Med. J. Cairo Univ., Vol. 87, No. 3, June: 1403-1406, 2019
www.medicaljournalofcairouniversity.net

Soluble Alpha Klotho Serum Level in Chronic Kidney Disease

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Abstract

Background: Chronic Kidney Disease (CKD) is a worldwide public health problem which has bad side effects. Soluble alpha klotho is a phosphate and calcium regulatory hormone which can be used as a biomarker in diagnosis of chronic kidney disease.

Aim of Study: Evaluation of the level of soluble alpha klotho and its role in diagnosis of chronic kidney disease.

Patients and Method: The study was done on eighty cases that were divided into two categories according to their health status and estimated Glomerular Filtration Rate (eGFR), diseased group including sixty patients with chronic kidney disease (eGFR <120ml/min/1.73m^2) and control group including twenty individuals (eGFR >120ml/min/1.73m^2). Patients group were subdivided into five subgroups according to variation in their eGFR. All subjects were subjected to full history taking, thorough clinical examination and assessment of age, sex and risk factors for CKD as hypertension, diabetes mellitus and urinary tract infection. Routine laboratory tests included urea, creatinine, Ca, Po4 level and protein in urine. Serum soluble alpha klotho was estimated by Enzyme Linked Immunosorbent Assay (ELISA).

Results: Our study found that there was significant decrease in soluble alpha klotho serum level with progression of chronic kidney disease which started to be more obvious in stage IIIB.

Conclusion: Soluble alpha klotho is a novel biomarker of chronic kidney disease that shows a significant decrease with disease progression and correlates with other mineral disorders of the disease, so it can be used in diagnosis of chronic kidney disease.

Key Words: *Chronic kidney disease – Soluble alpha klotho.*

Introduction

CHRONIC Kidney Disease (CKD) is a worldwide public health problem which has bad side effects including Cardiovascular Disease (CVD), metabolic bone disease, anemia and premature death [1]. In North Africa chronic kidney disease has additional side effects, including dialysis related infections such as HCV, HBV, and MRSA. In addition it represents an economic problem in these countries [2]. CKD is defined as any abnormality of kidney structure or function that lasts for more than three months. Early detection of CKD and managing risk factors may provide an opportunity to prevent progression of associated risks [3].

Soluble alpha klotho, as a phosphate and calcium regulatory hormone that directly or indirectly suppress PTH, 1,25-(OH)2-vitamin D3, and FGF23 production and release was found to be affected by chronic kidney disease [4].

Experimental models of CKD evidence early reduction of renal klotho mRNA expression with subsequent reduction of s-klotho ensuring its validity as a biomarker in diagnostic and prognostic chemistry for chronic kidney disease [5].

Patients and Methods

This study was done in Clinical Pathology Department in collaboration with Internal Medicine Department, Tanta University Hospitals from July 2017 to February 2018. This study was done on eighty cases that were divided into two main categories according to their health status and estimated Glomerular Filtration Rate (eGFR), diseased group including sixty patients diagnosed as chronic kidney disease (with eGFR<120ml/min/1.73m^2) and control group including twenty apparently healthy individuals (with eGFR >120ml/min/1.73m^2). Patients group were further subdivided into five subgroups according to variation in their eGFR.

All subjects were subjected to clinical evaluation including full history taking, thorough clinical examination and assessment of age, sex and risk factors for CKD which consist of hypertension,

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diabetes mellitus and urinary tract infection. Routine laboratory tests included urea, creatinine, Ca, Po4 level and protein in urine.

Serum soluble alpha klotho was estimated by enzyme linked immunosorbent assay supplied by Sun Red Biotechnology Company, purchased from Biogen Company.

Results

The current study involved investigation of a total number of 60 patients and 20 controls. The patients group was assigned into 5 stages. Stage I included 10 patients with eGFR 90:119ml/min/1.73m^2. Stage II included 10 patients with eGFR 60:89ml/min/1.73m^2. Stage IIIA included 14 patients with eGFR 45:59ml/min/1.73m^2. Stage IIIB included 13 patients with eGFR 30:44 ml/min/1.73m^2. Stage IV included 10 patients with eGFR 15:29ml/min/1.73m^2. Stage V included 3 patients with eGFR <15ml/min/1.73m^2.

Table (1) presents distribution of the studied cases according to stage.

Table (1): Distribution of the studied cases according to stage.

Stage	No.	%	eGFR (ml/min/1.73m^2)
I	10	16.7	90:119
II	10	16.7	60:89
IIIA	14	23.3	45:59
IIIB	13	21.7	30:44
IV	10	16.7	15:29
V	3	5.0	<15

Table (2) presents comparison between the different studied groups according to renal functions.

It shows significant positive correlation between both creatinine and urea levels and progression of CKD (with p-value <0.001).

Table (2): Comparison between the different studied groups according to creatinine and urea levels.

Renal function	Stage I (n=10)	Stage II (n=10)	Stage III A (n=14)	Stage III B (n=13)	Stage IV (n=10)	Stage V (n=3)	Control (n=20)	p
Creatinine (mg/dl):								
Min.-max.	0.7-1.2	1.3-1.8	1.3-2.5	1.6-7.9	2.1-7.9	4.8-10.8	0.5-0.9	<0.001
Mean ± SD.	0.93±0.14	1.4±0.16	1.66±0.32	2.6± 1.65	3.82± 1.99	7.13±3.21	0.68±0.12	
Median	0.95	1.35	1.6	2.2	3.2	5.8	0.7	
p_1	0.163	0.002*	<0.001*	<0.001*	<0.001*	<0.001*		
Urea (mg/dl):								
Min.-max.	29-53	21-105	30-162	43-237	83-162	102-241	10-39	<0.001
Mean ± SD.	41±8.19	52.1±29.59	86.64±46.35	132.54±55.55	122.9±31.99	192±78.04	26.05±8.69	
Median	41	44	72	139	125.5	233	28.5	
p_1	0.076	0.043*	<0.001*	<0.001*	<0.001*	<0.001*		

Fig. (1) presents comparison between the different studied groups according to serum soluble α-klotho levels.

