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Estimation of Salivary Creatinine and Urea as alternative to Plasma Creatinine and Urea in Sudanese Patients with Chronic Kidney Disease in Khartoum State-Sudan

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Abstract

Background: Many metabolic changes develop in patients with chronic kidney disease which often necessitate frequent biochemical analysis of blood. Saliva was found to reflect the changes that occur in plasma in case of endocrine, cardiovascular, autoimmune, and infectious disease. Saliva also exhibits biochemical indices of renal function and studies have shown association between salivary and serum creatinine and urea levels.
Objective: This study was designed to assess the levels of salivary creatinine and urea; to determine the correlation between the levels in saliva and blood as well as to evaluate the diagnostic potential of saliva in assessing levels of creatinine and urea in patients with CKD.
Materials and Methods: A case control study, involving 24 patients with late stage chronic kidney disease and 26 healthy individuals as control. Blood and saliva samples were analyzed for urea and creatinine levels. Comparison between patients and controls were done using Independent Samples t-test. Significant difference between plasma and salivary creatinine as well as urea was determined using pair sample t-test.
Results: mean of salivary creatinine levels were 2.54 mg/dl and 0.152 mg/dl while mean of salivary urea levels were 186.35 mg/dl and 10.60 mg/dl in patients with chronic kidney disease and controls respectively. Salivary levels of creatinine and urea were significantly elevated in chronic kidney disease patients ($p < 0.001$). In addition, there was no significant difference between blood and salivary urea level, but significant difference between blood and salivary creatinine was observed. There was no linear relationship between blood creatinine/ urea and salivary creatinine/ urea in patient R^2 were 0.0886 and 0.0084 respectively.
Conclusions: from this study we conclude that saliva sample can be used as alternative to plasma sample in estimation of urea and creatinine levels in patients with CKD.

Keywords: Chronic Kidney Disease, Urea, Creatinine, Sudanese.

1. Introduction

The kidneys are vital organs that perform a variety of important functions. The most prominent functions are removal of unwanted substances from plasma (both waste and surplus), homeostasis (maintenance of equilibrium) of the body's water, electrolyte and acid-base status, and participation in hormonal regulation [1]. Chronic kidney disease (CKD) is a type of kidney disease in which there is gradual loss of kidney function over a period of months or years [2, 3]. Early on there are typically no symptoms [2]. Later, leg swelling, feeling tired, vomiting, loss of appetite, or confusion may develop [2]. Complications may include heart disease, high blood pressure, bone disease, or anemia [4, 5, and 6]. Causes of chronic kidney disease include diabetes, high blood pressure, glomerulonephritis, and polycystic kidney disease [3, 7].

The usual laboratory tests which checks that the kidneys are working properly measures the level of urea, creatinine and electrolytes in the blood [8]. Creatinine is a waste product made by the muscles. Creatinine passes into the blood stream and is usually passed out in urine. A high blood level of creatinine indicates that the kidneys may not be working properly. Creatinine is usually a more accurate marker of kidney function than urea [8].

Urea is a waste product formed from the breakdown of proteins. Urea is usually passed out in the urine. A high blood level of urea ('uraemia') indicates that the kidneys may not be working properly, or that you have a low body water content (are dehydrated) [8]. Saliva is a watery substance formed in the mouths of animals, secreted by the salivary glands. Human saliva comprises 98% water, plus electrolytes, mucus, antimicrobial agents, epidermal growth factor, various enzymes, cells, opiorphin and haptocorrin [9]. Saliva as a biologic fluid secreted by the major and minor salivary glands plays the main role in oral health as well as systemic health [10].

Passive diffusion, ultrafiltration, transudation, and selective transport are the mechanisms that explain the movement of constituents from plasma to saliva [11]. Saliva was found to reflect the changes that occur in plasma in case of endocrine, cardiovascular, autoimmune, and infectious diseases. Saliva also exhibits biochemical indices of renal function and studies have shown association between Salivary and serum creatinine and urea levels [11].

Recently, saliva is being considered as an alternate biological sample to blood in the management of systemic disease in view of noninvasive collection method and providing similar information [11].

2. Materials and Methods

A case control study, this study was carried at Khartoum state. Patients participate in this study from Ibn Sina educational hospital, section of negative hemodialysis unit. During the period from April 2018 to August 2018. This study was included 50 participants (24 patients with CKD and 26 healthy controls). Data collected by questionnaire. The urea was measured by enzymatic method (urease method) and creatinine by jaff's method, the data obtained was analyzed by SPSS.

2.1. Sampling Technique

The study sample was collected by nonpropapility sampling "simple random Sampling" technique.

