ScienSage

Journal of Advanced Scientific Research

Available online through http://www.sciensage.info

ISSN
0976-9595
Research Article

ASSESSMENT AND CORRELATION OF SALIVARY AND SERUM UREA AND CREATININE LEVEL IN PATIENTS WITH CHRONIC KIDNEY DISEASE, DIABETES AND HYPERTENSION

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ABSTRACT

The biomarkers like creatinine and urea are most commonly useful for assessment of Chronic Kidney Disease (CKD) as well as susceptible diabetic and hypertensive patients. Blood collection is the invasive procedure, causing nervousness and distress to the patients whereas saliva collection is a noninvasive, simplest and cost effective procedure. Therefore, the main aim of the study was to assess and correlate salivary and serum urea and creatinine levels in CKD, diabetics and hypertensive patients and control group. This study consisted of total 60 patients involving 20 CKD, 20 diabetics, 20 hypertensive patients and 20 healthy controls. Ethical approval was taken from the institutional Human Research Ethics Committee. Saliva and blood samples were collected by standard procedure, then urea and creatinine levels were measured on automated biochemistry analyzer. Correlation between serum and salivary creatinine and urea was obtained in controls and patients using Pearson correlation coefficient in SPSS (version 15). Serum and salivary creatinine and urea levels were significantly higher in CKD patients followed by diabetics then hypertensive patients as compared to control group. Our findings suggest that analysis of salivary urea and creatinine in patients reflects their levels in blood. Thus, salivary urea and creatinine can be used noninvasively as diagnostic biomarkers in CKD, diabetics and hypertensive patients.

Keywords: Chronic Kidney Disease, Diabetes, Hypertension, Biomarkers, Urea, Creatinine

1. INTRODUCTION

Chronic kidney diseases (CKD) are characterized by loss in regulatory and excretory functions of kidney progressively [1, 2]. It becomes a larger global health problem which contributes most important mechanism to the morbidity and mortality [3, 4]. The prevalence incidences are elevated worldwide with the diabetes and hypertension is the leading cause [5]. Diabetes mellitus is usually linked with the dyslipidemia, hypertension, visceral adiposity, which collectively increases the risk of developing CKD [6]. It has been estimated that approximately 25-40% of diabetic and hypertensive patients usually develop CKD [1].

In India the numbers of prevalent CKD patients are increasing day by day reflected by rising elderly populations and rising number of patients with diabetes and hypertension. India is a biggest number of the diabetics in the world having the prevalence of 3.8% for the rural and 11.8% for the urban adults [3]. Hypertension is the established cardiovascular risk factor which contributes to the cardiovascular risk associated with CKD. The prevalence of the hypertension is noted that the range of 20-40% for the urban and 12-17% for the rural adults. Worldwide, over 1 million people survive on the dialysis [7].

Biochemical markers are played a significant role in accurate diagnosis and in assessing risk and adopting therapy to improve clinical outcome. Urea and Creatinine are good indicators of the normal functioning of the kidney [8]. Urea is the major nitrogenous ending product of the protein and amino acid catabolism, produced by liver and spread to the intracellular and extracellular fluid [9]. Creatinine is the breakdown product of the Creatinine phosphate and is released from the skeletal muscle by a steady rate [10].

Blood sample are collected for the serum analysis is the invasive procedure, causing nervousness and distress to the patients due to blood loss from frequent blood sampling and that increases of risk for the patient or health care professional to the blood born diseases [5]. Saliva is a multiconstituent biologic fluid secreting by salivary gland and contributes to the oral health. It is a

cutting edging over serum because saliva collection is a noninvasive, simplest and cost effective procedure that is performed by the patient with minimum participation from medical personnel [5]. Saliva is filtrated from the blood where a variety of molecules is passing from side to paracellular routes or transcellular into saliva. For the result, saliva may be representing correspondent to the serum [4]. CKD can affect the contents of salivary secretion as it is systemic disease. Saliva can indicates creatinine and urea level in CKD patients which are the parameters usually estimated in blood samples to know the normal functioning and any dysfunction of kidney [11].

The main aim of the present study was quantitative estimation of the Urea and Creatinine in the serum and saliva of the CKD, diabetic and hypertensive patients and their correlation and comparison with the control group.

2. MATERIAL AND METHODS

This cross sectional study involves total 60 patients that include 20 CKD, 20 diabetic and 20 hypertensive patients and 20 healthy individual as control group (age and gender mathched). The patients suffering from other diseases affected the electrolyte and water balance, patients under medication that could affect saliva production, patients with any salivary gland or oral diseases, alcoholics, smokers, pregnant women were excluded from the study. Ethical clearance was taken from the institutional human research ethics committee to perform this study. The patients were informed prior to study and written consent was taken.

