to detailed history taking, clinical examination and investigations as follows:

A- Laboratory investigations

All children were fasting for 6-12 hours. Samples were collected from patients on hemodialysis prior to dialysis session.

Five ml of venous blood sample were taken under complete aseptic condition in plain test tubes without anticoagulant. After coagulation, samples were centrifuged.

The separated serum was divided into 2 aliquots; one was designated for immediate assay of the following:

- Serum creatinine, blood urea, albumin, calcium, phosphorous, alkaline phosphatase, total cholesterol and triglyceride were assayed using fully automated clinical chemistry auto-analyzer system Konelab 20i (Thermo Electron Incorporation, Finland).
- Calcium × phosphorous product was calculated.
- Glomerular filtration rate (GFR) was calculated from serum creatinine according to Schwartz formula:

GFR (ml/min/1.73m²) = k × height (cm) / serum creatinine (mg/dl). Where, k is 0.33 for low birth weight infants younger than 1 year, 0.45 for term infants younger than 1 year, 0.55 for children and adolescent females, and 0.70 for adolescent males[6].

All subjects underwent measurements of carotid artery intima-media thickness using GE Vivid3 expert. IMT was defined as the distance between the leading edge of the first echogenic line (lumen-intima interface) of the far wall and the second echogenic line (media–adventitia interface) of the far wall (posterior wall).

RESULTS:

Table 1: Comparison between group Ia and control group as regard biochemical data.

Variables	Group Ia (n=20)	Control (n=38)	p
Urea (mg/dl)	49.2±31.9	24.1±5.6	0.002*
Creatinine (mg/dl)	1.47±0.71	0.7±0.2	0.0001*
Ca (mg/dl)	9±0.69	9.4±0.39	0.04*
Po4 (mg/dl)	5.3±1.4	4.7±0.65	0.03*
CaXPo4	47.5±11.1	43.1±6.3	0.05
Alkaline phosphatase	182.4±123.6	84.3±23	0.0001*
Cholesterol (mg/dl)	253.2±108.8	111.3±35.2	0.0001*
Triglycerides (mg/dl)	261.5±163.3	81.4±19.3	0.0001*

*= *significant difference, p < 0.05.*

This table demonstrated results of urea, creatinine, Ca, PO_4, $CaXPO_4$ product, alkaline phosphatase, cholesterol and triglyceride in group Ia. There was a significant decrease of Ca and a significant increase in urea, creatinine, PO_4, alkaline phosphatase, cholesterol and triglyceride in group Ia compared to control group.

Table 2: Comparison between group Ib and control group as regard biochemical data.

Variables	Group Ib (n=20)	Control (n=38)	p
Urea(mg/dl)	150.2±43.7	24.1±5.6	0.0001*
Creatinine(mg/dl)	6.5±1.5	0.7±0.2	0.0001*
Ca(mg/dl)	8.1±0.64	9.4±0.39	0.0001*
PO_4(mg/dl)	7.8±1	4.7±0.65	0.0001*
$CaXPO_4$	61.6±7.4	45.1±6.3	0.0001*
Alkaline phosphatase	284.1±126.9	84.3±23	0.0001*
Cholesterol(mg/dl)	196.2±75.9	111.3±35.2	0.0001*
Triglycerides(mg/dl)	179±53.9	81.4±19.3	0.0001*

*= *significant difference, p < 0.05.*

This table demonstrated results of urea, creatinine, Ca, PO_4, $CaXPO_4$ product and alkaline phosphatase in groupIb. There was a significant decrease of Ca and a significant increase in urea, creatinine, PO_4, $CaXPO_4$ product, alkaline phosphatase, cholesterol and triglyceride in group Ib compared to control group.

Table 3: Correlation of GFR with CIMT in group Ia.

Variable	GFR (ml/min/1.73 m²)	
	r	p
CIMT(cm)	-0.59	0.005*

*= *significant difference, p < 0.05.*

This table demonstrated that, GFR had a significant negative correlation with CIMT.

Table 4: Correlation of CIMT with duration of illness and $CaXPO_4$ product in group Ia and Ib.

