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RESEARCH ARTICLE

CAN SALIVARY UREA AND CREATININE LEVELS BE USED TO FOLLOW UP SUDANESE PATIENTS WITH RENAL FAILURE UNDER HEMODIALYSIS AS ACCURATELY AS SERUM CREATININE AND UREA LEVELS?

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ABSTRACT

Background*:** The uses of saliva markers have clear benefits than serum , the reason of this benefits saliva collection is a noninvasive, easy, and cheap. ***Objectives*:** The aim of this study was to compare the levels of urea and creatinine in plasma and saliva of Sudanese patients with renal failure under hemodialysis, and to investigate the potentiality of determination of saliva urea and creatinine levels instead of using plasma. ***Participants and Methods: A case-control study was conducted from May to Jun2018, involving fifty Sudanese Patients who had been diagnosed ofrenal failure, and had been admitted to Omer Alhag Musa Hospital, in GazeraState as cases(17 of them were females and 33 were males); and fifty healthy individuals were recruited as controls (16 of them were females and 34 of them were males), age ranged from 20 to 70 years in both groups, blood samples and saliva were collected and the levels of urea and creatinine were measured, using BioSystem (Apel/AP-101). Data analysis was carried out, using SPSS version, 21. Mean values werecalculated and independent t-test was used to compare mean values in case versus control group and Pearson's correlation was used to find the relationship between urea and creatinine levels in serum and saliva. ***Results*:** There were significant increase in the mean levels of plasma urea (mean ± SD: 179.9 ± 51.4 vs. 37.00 ± 253 mg/dL; p = 0.001) and creatinine (9.40 ± 2.38 versus 0.97 ± 0.6 mg/dL; p = 0.001) in patients with renal failure when compared to control group. Also there were a significant increase in the mean levels of saliva urea(214.1 ± 64.1 vs. 27.2 ± 27.5 mg/dL; p = 0.001) and creatinine (12.00 ± 3.89 vs. 1.01 ± 0.7 mg/dL; p = 0.001) in patients with renal failure when compared to control group.The result shows a significant positive correlation between plasma urea and saliva urea in patients with renal failure (r = 0.529; p = 0.001), also there wasa significant positive correlation between plasma urea and saliva urea in patients with renal failure (r=0.579; p =0.001).The plasma urea showed sensitivity of 99.9%, and specificity of 99.8% while the salivary urea showed sensitivity of 98% and specificity of 98%, but the plasma and saliva creatinine showed same sensitivity of 97% and same specificity of 97%. ***Conclusion*:** Sudanesepatients with renal failure under hemodialysis had increased levels of urea and creatinine in saliva and plasma. Sensitivity and specificity of saliva urea and creatinine levels are comparable to those of plasma.

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INTRODUCTION

Blood urea and creatinine are routinely estimated parameters for evaluation of kidney functions in two types of renal failure (acute and chronic). Multiple collection of blood sample cause pain, stress and might lead to infections. Saliva is more efficient to be a non-invasive alternative diagnostic fluid (Kovalcikova *et al.,* 2018). Saliva is not used in diagnosis in wild range, although the concentration of salivary biomarkers affected by many factors. Saliva, a multi-constituent biologic fluids excreted by the salivary glands, plays an important role in oral and systemic health (Renda, 2017). The use of saliva in clinical diagnosis is simple, easy to collect than blood. It also secures a cost effective method for screening large populations (Pham, 2017; Bagalad *et al.,* 2017; Lasisi *et al.,* 2016). Many systemic diseases; such as chronic kidney disease (CKD); have been reported to produce marked and identifiable changes in salivary secretion (Ark *et al.,* 2014; Elnahas and Bello, 2005). More importantly, saliva can indicate creatinine and urea levels in patients with CKD which are the parameters usually used in blood samples (Zuniga *et al.,* 2012; Blicharz *et al.,* 2008). The use of biomarkers in saliva to follow up and

monitoring the effectiveness of hemodialysis may be an effective alternative method (Summer *et al.,* 2007). Accordingly this study aimed to compare the levels of urea and creatinine in plasma and saliva of Sudanese renal failure patients and to investigate the potentiality and effectiveness of using of saliva urea and creatinine levels in renal failure patients instead of using plasma.

PARTICIPANTS AND METHODS

Setting: This is a case-control study conducted in Gazera State, from May to June 2018. It enrolled fifty Sudanese patients with renal failure admitted to Omer Alhag Musa Hospital, aged between 20 and70 years, and, fifty normal healthy individual as controls. The cases and control were age-matched. 17 of patients were females and 33 were males and 16of controls were females and 34 of themwere males. Patients attending Omer Alhag Musa Hospitalin-patients with renal failure under hemodialysis were included. Patients with liver disease and pulmonary problem were excluded. The study was approved by the scientific committee of Faculty of Medical Laboratory Science, Alneelain University. An Informed consent was obtained from all the anonymously enrolled participants. Demographic data was collected by using questionnaire.

