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ORIGINAL RESEARCH

Assessment of Salivary Urea in Different Stages of Chronic Renal Failure Patients

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ABSTRACT

Background: Renal diseases are classified, based on onset, as acute and chronic renal failure (CRF). With growing awareness of the interrelationship between medical and dental problems, need was felt for a simple, noninvasive, rapid method for assessing urea levels in CRF patients. So the study was designed to assess salivary urea (SaU) in CRF patients and controls, and also to confirm the reliability and feasibility of using SaU levels for diagnosing and monitoring uremic status in CRF patients.

Materials and methods: A total of 200 subjects (120 CRF cases and 80 controls) were assessed for SaU levels enzymatic colorimetric method. In total, 120 cases were of different stages under CRF. Student's *t*-test was performed to find significant differences between levels of SaU of controls and CRF cases. ANOVA test was performed to compare levels of SaU with different stages of CRF cases.

Results: A positive correlation was observed between SaU and stages in CRF cases with the p value 0.0000. Also, comparison of SaU with respect to different stages showed statistically significance with the p value 0.0000.

Conclusion: The present study showed a significant relationship of SaU and different stages of chronic renal failure, hence SaU can be used as a biomarker in assessment of different stages.

Keywords: Blood urea nitrogen, Chronic renal failure, Glomerular filtration rate, Saliva, Salivary urea.

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INTRODUCTION

The human kidneys are bean-shaped organs located in the retroperitoneum at the level of the waist. Each adult kidney weighs approximately 160 g and measures 10 to 15 cm in length.[1]

The kidneys are vital organs for maintaining a stable homeostasis. Kidney has many functions like regulating the acid–base and fluid electrolyte balance of the body by filtering blood, reabsorbing water and electrolytes, and excreting urea and other toxic metabolites. Renal diseases are classified based on onset as acute and chronic renal failure (CRF). Acute renal failure is reversible, whereas chronic is irreversible and progresses to end-stage renal failure.[1-4]

The term "uremia," which was originally applied by Piorry and Heritier in 1840 for cases of renal failure and which at that time was taken to imply the retention of urine in the blood, has been used for the various syndromes associated with nitrogen retention. Chronic renal failure is now termed "chronic kidney" disease or (CKD).[5]

A system to classify stages of CKD is justified to permit a logical approach to diagnosis and therapy in these patients. A working group of the National Kidney Foundation (NKF) recently published clinical practice guidelines to aid physicians in diagnosing and managing CKD.[6]

Chronic renal failure is divided into stages according to the level of renal function present or the glomerular filtration rate (GFR). The glomerular filtration rate is the best overall measure of kidney function. Factors that influence GFR include both structural (or functional) kidney disease as well as patient age. In stage I CKD, patients have normal renal function (glomerular filtration rate > 90 cc/minute) but may have proteinuria or hematuria. In stage 2 CKD, patients have reduced renal function with GFR between 60 and 90 cc/minute. Stage 3 CKD reflects a GFR between 30 and 60 cc/minute. During stage 3 CKD, patients often start developing manifestations related to CKD, such as anemia and secondary hyperparathyroidism (HPTH). These patients are more likely to die from other comorbidities than

before they progress to advanced CKD or end-stage renal failure disease (ESRD). Stage 4 CKD reflects a GFR of 15 to 30 cc/minute, and during this stage of CKD, patients are medically prepared for dialysis. Stage 5 CKD or GFR of < 15 cc/minute reflects significantly reduced renal function, and this is the stage when patients will require long-term chronic dialysis treatment.[6]

Urine analysis for the presence of protein, blood, and creatinine levels will be a very important diagnostic tool in renal diseases. Similarly, serum has been also used as a diagnostic tool in which the levels of urea, sodium, calcium, potassium, and creatinine will be assessed. Estimation of serum urea, though an invasive procedure, is an important marker for the GFR. Measurement of pre- and posttreatment blood urea nitrogen (BUN) is a gold standard test for evaluating dialysis efficacy.[1]

With the increase in the blood urea levels, there is concomitant increase in salivary urea (SaU) levels due to diffusion of nitrogenous waste into saliva. The normal salivary urea is 12–70 mg/dl.[7] Urea concentrations in the whole saliva of healthy subjects are on the order of 2–4 mmol/l, but those in minor mucous gland secretion average over 5 mmol/l. Urea was reported in saliva by Stephen on an average of 20 mg/100 ml of resting saliva and 13 mg/100 ml of stimulated saliva.[8]