Variable	CIMT in group Ia		CIMT in group Ib	
	r	p	r	p
Duration of illness	0.652	0.002*	0.809	0.0001*
CaXPo4	0.445	0.050*	0.739	0.0001*

*= *significant difference, p < 0.05.*

This table demonstrated that, CIMT had a significant positive correlation with duration of illness and $CaXPO_4$ product in both group Ia and Ib.

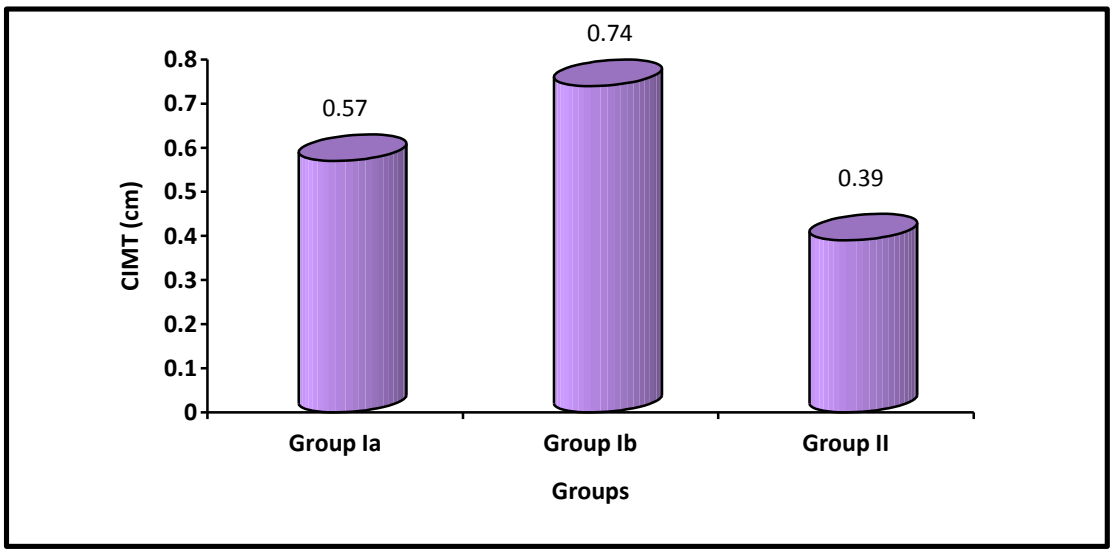

Figure 1: Comparison of CIMT in studied groups.

This figure is showing comparison of CIMT in studied groups. There was a significant increase of carotid artery intima media thickness (CIMT) in group Ia and group Ib when each group was compared to group II, p=0.0001*, and in group Ib compared to group Ia, p=0.0001*.
*= *significant difference, p < 0.05.*

DISCUSSION:

Vascular calcification is widely held to be an important contributor to the cardiovascular morbidity and mortality of patients with advanced atherosclerosis linked to aging, diabetes mellitus and chronic kidney disease. It is associated with fragmentation and reduction of elastic fibers in the arterial wall, vascular stiffening and hence increased cardiac afterload[7]. Early detection of the extent of arterial degeneration caused by atherosclerosis using noninvasive techniques, based on ultrasound, has provided an important stimulus to develop early detection programs and to assess the effects of intervention in the pediatric population[8].

Increased intima-media thickness of the large arteries is an early marker of atherosclerotic changes and a predictor of cardiovascular events in adult dialysis patients[9]. Chronic kidney disease, renal replacement therapies and various treatments induce complex biochemical disturbances of the calcium–phosphate metabolism with a wide spectrum of bone, vascular and soft tissue abnormalities. Changes in mineral metabolism and bone structure are an almost universal finding in progressive chronic kidney disease[10].

Chertow et al., (2004)[11] suggest that serum Ca, PO_4 and $CaXPO_4$ product are responsible for cardiovascular calcifications or for the link between bone and vascular calcifycations. We observed in our study that aortic stiffness and CIMT had a significant positive correlation with $CaXPO_4$ product in CKD patients on conservative therapy and hemodialysis group. The same finding was found by Bakiler et al., (2007)[12] and Moldovan et al., (2010)[13].