2.1. Sample collection

The patients were selected on the basis of inclusion and exclusion criteria. Most of the CKD patients were undergoing dialysis treatment. Under aseptic conditions 2 ml of the patient's intra-venous blood was obtained and centrifuged at 3000 rpm for 10 minutes and serum was separated for further testing.

The participants were instructed to refrain from eating and drinking at least 1 or 2 hours. 2 ml of whole saliva was collected in between 9.00 a.m. to 12:30 p.m. to avoid diurnal variations into a disposable test tube and then centrifuged at 2000 rpm for 2-3 minutes. The supernatant saliva samples were obtained for further analysis.

The serum and salivary urea and creatinine levels were estimated by using Berthelot-urease kit method [12] and Jaffe's kit method [13] respectively on Automated Biochemistry Analyzer.

2.2. Statistical analysis

Entire data obtained from the study was entered in to excel sheet. The Mean, Standard Deviation (SD) values was calculated and statistically analysis was done by using SPSS (version 15) software [14]. Spearman's correlation test was used for correlations between serum and salivary urea and creatinine [14]. The p-value <0.05 was considered as statistically significant.

3. RESULTS

The study population comprised a total of 60 patients suffering from CKD, diabetes and hypertension and 20 healthy individual. Out of 60 patients, 36 (60%) were male and 24 (40%) were female patients. No significant difference observed among the group with age and gender as shown in table 1.

Table 1: Gender wise distribution

	Control Group (n = 20)	Study Group (n = 60)
Age (in years)	56.75 ± 7.83	58.2 ± 9.71
Male	12 (60%)	36 (60%)
Female	8 (40%)	24 (40%)

The mean age of the control group was 56.75±7.83 years and the mean age of the study group was 58.2±9.71 years. In control group and study group, significant difference was not found with respect to age and gender.

Table 2: Comparison of serum and salivary creatinine level

Study Group	Creatinine		p-value
	Serum creatinine (mg/dl) (Mean ± STD)	Saliva creatinine (mg/dl) (Mean ± STD)	
Control	0.99 ± 0.31	0.17 ± 0.02	0.867
CKD patients	4.31± 1.99	0.7 ± 0.34	0.034
Diabetic patients	1.29± 0.4	0.56 ± 0.31	0.938
Hypertensive patients	1.23 ± 0.4	0.37 ± 0.19	0.211

The serum & salivary creatinine levels were higher in all study groups as compared to control. The comparison between serum and salivary creatinine levels showed that in all the groups, the serum creatinine level was higher as compared to the salivary creatinine level. Among all groups the serum and salivary creatinine levels were highest increased in CKD patients followed by diabetics then hypertensive patients. The significant positive correlation was detected between serum and salivary creatinine values in CKD patients as shown in table 2.

The salivary and serum urea levels were higher in all study groups as compared to control group. We also found that the urea level in serum and saliva was almost similar. The correlation for salivary and serum urea showed very strong positive relation. It means as serum urea level increases, salivary urea level also increases. Among all groups the serum and salivary urea levels were highest increased in CKD patients followed by diabetics then hypertensive patients The highly significant positive correlation was detected between serum urea values with salivary urea values in CKD and hypertensive patients as shown in table 3.

Table 3: Comparison of serum and salivary urea level

Group	Urea		p-value
	Serum urea (mg/dl) (Mean ± STD)	Saliva urea (mg/dl) (Mean ± STD)	
Control	25.67±3.04	36.61±5.47	0.158
CKD patients	242.18±127.3	249.05±126.96	0.000
Diabetic	102.12±43.94	108.79±40.18	0.332
Hypertensive patients	86.59±27.75	91.86±20.76	0.014

4. DISCUSSION

Kidneys regulate the volume and construction of the extracellular and intracellular fluid to maintain homeostasis of the body by constant processing of the plasma through filtration, reabsorption and secretion of the substances [4]. Creatinine is unable to easily diffuse across the cells and stronger intercellular junction of the salivary gland in the healthy state under normal conditions. But in diseased state, creatinine value increases in saliva possibly due to an alteration in the permeability of salivary gland cells and the high serum creatinine levels in CKD patients create a concentration gradient that facilitates diffusion of creatinine from serum in to saliva. The normal range of serum creatinine is 0.6-1.5mg/dl and salivary creatinine is 0.05-0.2mg/dl [1]. Thus, serum creatinine is used for monitoring disease progression [15]. Whenever there is an increase in the blood urea there is concurrent increase in salivary urea also because the kidneys are unable to excrete urea in the renal failure and its concentration in blood increases with increased concentration in saliva because of increased serum urea which creates an increased concentration gradient in turn increasing the diffusion of urea from serum to saliva. Normal blood urea concentration is 30-40 mg/dl where as normal salivary urea is 12-70 mg/dl. Therefore, salivary creatinine and urea levels correlate well with the serum creatinine and urea respectively so that saliva can be used as a noninvasive diagnostic tool [1].

