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SALIVARY UREA AND CREATININE'S EFFECTIVENESS AND CORRELATION WITH BLOOD UREA AND CREATININE IN PATIENTS WITH SEVERE RENAL DISEASE

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ABSTRACT

Background: Because of aging and the growing burden of non-communicable illnesses, there is an increasing prevalence of chronic kidney disease (CKD) worldwide. CKD patients accumulate a number of waste products as a result of impairment, which leads to a number of metabolic problems. They must thus have hemodialysis repeatedly in order to survive. As a result, blood urea and creatinine levels must be regularly checked. Saliva is becoming a popular medium for assessing these characteristics, nevertheless, because it is non-invasive.

Aim: The purpose of this study was to evaluate the effectiveness of serum urea and creatinine in patients with severe renal disease as well as the relationship between these parameters and salivary urea and creatinine in patients with chronic kidney disease.

Methods: The 200 participants in this study were split into two groups of 100 each, with CKD individuals in Group I and age- and gender-matched control subjects in Group II. Samples of blood and saliva were taken from each individual, and the levels of creatinine and urea were measured and compared. The collected data were subjected to statistical analysis.

Results: The study's findings demonstrated that the levels of creatinine and urea in the blood and saliva samples of the two groups differed significantly. Salivary urea and creatinine levels were also shown to be strongly positively correlated with serum urea and creatinine levels, respectively. The maximum specificity and sensitivity were seen for salivary creatinine at a cut-off value of 0.8 mg/dl and blood urea at 40 mg/dl.

Conclusion: salivary urea and creatinine levels can be utilized in place of blood urea and creatinine for determining eGFR and staging chronic renal disease. Additionally, as saliva collection is non-invasive, it may be utilized in place of blood sample collection, which is invasive, for the diagnosis and follow-up of CKD patients.

Keywords: urea, creatinine, serum, saliva, and chronic kidney disease

INTRODUCTION

Chronic kidney disease (CKD) causes aberrant kidney function as a result of many pathophysiological processes, resulting in a persistent decline in glomerular filtration rate (GFR). Chronic kidney disease is a clinical illness caused by permanent kidney dysfunction that results in metabolic, excretory, and synthetic failure. This buildup of nonprotein nitrogenous chemicals causes a variety of clinical symptoms. According to reports, the prevalence of chronic kidney disease (CKD) in India is between 0.79 and 0.9%, and as the country's population grows, 1.65 to 2.2 million more people are predicted to develop end-stage renal disease (ESRD) year. Due to the decrease of kidney function in individuals with chronic kidney disease (CKD), waste end products of various metabolites accumulate, affecting several organs. Along with other hematologic indicators, endocrine markers, and electrolytes, they include elevated blood creatinine and urea levels.

Saliva, a biological fluid with many components released by salivary glands, has been shown to be essential for both systemic and dental health. Because saliva can be taken often, is affordable, and is a simple fluid to collect, it is a better option for biochemical marker analysis than blood collection, which is an intrusive procedure. Additionally, saliva collection may be utilized for screening huge sample volumes and is more affordable than blood collection.²

Many systemic disorders, including chronic kidney disease, are known to influence the composition of salivary secretions. Along with measuring salivary urea and creatinine, routine markers measured in CKD participants' blood can also be examined from their saliva. Blood collection is an invasive procedure that is typically associated with anxiety and suffering. CKD patients have some blood loss during the hemodialysis and routine blood collection procedures.³

Additionally, doctors and other healthcare professionals are more susceptible to blood-borne infections. Saliva collection, a non-invasive technique requiring little expertise, is therefore seen as a superior choice that offers a comparative evaluation of medical issues with the least amount of danger to participants and medical personnel.⁴

Therefore, the purpose of the current study was to evaluate the effectiveness of salivary urea and creatinine in patients with chronic renal disease as well as their relationship to blood urea and creatinine in patients with severe kidney disease.

MATERIALS AND METHODS

The current case-control clinical investigation sought to evaluate the relationship between blood urea and creatinine in patients with severe renal disease and the effectiveness of salivary urea and creatinine in patients with chronic kidney disease. The research participants came from the Institute's Department of Medicine.

Prior to participation, all individuals gave their written and verbal informed permission. Using KDIGO recommendations, 100 patients of both genders and ages with CKD stages 4 and 5 were evaluated for the research. As controls, the research also evaluated a comparable number of healthy individuals who were matched by age and gender and had no history of serious systemic illness.