Increased intima-media thickness of the large arteries is an early marker of atherosclerotic changes and a predictor of cardiovascular events in adult dialysis patients[9]. Carotid artery ultrasound, which measures CIMT and detects atheromatous plaques, is a strong indicator of overall vascular health. CIMT is a well-recognized and accepted marker to predict cardiovascular disease and was accepted as a surrogate marker of atherosclerosis by the US Food and Drug Administration (FDA) and the European Agency for the Evaluation of Medicinal Products[5].

In our study, we found that CIMT increased significantly in patients with CKD on conservative therapy and in hemodialysis group compared to control group and more in dialysis group compared to group of CKD patients on conservative therapy. This result was supported by Stephanie et al., (2009)[14], Alejandro et al., (2011)[1] and Tanaka et al., (2012)[15] who found that CIMT in patients with CKD was significantly higher compared to control group and CIMT value in hemodialysis patients were significantly higher compared to predialysis patients.

CONCLUSIONS:

CKD is associated with significant arterial wall abnormalities in children. This suggests that even in young children, uremia and/or metabolic alterations have a profound impact on arterial structure and function leading to cardiovascular morbidity and mortality. Functional change in the cardiovascular system may start when kidney function is mildly impaired. Duration of illness has an impact on increased aortic stiffness and CIMT.

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دراسة سمك الطبقة المبطنة و الوسطى للشريان السباتى في أمراض الكلى المزمنة في الأطفال

تعتبر أمراض القلب و الأوعية الدموية من أكثر الأسباب المؤدية إلى الوفاة في الأشخاص الذين يعانون من أمراض الكلى المزمنة. و تبدأ التغيرات التركيبية و الوظيفية بالإضافة إلى التكلس في الأوعية الدموية الكبرى من العقد الأول من العمر في هؤلاء المرضى. و قد وجد أن قياس سمك الطبقة المبطنة و الوسطى للشريان السباتى دلالة ممتازة لتشخيص تصلب الشرايين الغير واضح إكلينيكيا.

الدراسة و طرق البحث:

شملت هذه الدراسة ثمانية و سبعون طفلا يعانون من أمراض الكلى المزمنة المترددين على قسم طب الأطفال بمستشفى المنيا الجامعي و وحدة الغسيل الكلوي بمستشفى المنيا العام في الفترة من أغسطس 2010 إلي يونيو 2011 وتم تقسيمهم إلى مجموعتين فرعيتين:

المجموعة الفرعية (أ): شملت 20 طفلا يعانون من أمراض الكلى المزمنة يتلقون العلاج التحفظي.

المجموعة الفرعية (ب): شملت 20 طفلا يعانون من أمراض الكلى المزمنة يعالجون بالاستصفاء الدموي المنتظم.

من الأصحاء كمجموعة ضابطة في نفس العمر والجنس 38 كما تم اختيار

وقد خضع جميع الأفراد قيد الدراسة إلى اخذ التاريخ المرضى, الفحص الاكلينيكى والفحوصات الآتية: الفحوصات المعملية: نسبة البولينا, الكرياتينين, نسبة الألبومين, نسبة الكالسيوم والفوسفور, الكولسترول, الدهون الثلاثية. تم حساب معدل الترشيح الكبيبى من الكرياتنين وفقا لصيغة شوارتز. قياس سمك الشريان السباتى بواسطة الدوبلر.

النتائج:

أظهرت النتائج أن سمك الطبقة المبطنة والوسطى للشريان السباتى زادت بشكل ذو دلالة إحصائية عالية في مرضى الكلى المزمن تحت العلاج التحفظي وفي مرضى الكلى المزمن تحت الاستصفاء الدموي عند مقارنتهم بالمجموعة الضابطة وزادت أيضا بشكل ذو دلالة إحصائية عالية في مرضى الكلى المزمن تحت الاستصفاء الدموي عند مقارنتهم بمرضى الكلى المزمن تحت العلاج التحفظي

الاستنتاج:

يستخلص من ذلك أن زيادة سمك الطبقة المبطنة و الوسطى للشريان السباتى و يمكن أن يستخدم بمثابة دلالة تكلس الأوعية الدموية و تصلب الشرايين المبكر في الأطفال المصابين بأمراض الكلى المزمنة.