Sampling and clinical chemistry investigations: 2.5 mL of venous blood samples and about 1 mL of saliva were collected from both patient and healthy individual; under aseptic conditions; using disposable syringe (for blood sample) and wide mouth container(for Saliva sample). The collected blood was drawn into heparin containers, gently mixed, centrifuged at 5000 rpm for 5min to obtain plasma. The levels of plasma and saliva urea and creatinine were measured by using Bio system (Apel/AP-101). As a quality control measure, pathological and normal control sera were used to assure accuracy and precision of results.

Data analysis: Data were analyzed using SPSS, version 21. The results were expressed as frequencies (n and %), and, mean ± SD. Independent t-test was used to compare mean values in case versus the control group. Pearson's correlation test was done to study the relationship between plasma and saliva urea and creatinine. (Calculation of specificity and sensitivity by Roc carve) P value <0.05 was considered significant.

RESULTS

One hundred participants were enrolled in this study; 50 patients with renal failure (17 females and 33 males) with age of46.9±15.6 years and 50 controls (16 females and 34 males) with age of46.0 ±15.1years. The result showed that, 68% above40years old and 32% below 40 years old. There were significant increase in the mean levels of plasma urea and creatinine in patients with renal failure when compared to control groups. Also there were significant increase in the mean levels of saliva urea and creatinine in patients with renal failure when compared to control groups (Table 1). There were significant positive correlation between plasma and saliva urea and creatinine in patients with renal failure (Figures: 1, 2). The results revealed very little difference in sensitivity and specificity of plasma urea and saliva urea levels, but same sensitivity and specificity of plasma and saliva for creatinine levels (Table 2 and Figure 3).

Table 1. Comparison of plasma and saliva urea and creatinine levels in renal failure patients vs. healthy controls. Data shown are mean ± SD.

Parameter	Cases	Controls	p
Plasma Urea	179.9 ± 51.4	37.0 ± 25.3	0.001
Saliva Urea	214.1 ± 64.1	27.2 ± 27.5	0.001
Plasma Creatinine	9.40 ± 2.38	0.97 ± 0.61	0.001
Saliva Creatinine	12.00 ± 3.89	1.01 ± 0.75	0.001

Table 2. Specificity and sensitivity of plasma and saliva urea and creatinine

Parameter	Area	Sensitivity	Specificity
Plasma Urea	1.00	99.9	99.8
Saliva Urea	0.991	98	98
Plasma Creatinine	0.974	97.9	97.9
Saliva Creatinine	0.976	97	97

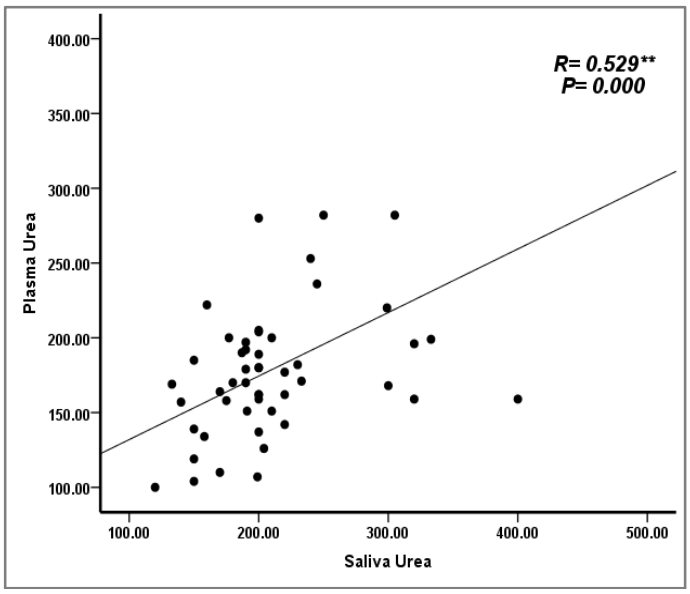

Figure 1. Correlation between plasma and saliva urea levels in renal failure patients

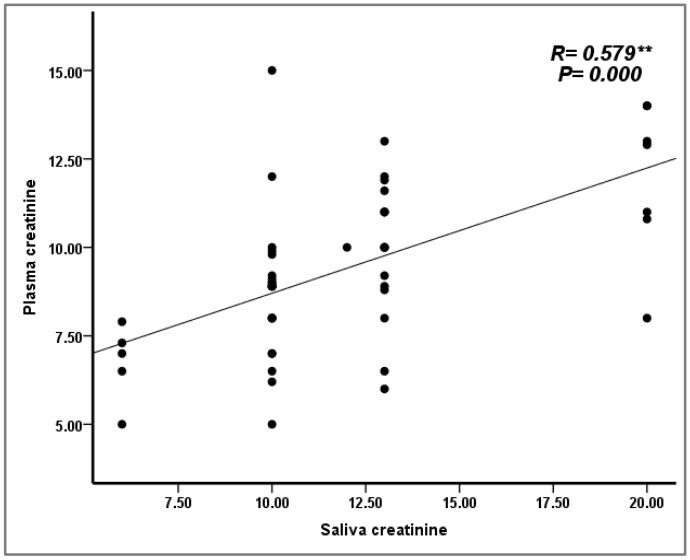

Figure 2. Correlation between plasma and saliva creatinine levels n renal failure patients