With growing awareness regarding the interrelationship between medical and dental problems, need was felt for a simple, noninvasive, rapid method for assessing urea levels in CRF patients. Monitoring of markers in saliva instead of serum is advantageous because saliva collection is a noninvasive, simple, and inexpensive approach with minimal infectious risk that can be performed by the patient with no need for involvement from medical personnel.[9]

Most data available on SaU are limited to the study of oral health and the diagnostic value of SaU as an alternative to blood urea in clinical practice is still unclear. Hence, a study was designed to assess SaU in CRF patients of different stages and controls, and also to confirm the reliability and feasibility using SaU levels for diagnosing and monitoring uremic status in CRF patients.

MATERIALS AND METHODS

The present study includes 120 patients of 16 to 70 years, who were selected from OPD and Nephrology Department and Dialysis Unit of a medical college. About 80 healthy individuals were selected as controls.

The study subjects were categorized as group I and group II. Group I comprised 80 healthy subjects with absence of any systemic diseases with GFR >90 ml/minute and normal serum urea levels. Group II comprised patients with five stages of chronic renal failure undergoing therapies and dialysis with GFR <50 ml/minute, according to the working group of the NKF.[6]

Patients suffering from any other systemic disease that could affect GFR and/or saliva characteristics were excluded from the study. All the data regarding disease status, investigations, medical therapies, and dialysis details were recorded on special proforma.

Approximately 3 ml of whole unstimulated saliva was collected in the morning from study and control groups. Patients were asked not to eat, drink, and smoke for 2 hours prior to collection. For the patients on dialysis, saliva samples was obtained before dialysis.

Saliva was collected after rinsing of mouth with distilled water. It was collected in a sterile graduated tube by expectoration method over a period of 5 minutes. Saliva, thus obtained, was maintained at 0.4°C and sent to laboratory within 1 hour. The collected saliva was centrifuged at 1000 rpm for 10 minutes. After centrifugation, the supernatant fluid was used for biochemical analysis. ERBA Company's test kit was used to assess the levels of urea in the saliva sample, using Enzymatic Colorimetric method.

Results obtained were statistically analyzed and interpreted appropriately. The mean and standard deviation (SD) of levels of salivary urea in controls and diseased were calculated. Student's *t*-test was performed to find significant differences between levels of SaU of controls and CRF cases. ANOVA test was performed to compare levels of SaU with different stages of CRF cases.

RESULTS

The present study consisted of 200 samples, out of which 120 were known CRF patients (stages II, III, IV and V) and 80 were age- and sex-matched healthy controls. The percentage of different stages of CRF cases are 15%, 15.83%, 33.33%, and 35.83 for stages II, III, IV, and V respectively (Table 1).

The mean age was 40.89 ± 10.77 years in control group and 52.60 ± 11.9 years in diseased group. The present study showed 66.67% of male and 33.33% of females.

Table 1: Distribution of subjects among case groups according to the stages of CRF cases

Staging	*No of respondents (%)*
Stage II	18 (15.00%)
Stage III	19 (15.83%)
Stage IV	40 (33.33%)
Stage V	43 (35.83%)
Total	120 (100.00%)

Table 2: Comparison of control and disease groups with respect to salivary urea (mg/dl)

Group	*Mean (SD)*	*t-value*	*p-value*
Control	41.9375 ± 15.4021	–14.2225	0.0000*
Disease	115.9937 ± 44.8092		

*p < 0.05

Table 3: Comparison of salivary urea level among various stages of CRF

Stage	*Mean salivary urea*
Stage II	76.07 ± 12.26
Stage III	95.82 ± 44.77
Stage IV	110.93 ± 30.47
Stage V	146.33 ± 45.53
F-value	18.3979
p-value 0.0000*	

The mean value of SaU in controls was 41.9375 ± 15.4021 mg/dl. The mean value of SaU in CRF cases was 115.9937 ± 44.8092 mg/dl. Comparison of control and disease groups with respect to salivary urea was done by Student's *t*-test. The results showed a statistically significant relation between controls and CRF cases with the p-value 0.0000 (Table 2).

