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Association between phosphate levels and Gradual Renal Function Decline in Children Afflicted with Chronic Kidney Diseases

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Abstract: Chronic kidney disease (CKD) in children is a devastating illness that has severe long-term negative outcomes to the well-being of affected children, as it severely worsens mortality and morbidity rates and deteriorates their quality of life. Accumulation of phosphate as a result of impaired renal function may induce kidney damage and accelerate CKD progression. Additionally, hyperphosphatemia may contribute to several CKD associated complications such as vascular diseases and hypertension. Therefore, we aim to study the association between progressive loss of renal function and phosphate levels in blood samples of our study group of children with CKD, in order to enhance our understanding to the correlation between hyperphosphatemia and compromised renal function

keywords: Chronic kidney disease, CKD, creatinine, phosphate, CKD in children.

1.Introduction

Chronic kidney disease (CKD) is a major challenge to public health on the global scale as it affects nearly 13.4% of the global population [1, 2]. CKD is a progressive disease that is distinguished by cumulative loss of functional renal mass and is defined as abnormalities observed in kidney structure or function that persists for at least three months or more [3]. CKD mostly affects adults with lifelong incidence rate up to 60 % in the general population [4]. In adults, CKD mostly occurs as a complication for hypertension and diabetes mellitus [5]. On the other hand, prevalence of CKD in children is much lower than that in adults and is mostly attributed to by congenital abnormalities of the kidneys and urinary tract (CAKUT) [6]. Nevertheless, children who suffer from CKD are at high risk of developing destructive complications such as growth impairment, neurocognitive degeneration, anemia, cardiovascular diseases, bone fractures and deformities, high rates of morbidity and mortality, and reduced quality of life [7].

The most reliable tool for monitoring renal function deterioration in children with CKD is obtaining estimated glomerular filtration rate by using Schwartz bedside formula 2009 version based on both serum creatinine and height [8]. Serum creatinine is the most frequently used biomarker for monitoring progressive CKD, as creatinine levels are elevated as kidney function is gradually lost in CKD [9]. Additionally, progressive impairment of renal function leads to accumulation of uremic toxins, especially phosphate, leading to hyperphosphatemia in CKD patients [10].

Hyperphosphatemia is a major repercussion of progressive CKD, and an inducer for further CKD progression, since hyperphosphatemia has been associated with accelerated nephron damage due to elevated oxidative stress in renal tubular epithelial cells [11, 12], furthermore, hyperphosphatemia might be associated with hypertension, which is considered a principal risk factor for CKD progression [13].

Hyperphosphatemia may have a major role in the pathogenesis of CKD associated health complications, since hyperphosphatemia have been associated with elevated inflammation, which might induce anemia and loss of muscle mass in CKD patients [10]. Furthermore, Phosphate is a major vascular toxin,

hyperphosphatemia has been associated with several vascular abnormalities in CKD patients such as, endothelial dysfunction, endothelial cell apoptosis, vascular calcification, and osteogenic differentiation of vascular smooth muscle cells [13–15]. On the other hand, maintenance of normal blood phosphate level in CKD patients by phosphate dietary restrictions and by treatment with phosphate binders may mitigate the negative repercussions of hyperphosphatemia in patients with CKD [16, 17].

In this context aimed to investigate the association between serum creatinine and serum phosphate levels in our study group of children with CKD.

2.Subjects and methods

Study population

The current study was authorized by the Medical Research Ethics Committee, Institutional Review Board, Faculty of Medicine, Mansoura University, code number MS.21.10.1720. All patients signed a written informed agreement before the inclusion in the study.

This study included 91 children with CKD, 52.7% of the study population were males and while 47.3% were females, in addition to 50 healthy control subjects of matched age and gender.

Sample collection

Whole blood samples (3mL) were collected from CKD patients and control subjects in plain vacuum tubes and let to clot in room temperature, then the tubes were centrifuged at 2000 rpm for 5 minutes, serum was obtained from samples, and Creatinine and phosphate levels were measured soon after sample collection.

Biochemical analysis:

Serum creatinine was measured by commercially available enzymatic method kit (Agappe Diagnostics LTD, 'Agappe Hills', Dist. Ernakulam, Kerala, India-683 562). [18, 19]

Serum phosphate levels were measured by a commercially available kit (Agappe Diagnostics LTD, 'Agappe Hills', Dist. Ernakulam, Kerala, India-683 562). [20, 21]

Statistical analysis

Results were analyzed by the Statistical package for Social Science (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.), A probable value (p value) is considered significant if $p<0.05$ at confidence interval 95%.

3.Results and Discussion

Table 1. Demographic data of patients and control group.

	Control N = 50		CKD N = 91		Test (p)
	№	%	№	%	
Gender					
Male	27	54.0	48	52.7	X^2=0.020 p=0.887
Female	23	46.0	43	47.3	
Age (years)					
Mean ± SE.	8.29 ± 0.59		9.05 ± 0.48		U=2486.0 p=0.362
Median (Range)	8.0 (2.0 – 18.0)		9.0 (1.50 – 17.50)		

SE. Standard error, Range: Min. – Max; X2, Chi-Square; U, Mann Whitney test. *: P value Significant <0.05.