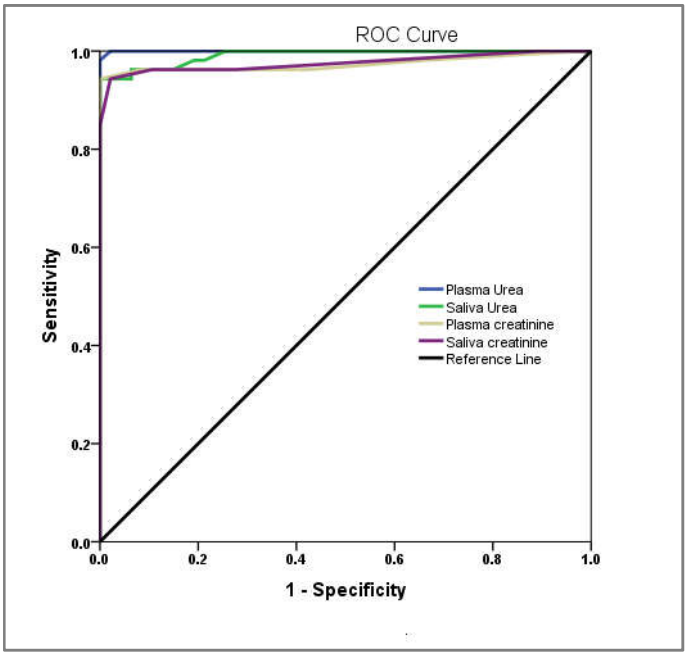

Figure 3. ROC curve for calculation of specificity and sensitivity of plasma and saliva urea and creatinine levels in renal failure patients

DISCUSSION

The uses of saliva markers have clear benefits than serum because saliva collection is cheap, easy to perform a noninvasive, and need minimum skills. Saliva remains a largely untapped source of medical information that can enhance diagnostic accuracy while saving the patient from some of the discomfort associated with a blood test or other more invasive procedures (Kovalcikova *et al.,* 2018). For monitoring the effectiveness of hemodialysis, measurement of biomarkers in saliva maybe an effective alternative method (Summer *et al.,* 2007). This study conducted in Gazira state to measure saliva and plasma urea and creatinine in renal failure patients under hemodialysis. The results revealed significant increase in the mean levels of plasma and saliva urea and creatinine in patients with renal failure when compared to control groups. This result agreed with previous studies results which showed significant elevation in mean level of urea and creatinine in saliva and plasma in patients with renal failure compared to control group (Summer *et al.,* 2007; Chuang *et al.,* 2005; Dela *et al.,* 2006). It is reported in the literature that any constituents of the blood pass through saliva, for this reason saliva used as indicator of the current state of the blood and of the rest of the body; accordingly biomarkers, or substances used as indicators of biological states, can be readily found in saliva (Chuang *et al.,* 2005). The current study results revealed significant positive correlation between plasma and saliva urea and creatinine levels in patients with chronic renal failure. This finding was in agreement with results of some previous studies; in which some of them were conducted in Central Africa and Nigeria; which showed significant positive correlation between plasma and saliva urea and creatininein patients with renal failure (Dela *et al.,* 2006; Schoolwerth *et al.,* 2006; Nagler *et al.,* 2002; Xia *et al.,* 2012). Indeed; because urine forms mainly through passive diffusion, just like saliva, many components of the blood exchanged at the kidney are also exchanged at the salivary glands (Nagler *et al.,* 2002). In the present study; the plasma urea showed sensitivity of 99.9%, and specificity of 99.8% while the salivary urea showed sensitivity of 98% and specificity of 98%, but the plasma and saliva creatinine showed same sensitivity of 97% and same specificity of 97%.This suggested that salivary urea and creatinine has excellent diagnostic accuracy which was also confirmed by its score of 0.9 of area under the curve in ROC. This result in agreement with another result demonstrated by Xai et al, which found sensitivity of 80%, specificity of 90%, and area under the curve of 0.898 in ROC (Xia *et al.,* 2012). This result also agreed with previous result which demonstrated that sensitivity and specificity of saliva urea and creatinine are similar to those of plasma urea and creatinine (Bader *et al.,* 2015).

Conclusion

Patients with renal failure had increased levels of urea and creatinine in both plasma and saliva, and there is a positive correlation between urea and creatinine levels in plasma and saliva.Salivary urea and creatinine has excellent diagnostic accuracy and so; could be used for investigations of urea and creatinine levels instead of using of plasma.

Limitations of the Study: The study was done in Omer Alhag Musa Hospital, in Gazera State, but not covered the rest of states in Sudan.

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