The mean value of SaU in CRF cases was calculated. Stages II, III, IV, and V were having a mean value of 76.07 ± 12.26 mg/dl, 95.82 ± 44.77 mg/dl, 110.93 ± 30.47 mg/dl, and 146.033 ± 45.53 mg/dl respectively. A comparison of SaU with respect to different stages was done using ANOVA test, which showed statistically significance with the p-value 0.0000 (Table 3).

DISCUSSION

Renal diseases are life threatening in nature, next to cardiovascular diseases. Malfunction of the kidney may lead to increased BUN. Most laboratory investigations to diagnose renal diseases are estimation of BUN and serum creatinine. Other laboratory investigations include examination of urine for its quantity, pH, and specific gravity.[1]

Most data available on SaU are limited; very minimal studies are present regarding the use of SaU as a diagnostic tool and its correlation with different stages of CRF cases. Hence, the present study was designed to assess the urea levels in saliva in CRF patients. The study also evaluated the level of SaU in different stages of CRF.

Various components of saliva, namely, urea and uric acid, are either passively diffused or actively transported directly from the serum into the saliva through the oral mucosa and/or gingiva. The levels of such components in saliva may or may not reflect their serum levels. Monitoring of markers in saliva instead of serum is advantageous because saliva collection is a noninvasive, simple, and inexpensive approach with minimal infectious risk that can be performed by the patient with no need for involvement from medical personnel. Saliva can be tested at home, thus saving the need for a visit to the clinic or hospital.[9,10]

Various methods have been used for the SaU estimation, such as test strip, colorimetric kinetics, and microdiffusion method with varying results in literature. Enzymatic colorimetric method is the most commonly adopted method in recent literature with promising results.[10]

The present study included 200 subjects; out of which, 80 (40%) were controls. The control group consisted of 41 (51.25%) males and 39 females (48.75%). The observation of the study showed the mean and the SD of the age of CRF cases as 52.60 and ± 11.97 respectively. Gavaldá C et al[11] studied the level of urea in CRF cases in which the mean and SD of age of samples were 58.9 ± 14.9 years. Tomás I et al[12] reported mean age of 64 ± 11 years for CRF cases.

The present study noted higher percentage of male patients (66.67%) in CRF group as compared to females (33.33%). In agreement to our finding, Akai T et al[13] reported higher male percentage (65.9%) than females (34%) in his study.

Nandan et al[7] in his study observed the normal SaU as 12–70 mg/dl. In accordance with the above study, the present study showed the mean salivary urea in controls 41.9375 mg/dl.

Arora et al[14] studied SaU values in children who were undergoing dialysis with the mean value of SaU, 92.30 mg/dl and ± 15.27 as standard deviation. Their study suggested that the SaU levels were higher in patients with CRF when compared to controls. Similarly, the present study showed mean and standard deviation of SaU in CRF cases 115.9937 mg/dl and ± 44.8092 respectively, which was higher than control group with the mean and standard deviation as 41.9375 mg/dl and ± 15.4021 respectively.

In this study, the mean values of SaU in CRF cases were calculated in stages II, III, IV, and V. The mean values of SaU were 76.07 mg/dl, 95.82 mg/dl, 110.93 mg/dl, and 146.033 mg/dl respectively. These findings indicate increase in the levels of SaU with stages of CRF. Similarly, Tomás et al[12] have reported that the SaU levels increased with increasing stages of CRF cases.

Khramov VA et al[15] studied the correlation between the levels of SaU and different grades of CRF cases. They observed higher levels of SaU in stage III CRF cases than in stages I and II. They concluded that SaU levels reflect the progression of renal dysfunction and may serve as a diagnostic criterion. According to Khramov VA et al, the

present study also showed statistically significant relation between SaU levels and different stages of CRF cases with the p-value 0.0000 (Table 3).

CONCLUSION

To summarize, the present study suggests the use of saliva as an adjunct tool in diagnosing and staging of CRF cases. However, large-scale studies are required to further establish it as a "gold standard," like the use of serum in CRF cases. Since the salivary sampling is a noninvasive, simple, and rapid technique, the use of this as a biomarker in diagnosing and staging of CRF cases can become a potential diagnostic tool.

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