The mean salivary & serum creatinine level in CKD patients was 0.7±0.34 & 4.31±1.99. In Urea level was CKD patients was 249.05±126.96 and 242.18±127.3. We observed a significantly high creatinine and urea level both in serum and saliva of CKD patients as compared with controls. Similar observation was made by Xia et al. [16], Davidovich et al. [17] and Zuniga et al. [18]. A highly significant difference was observed for the serum urea and creatinine values between CKD patients showing highest range of the serum urea followed by diabetic patients as compared to controls. Similar results were seen in study done by Mittal A et al. [19]. Renal damage reduces the glomerular filtration capacity of kidneys and leads to increased levels of metabolic waste product such as urea and creatinine which are main indicators of the renal function alterations [4].

In diabetic patients, the mean salivary & serum creatinine level was 0.56±0.31 & 1.29±0.4 and in urea level was 108.79±40.18 & 102.12±43.94. Our study result showed high creatinine level in both saliva and serum as compared to control in diabetic patients. Similar results were seen in study done by Deepa K et al. [20]. Urea level also increased in both saliva and serum in almost all diabetic patients. Similar results were seen in the study done by Rohitash K et al. [21] and Kamal A [22]. High

blood sugar levels damage millions of nephrons resulting in inability of the kidney to maintain fluid and electrolyte homeostasis [1].

The mean salivary & serum creatinine level in hypertensive patients was 0.37±0.19 & 1.23±0.4 and urea level was 91.86±20.76 & 86.59±27.75 in this study. Results of our study were consistent with the results of study done by Pooja and Mittal Y. [23] and Yadav R et al. [24]. In hypertensive patients, the kidney is main target organ and long term exposure to elevations in blood pressure can induce early renal damage [25]. In all the groups serum creatinine values were significantly higher than salivary creatinine. Similar findings were obtained by study done by Ali SP et al. [26]. Overall correlations (n=20) were significant between serum urea and salivary urea in all the groups and demonstrated that as serum urea and salivary urea increases. Our finding was also similar to the study done by Cardoso EML et al. [27].

5. CONCLUSION

The highest numbers of CKD, diabetic and hypertensive patients were seen in the old age group of above 50 years. Among all groups, serum and salivary creatinine levels were highest increased in CKD patients followed by diabetes then hypertensive patients as compared to control group. The comparison between serum and saliva creatinine levels showed that in all the groups, the serum creatinine level was higher as compared to the salivary creatinine level. Serum and salivary urea levels were highest increased in CKD patients followed by diabetes then hypertensive patients as compared to the control. The comparison of urea levels in serum and saliva showed that the values were almost similar in all the study groups. The correlation for salivary and serum urea showed very strong positive relation and highly significant as compared to the control.

In our study, increase amount of salivary and serum creatinine and urea levels were seen in CKD, diabetic and hypertensive patients as compared to controls. Thus, salivary urea and creatinine can be used for screening of renal status in CKD, diabetic and hypertensive patients. As a result, saliva may represent the same to serum, thereby reflecting the physiological body state. Thus, it has been proposed, to be a good source for the diagnostic purposes, several chronic diseases, cardiovascular diseases, renal diseases especially Chronic Kidney Disease.

Our findings recommend that salivary creatinine and urea can be used as a noninvasively diagnostic parameter in CKD, diabetics and hypertensive patients and saliva may be used as noninvasive diagnostic tool. Thus, it can prevent the avoidable and periodic withdrawal of the blood which is not only burdensome but also increase the risk of infection. This study was an attempt to harness the benefit of saliva as a noninvasive diagnostic fluid in the chronic kidney disease patients, which has the potential to dramatically decrease worry and discomfort associated with blood sampling procedures. However, lack of sensitive detection methods, lack of correlation between the biomolecules in the blood and saliva and the cardian variation in saliva may affect the result outcome.

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