2.2. Ethical Approval

Approval was taken from university management and ministry of health. The collection of sample was done by appropriate ways and participants were provided by informations about study and their verbal consent was obtained.

2.3. Data Collection

Data was obtained by direct interviewing questionnaire which done for patients.

2.4. Samples Collection

Blood and saliva samples was collected from each participant after their consent. the vein puncture technique was used for collection of plasma sample, and the spitting method used to collect saliva sample after rinsing with clean water.

2.5. Data Analysis

SPSS version 16 was used for analysis of data.

2.6. Quality Control

For internal quality control, normal control sera (normal) and pathological control sera (pathological) were included in every batch of chemical analysis.

3. Results

Table (3.1): means and Std. Deviation for plasma urea and creatinine in patients and control.

Variable	Control (mean SD)	CKD (mean SD)	p-value
Plasma urea No	20.40 11.87 26	162.91 59.13 23	0.001
Plasma creatinine No	0.73 0.44 26	10.08 4.54 23	0.001

Table (3.2): means and Std. Deviation for Salivary urea and creatinine in patients and control.

Variable	Control (mean SD)	CKD (mean SD)	p-value
Salivary urea No	10.60 7.25 26	186.35 74.46 23	0.001
Salivary creatinine No	0.152 0.14 26	2.54 1.84 24	0.001

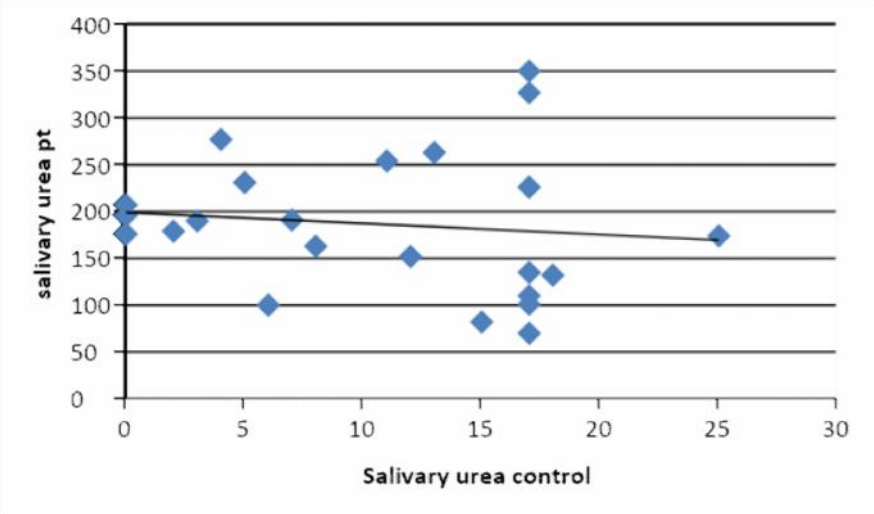

Figure (3.1): scatter plot shows relationship between salivary urea control and patients.

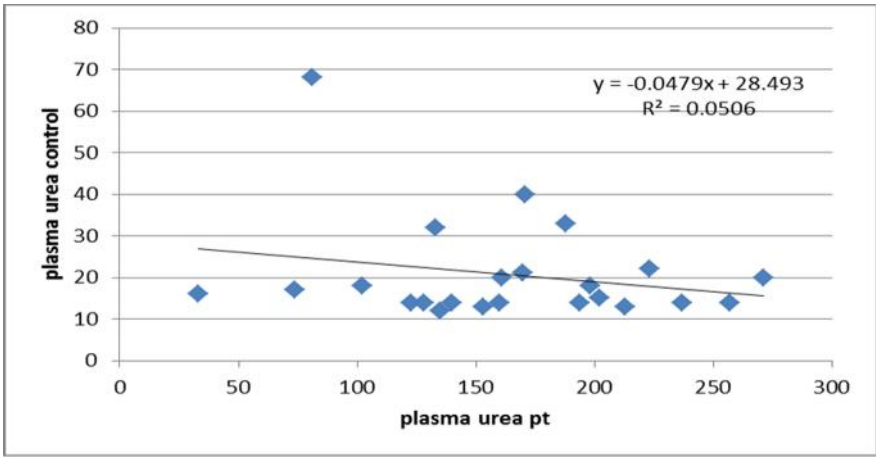

Figure (3.2): scatter plot shows relationship between plasma urea control and patients.