All of the individuals had their samples taken for the study at any time of day. Prior to hemodialysis, all CKD patients had blood and saliva samples taken under very rigorous aseptic and sterile guidelines.

Two milliliters of blood were drawn from the antecubital vein in a simple tube, and two milliliters of saliva were extracted using the spitting technique and placed in a sterile, graded container. Prior to sample collection, no food or liquids were permitted, and distilled water was used to completely rinse the mouth.

After that, the participants were instructed to sit comfortably while having their mouth and swallowing motions restrained. The participants were directed to collect their saliva on the bottom of their mouths, and spitting was done every 60 seconds until two milliliters of the salivary sample was obtained. Following sample collection, centrifugation at 3000 rpm was used to separate the serum from the blood sample and the saliva supernatant.

Saliva and serum were tested using commercially available standard kits in accordance with manufacturer directions, and urea levels were determined using the enzymatic kinetic technique and creatinine using Jaffe's method.

The collected data was statistically evaluated using the Student t-test, ANOVA (analysis of variance), Chi-square test, and SPSS (Statistical Package for the Social Sciences) software version 24.0 (IBM Corp., Armonk, NY, USA) for evaluating descriptive measures. To evaluate correlation across different factors, the Pearson correlation coefficient was employed. The findings were presented as frequency, percentages, mean, and standard deviation. A p-value of less than 0.05 was taken into account.

RESULTS

Assessing the effectiveness of salivary urea and creatinine in patients with chronic kidney disease and their correlation with blood urea and creatinine in patients with severe renal disease were the goals of the current case-control clinical investigation. The 200 participants in the current study were split into two groups of 100 each, with CKD individuals in Group I and age- and gender-matched control subjects in Group II. Samples of blood and saliva were taken from each individual, and the levels of creatinine and urea were measured and compared. There were 74 and 70 men and 26 and 30 females among 100 cases and 100 controls, respectively, and these numbers were statistically equivalent ($p=0.84$). Additionally, the mean age of the controls was 46.84 ± 12.84 years, while the mean age of the cases was 48 ± 13.85 years, which was not significant ($p=0.42$).

Diabetes mellitus was the most prevalent comorbidity among CKD cases in the current study, occurring in 62% ($n=62$) of the subjects, followed by hypertension in 60% ($n=60$), coronary artery disease in 8% ($n=8$), obstructive uropathy in 6% ($n=6$), and atrial fibrillation, stroke, gout, peripheral neuropathy, polycystic kidney disease, and SLE (systemic lupus erythematosus) in 2% ($n=2$) of each study participant (Table 1).

Serum urea levels were substantially higher in CKD participants than in controls ($p<0.01$) when comparing the mean creatinine and urea values in serum and saliva samples from the two groups. Serum creatinine levels showed similar trends, with CKD individuals having considerably greater levels than controls ($p<0.01$). Subjects with CKD had substantially higher levels of salivary urea and creatinine than those in the control group ($p<0.01$) (Table 2).

The correlation between the study participants' serum and salivary urea and creatinine levels was shown to be 0.96 for salivary urea vs serum urea, indicating a statistically significant association with $p<0.01$. Salivary creatinine levels and serum creatinine levels showed a comparable substantial correlation, with r and p -values of 0.93 and less than 0.01 respectively (Table 3).

According to the study's findings, the 95% CIs for the levels of salivary urea and creatinine in two groups of research participants were 0.94-1.00 and 0.98-1.00, respectively, with $p<0.01$ for both, indicating statistically significant outcomes (Table 4).

Salivary urea cut-off values, sensitivity, and specificity were 40, 92%, and 98%, respectively, for study participants with the highest specificity and sensitivity in CKD subjects. In contrast, salivary creatinine cut-off values, sensitivity, and specificity were 0.2, 100%, and 100%, respectively (Table 5).

DISCUSSION

The 200 participants in the current study were split into two groups of 100 each, with CKD individuals in Group I and age- and gender-matched control subjects in Group II. Samples of blood and saliva were taken from each individual, and the levels of creatinine and urea were measured and compared. There were 74 and 70 men and 26 and 30 females among 100 cases and 100 controls, respectively, and these numbers were statistically equivalent ($p=0.84$).