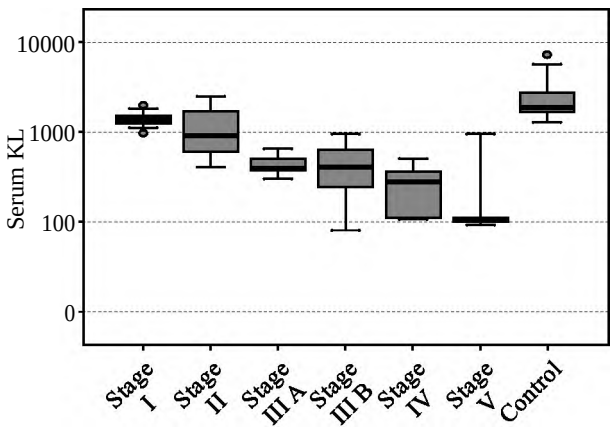

Fig. (1): Comparison between the different studied groups according to Serum KL.

It shows a significant negative association between level of soluble α-klotho and progression of CKD.

Table (3): Relation between serum KL and different parameters in cases group.

	Serum KL	
	r_s	p
Age (years)	–0.380*	0.003*
Weight (kg)	0.172	0.189
Creatinine (mg/dl)	–0.738*	<0.001*
Urea (mg/dl)	–0.589*	<0.001*
eGFR (ml/min./1.73m^2)	0.564*	<0.001*
Ionized Ca (mmol/L)	0.576*	<0.001*
PO4 (mg/dl)	–0.377*	<0.001*
Protein in urine (mg/24h.)	–0.595*	<0.001*

Table (3) represents relation between serum KL and different parameters in cases group. It

shows that there was significant positive correlation between level of soluble α-klotho and eGFR and ionized calcium level, while there was significant negative correlation between soluble α-klotho and age, creatinine level, urea level, phosphorus level and level of protein in urine (p-value <0.001) while there was no significant correlation between soluble α-klotho level and weight (p-value 0.189).

Discussion

Our study found that there was statistically significant decrease in soluble alpha klotho serum level with progression of chronic kidney disease which started to be more obious in stage IIIB.

The current study also found that there was a statistically significant positive correlation between level of soluble α-klotho and eGFR and ionized calcium level, while there was significant negative correlation between soluble α-klotho and age, creatinine level, urea level, phosphorus level and level of protein in urine (p-value <0.001) while there was no significant correlation between soluble α-klotho level and weight (p-value 0.189).

Our results are in accordance with Lindberg et al., 2014 who believed that α-klotho deficiency plays strong role in kidney fibrosis which made patients enter a vicious circle of more decrease in klotho level and more progression of the disease, he also suggested that α-klotho may be used as therapeutic agent for CKD. He also found that soluble α-klotho plays its role mainly via its role as a co-receptor for Fibroblast Growth Factor 23 (FGF 23) which decreases dietary absorption and renal reabsorption of phosphate **[6]**.

Our study was in accordance with Shimamura et al., 2012 who also found that serum level of soluble α-klotho was decreasing with age and also its level was inversely proportional to serum phosphorus level **[7]**.

Conclusion:

The results of this research showed that level of soluble alpha klotho showed significant decrease in patients with chronic kidney disease than in normal control group and that its level started to decrease early in the disease. It could be considered a novel biomarker of chronic kidney disease that shows a significant decrease with progression of chronic kidney disease and correlates significantly with other mineral disorders of the disease, so it can be used in diagnosis of chronic kidney disease.

Acknowledgment:

This research was carried out without funding.

Conflict of interest:

No conflict of interest declared.

Authors' contribution:

All authors had equal role in design, work, statistical analysis and manuscript writing. All authors have approved the final article work.

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دراسة مستوى الآلفا كلوثو الذائب فى مرضى القصور الكلوى المزمن

يعتبر القصور الكلوى المزمن مشكلة عالمية بما يشمله من آثار ومضاعفات. الآلفا كلوثو الذائب هو هرمون منظم لمستوى الفسفور والكالسيوم فى الدم ويمكن آن يستخدم لتشخيص مرض القصور الكلوى المزمن.

الهدف من الدراسة: تقييم مستوى الآلفا كلوثو الذائب ودوره فى تشخيص مرض القصور الكلوى المزمن.

طرق البحث: إشتملت الدراسة ثمانين عضوا تم تقسيمهم إلى مجموعة المرضى وتشمل ستون مريضا تم إعادة تقسيمهم إلى خمسة مجموعات فرعية على حسب إختلاف معدل الترشيح الكلوى ومجموعة الآصحاء وتضم عشرون عضوا صحيحا (معدل الترشيح الكلوى ١٢٠مل/دقيقة/١.٧٣م٢) جميعهم خضع لآخذ التاريخ المرضى كاملا، الفحص الطبى الشامل، والفحوصات المعملية الروتينية كقياس مستوى البولينا والكرياتينينو الكالسيوم والفسفور والبروتين فى البول. تم قياس مستوى الآلفا كلوثو الذائب بإستخدام الإليسا.

النتائج: آظهرت الدراسة وجود نقص ملحوظ فى مستوى الآلفا كلوثو الذائب مع تطور مرض القصور الكلوى المزمن والذى ظهر واضحا إبتداء من المرحلة (٣آ) من المرض مما يجعل منه مؤشر بيولوجى جديد يمكن إستخدامه لتشخيص المرض.