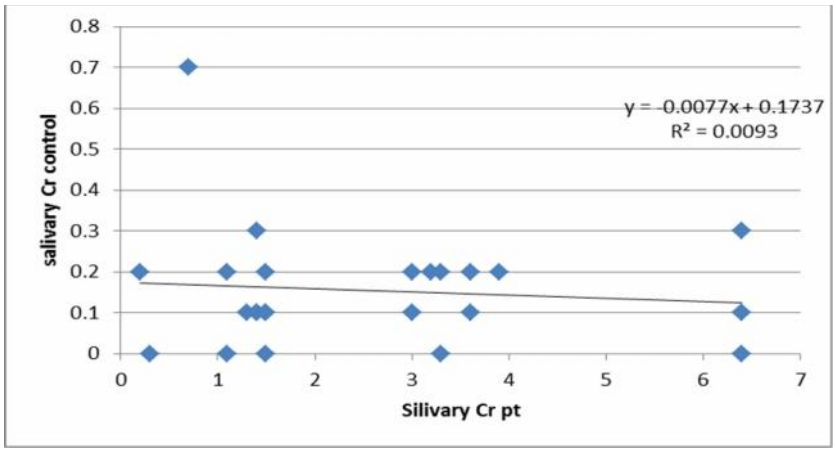

Figure (3.3): scatter plot shows relationship between salivary creatinine control and patients.

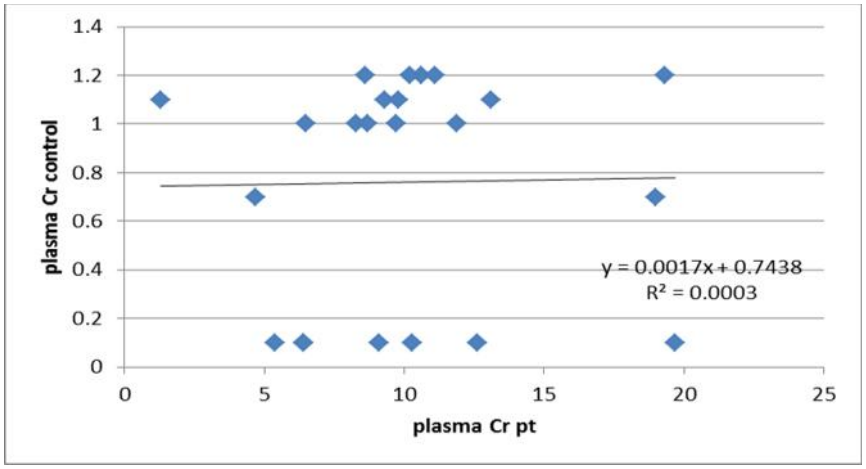

Figure (3.4): scatter plot shows relationship between plasma creatinine control and patients.

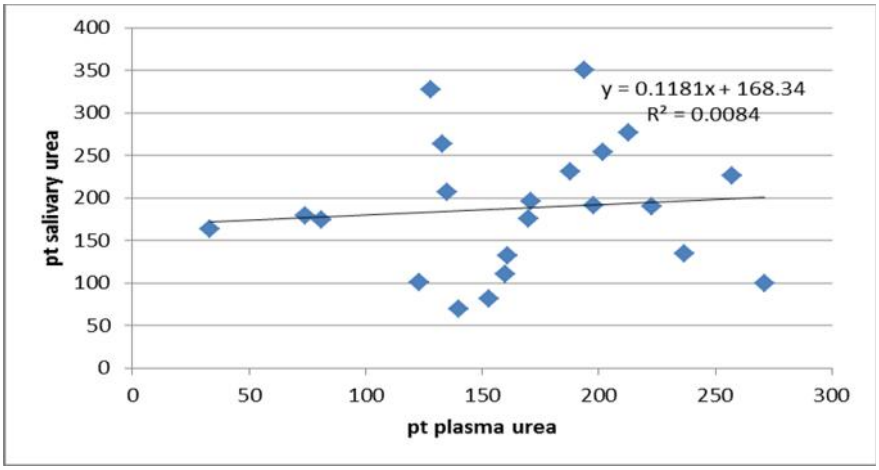

Figure (3.5): scatter plot shows relationship between patient salivary urea and patient plasma urea.