Additionally, the mean age of the controls was 46.84 ± 12.84 years, while the mean age of the cases was 48 ± 13.85 years, which was not significant ($p=0.42$). Diabetes mellitus was the most common comorbidity in CKD cases in this study, occurring in 62% ($n=62$) of the subjects, followed by hypertension in 60% ($n=60$), coronary artery disease in 8% ($n=8$), obstructive uropathy in 6% ($n=6$), and atrial fibrillation, stroke, gout, peripheral neuropathy, polycystic kidney disease, and SLE (systemic lupus erythematosus) in 2% ($n=2$) of the study participants each. These findings were similar to those of earlier research by Lasisi TJ et al. (2012) and Yajamanam N et al. (2016), who evaluated participants using demographic information similar to those of the current study.

According to the study's findings, CKD sufferers had substantially higher serum urea levels than controls ($p<0.01$) when comparing the mean creatinine and urea values in their serum and saliva samples to those of the control group. Serum creatinine levels showed similar trends, with CKD individuals having considerably greater levels than controls ($p<0.01$). Subjects with CKD had substantially greater levels of salivary urea and creatinine than those in the control group ($p<0.01$).

These findings were in line with those of Kurokawa K et al. (2002) and Bader RS et al. (2015), who found that the mean creatinine and urea levels in serum and saliva samples from CKD patients and control study participants were comparable to those of the current study. Regarding the relationship between research participants' serum and salivary urea and creatinine levels, the r -value for salivary urea vs serum urea was 0.96, indicating a statistically significant association with $p<0.01$. Salivary creatinine levels and serum creatinine levels showed a comparable substantial correlation, with r and p -values of 0.93 and less than 0.01 respectively (Table 3).

According to the study's findings, the 95% CIs for the levels of salivary urea and creatinine in two groups of research participants were 0.94-1.00 and 0.98-1.00, respectively, with $p<0.01$ for both, indicating statistically significant outcomes. These results were consistent with those of Xue JL et al. (2001) and Dash SC et al. (2006), who also observed correlations between serum and salivary urea and creatinine levels similar to those in the current investigation.

Salivary urea cut-off values, sensitivity, and specificity were 40, 92%, and 98%, respectively, for study participants with the highest specificity and sensitivity in CKD subjects. In contrast, salivary creatinine cut-off values, sensitivity, and specificity were 0.2, 100%, and 100%, respectively. These findings were consistent with those of Arvind PS et al. (2018) and Bagalad BS et al. (2017), whose studies' cut-off values, sensitivity, and specificity of salivary urea and creatinine were similar to the current study's findings.

CONCLUSIONS

The present study, within its limitations, concludes that salivary urea and creatinine levels can be used as an alternative to serum urea and creatinine in the calculation of eGFR and staging of chronic kidney disease. Also, saliva collection being a non-invasive method can be used as an alternative to blood sample collecting which is an invasive method for diagnosis and monitoring of subjects with CKD. However, further prospective longitudinal studies with larger sample sizes and longer monitoring are needed to reach a definitive conclusion.

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Comorbidities	Number (n)	Percentage (%)
SLE	2	2
Polycystic kidney disease	2	2
Peripheral neuropathy	2	2
Gout	2	2
Stroke	2	2
Atrial fibrillation	2	2
Obstructive uropathy	6	6
Coronary artery diseases	8	8
Hypertension	60	60
Diabetes mellitus	62	62

Table 1: Distribution of CKD subjects based on the comorbidities

Variables	CKD cases (n=100)	Controls (n=100)	p-value
Serum urea	119.82±55.00	28.92±6.92	<0.01
Serum creatinine	4.32±2.27	0.79±0.19	<0.01
Salivary urea	115.70±58.85	24.04±7.93	<0.01
Salivary creatinine	0.86±0.69	0.08±0.01	<0.01

Table 2: Mean creatinine and urea values in serum and saliva samples in CKD subjects and control study subjects

Pearson correlation	r-value	p-value
Salivary urea vs serum urea	0.96	<0.01
Salivary creatinine vs serum creatinine	0.93	<0.01

Table 3: Correlation of serum and salivary urea and creatinine values in study subjects

Variables	Mean	95% CI	p-value
Salivary urea	0.96±0.01	0.94-1.00	<0.01
Salivary creatinine	0.98±0.00	0.98-1.00	<0.01

Table 4: Salivary urea and creatinine levels concerning 95% CI in two groups of study subjects

Variables	Cut-off value	Sensitivity	Specificity
Salivary urea	40	92	98
Salivary creatinine	0.2	100	100
Variables	Cut-off value	Sensitivity	Specificity
Salivary urea	40	92	98
Salivary creatinine	0.2	100	100

Table 5: Cut-off values for salivary urea and creatinine in study subjects with the highest specificity and sensitivity in CKD subjects