The Current study was conducted on 91 CKD patients. Their mean age was 9 years, ranging from 1.5 to 17.5 years. They were 52.7% males and 47.3% females. In addition to 50 healthy control subjects of matched age and gender. There were no significant statistical differences between CKD patients and control subjects in terms of age and gender (P>0.05)

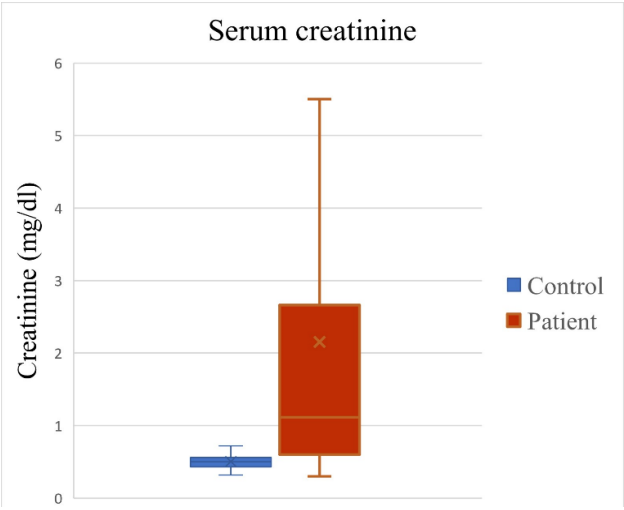

Figure 1. Comparisons of serum creatinine levels between CKD patients and controls

Table 2. Creatinine and phosphate levels of patients and control group.

	Control N = 50	CKD N = 91	Test (p)
Creatinine (mg/dl)			
Mean ± SE.	0.50 ± 0.01	2.20 ± 0.30	U=3894.0 p<0.001*
Median (Range)	0.50 (0.32 – 0.72)	1.14 (0.40 – 21.40)	
Phosphate (mg/dl)			
Mean ± SD.	4.40 ± 0.61	5.01 ± 1.07	t=4.321 p<0.001*
Median (Range)	4.38 (3.20 – 5.89)	4.80 (3.20 – 9.10)	

SE. Standard error, SD. Standard deviation

Range: Min. – Max., *: P value Significant <0.05, U, Mann Whitney test, t, student t test.

The results illustrated in Table 2, Figure 1 and 2 demonstrate that Creatinine levels has significantly increased in CKD patients compared to control subjects (p<0.001). Additionally, serum phosphate levels in CKD patients showed significant increase compared to control group (p<0.001).

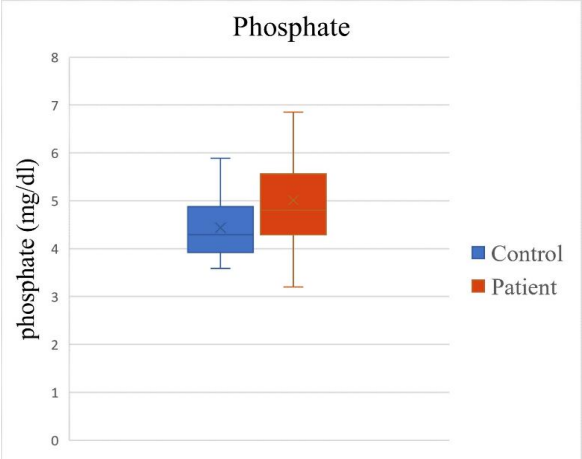

Figure 2. Comparisons of phosphate levels between CKD patients and controls.

Table 3. Correlation between Creatinine and phosphate levels among CKD patients

CKD N=91	**Creatinine (mg/dl)**	
	ρ	**p**
Phosphate (mg/dl)	0.633	0.0025*

ρ, Correlation coefficient; *: P value Significant <0.05.

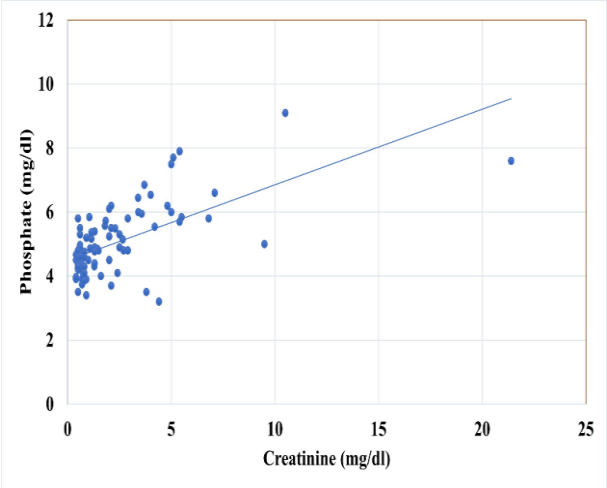

Figure 3. Correlations between Creatinine and phosphate among CKD patients

1.Conclusion and recommendations

CKD in children is a major threat to affected children's health and quality of life, as it does not only affect the kidneys, but it has long-term destructive effects on every compartment of the human body. Hyperphosphatemia that develops with progressive CKD is a major contributor to CKD progression and its complications, thereby, we recommend that it is of the utmost importance to manage hyperphosphatemia in order to slow CKD progression and mitigate its complications in order to improve the quality of life of children with CKD.

4. Conclusion and recommendations

CKD in children is a major threat to affected children's health and quality of life, as it does not only affect the kidneys, but it has long-term destructive effects on every compartment of the human body. Hyperphosphatemia that develops with progressive CKD is a major contributor to CKD progression and its complications, thereby, we recommend that it is of the utmost importance to manage hyperphosphatemia in order to slow CKD progression and mitigate its complications in order to improve the quality of life of children with CKD.

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