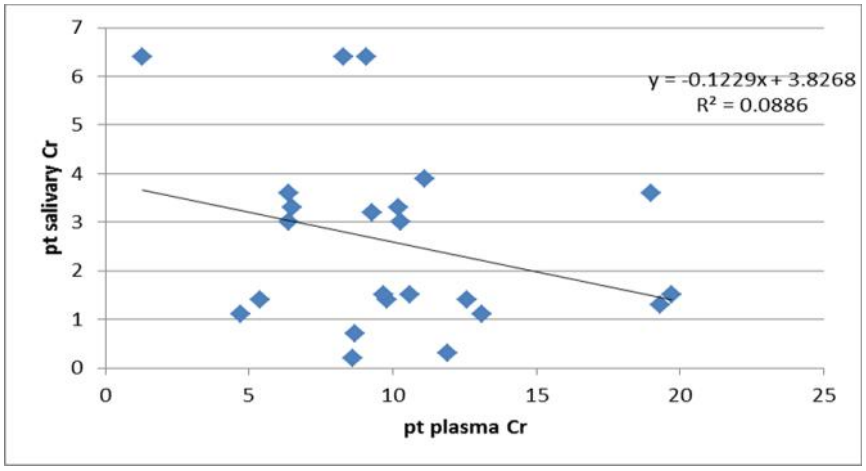

Figure (3.6): scatter plot shows relationship between pt patient salivary creatinine and patient plasma creatinine.

Table (3.3): paired sample t-test to compare mean of salivary urea and plasma urea patient.

a. Means:

Means	Mean	N	Std. Deviation	Std. Error Mean
Patient salivary urea	183.22	23	77.426	16.144
Patient plasma urea	162.913	23	59.1369	12.3309

b. Pair sample difference

Paired Differences						t	df	Sig. (2-tailed)
	Mean	Std. De	Std. Error Mean	95% Confidence interval of the Difference				
				Lower	Upper			
Patient salivary urea Patient plasma urea	20.3043	90.0547	18.7777	-18.6382-	59.2469	1.081	22	0.291

Table (3.4): paired sample t-test to compare mean of plasma creatinine and salivary creatinine patient.

a. means

Means	Mean	N	Std. Deviation	Std. Error Mean
Patient plasma creatinine	10.087	23	4.5436	0.9474
Patient salivary creatinine	2.587	23	1.8765	0.3913

b. Pair sample difference

Paired Differences						T	df	Sig. (2-tailed)
	Mean	Std. De	Std. Error Mean	95% Confidence interval of the Difference				
				Lower	Upper			
Patient plasma creatinine Patient salivary creatinine	7.50	5.4074	1.1275	5.1617	9.8383	6.652	22	0.000

Table (3.5): correlation between patient age and measurement of salivary and plasma Creatinine and Urea.

		Salivary urea	Plasma urea	Salivary Cr	Plasma Cr
Patient age	Pearson Correlation	0.068	0.153	-0.122-	-0.196-
	Sig. (2-tailed)	0.759	0.486	0.569	0.371
	N	23	23	24	23

4. Discussion

This study was case control study done to estimate salivary creatinine and urea as alternative to plasma creatinine and urea in CKD patients in stage 5 before hemodialysis. The study was done in 26 healthy individuals as control group and 24 patients with CKD (16 male and 8 female) with age range between 16–72 years.

The study shows that; the mean ± STD for salivary creatinine and urea in patients (2.54 ±1.84, 186.35 ± 74.46) and controls (0.152 ± 0.14, 10.60±7.25) mg/dl respectively. And there was significant difference in patients and control (p value less than 0.01). This result was agreed with (Taye Jemilate et al, 2016 and Venkatapathy R, et al 2014).

The study found that plasma creatinine and urea in patients (10.08 ± 4.54, 162.91 ± 59.13) and control (0.73 ± 0.44, 20.4 ± 11.87) mg/dl respectively; there was significant difference in patients and controls. The study clarify that salivary creatinine and urea were elevated in CKD such as plasma creatinine and urea, and can be used as alternative for diagnosis (Independent sample t-test). The elevated levels of salivary creatinine and urea observed in patients with CKD are reflections of the blood level. These elevated salivary levels of creatinine and urea could be responsible for the complaints of mouth odor or uremic breath as well as tongue coating and other oral complications of CKD.

The study found that no significant difference between plasma and salivary urea (P value 0.291) > 0.05, (t value 1.08) this mean that salivary urea can be used instead of plasma urea for diagnosis of CKD. This result agrees with (Taye Jemilate et al, 2016). The study reveal that there was significant difference between salivary creatinine and plasma creatinine in patients with CKD as (P value less than 0.01, (t value 6.65) with 95% confidence interval to plasma creatinine; this clarify that although salivary creatinine can be used as alternative of plasma creatinine for diagnosis of CKD, it needs another marker suport it. (Pair sample t-test). This result is not agreeing with (Taye jemilate et al, 2016). And this may return to high molecular weight of creatinine which reduce its diffusion and permatibility in salivary gland.

5. Conclusion

From this study we conclude that saliva sample can be used as alternative to plasma sample in estimation of urea and creatinine levels in patients with CKD.

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