Assessment and Correlation of Urea and Creatinine Levels in Saliva and Serum of Patients with Chronic Kidney Disease, Diabetes and Hypertension– A Research Study

DIVYA PANDYA[1], ANIL KUMAR NAGRAJAPPA[2], K.S RAVI[3]

ABSTRACT

Introduction: Serum urea and creatinine are most widely accepted parameters to assess Chronic Kidney Disease (CKD) status as well as to assess renal status in susceptible diabetic and hypertensive subjects.

Aim: To assess and correlate the serum and salivary urea and creatinine levels of CKD, diabetes mellitus and hypertensive subjects.

Materials and Methods: This cross-sectional study was done on 120 subjects involving 30 CKD, 30 diabetic, 30 hypertensive subjects and 30 healthy controls. After collection of saliva and blood samples, urea was analyzed by enzymatic calorimetric method and creatinine by Jaffe's method. Kruskal Wallis test and Mann Whitney U test were used for comparison between different groups and correlations between serum and salivary parameters were evaluated by applying Spearman's correlation test. The p-value <0.05 was considered statistically significant.

Results: The median serum and salivary urea and creatinine levels were highest in CKD group followed by diabetic, hypertensive groups and controls. The correlation coefficient for serum urea and salivary urea was 0.977 and for serum creatinine and salivary creatinine was 0.976, with p-value <0.001.

Conclusion: This study showed that there is a significant positive relationship between salivary and serum urea and creatinine. Thus, salivary urea and creatinine levels can be used non-invasively to detect serum urea and creatinine levels respectively in renal disease and diabetic and hypertensive nephropathic cases.

INTRODUCTION

Chronic Kidney Disease (CKD) is a progressive reduction in renal function [1]. It is a condition where the kidneys lose their normal function, especially excretory and regulatory functions which can be due to infections, autoimmune diseases, diabetes, hypertension, cancer and toxic chemicals [2]. CKD is heading towards becoming a major health problem [3] and is rapidly assuming epidemic proportions globally [4]. India has highest number of diabetics in the world having a prevalence of 3.8% in rural and 11.8% in urban adults [3]. It is associated with adverse outcomes in all stages of CKD [5]. The prevalence of hypertension is reported to range between 20-40% in urban adults and 12-17% among rural adults [3]. It also contributes to cardiovascular risk associated with CKD. Systolic blood pressure is more strongly associated with cardiovascular death in dialysis patients than diastolic or pulse pressure [5]. It has been estimated that approximately 25-40% of diabetic and hypertensive patients usually develop CKD (Nephropathy) [3]. Studies conducted on renal patients revealed that up to 90% were found to have oral symptoms of uremia like ammonia like taste and smell, stomatitis, gingivitis, decreased salivary flow, xerostomia and parotitis [2]. The objectives of early diagnosis is identification of asymptomatic disease at that time when intervention has a reasonable potential of a positive impact on outcome [3].

Biochemical markers play an important role in accurate diagnosis and in assessing risk and adopting therapy to improve clinical outcome. Instead of urine analysis which is relatively discomforting for patient, serum analysis of renal function markers like urea, creatinine, uric acid and electrolytes are used routinely [6]. Blood tests for Blood Urea Nitrogen (BUN) [7] which is a major nitrogenous end product of protein and amino acid catabolism [6] and creatinine [7] which is a breakdown product of creatine phosphate in muscle [6] are excreted by kidneys. BUN is an indirect and rough measurement of renal function that measures the amount of urea nitrogen in blood and is directly related to excretory function of kidney. Creatinine tests diagnose impaired renal function and measure the amount of creatinine phosphate in blood. Urea and creatinine are good indicators of a normal functioning kidney and increase in the serum are indications of kidney dysfunction [7] BUN and serum creatinine are widely accepted and most commonest parameters to assess renal functions [7,8]. Collection of blood for serum analysis is an invasive technique and thus, causes anxiety and discomfort to patients due to blood loss from frequent blood sampling and thereby potentially increases the risk for patients as well as health care professionals to blood borne diseases. Hence, a simple diagnostic test that provides a reliable evaluation of disease status and stages and is of value to both clinicians and patients is required [1]. As blood is the most common sample in clinical chemistry for identification of diseases and to follow progress of affected individuals under medical treatment, similar use has been envisioned for saliva [9].

The potential of saliva as a diagnostic aid has attracted the attention because of its virtue of being non-invasive in nature, relative simplicity of collection, economic procedure that can be performed by the patient with minimal involvement of medical personnel. Whenever required a repeat sample can also be easily

obtained, is suitable to all age groups, can screen large populations and can be used as a diagnostic medium and thus, is considered as a boon to patients suffering from clotting disorders such as hemophilia and in patients with compromised venous access [1]. Thus, it's a fluid that lacks the drama of blood, the sincerity of sweat and emotional appeal of tears [9].

Elevation of BUN and creatinine in renal diseases results in high concentration of these byproducts in saliva due to passive diffusion of these nitrogenous waste into the saliva as well as alteration in salivary gland permeability that allows diffusion of nitrogenous products, Saliva acts as an alternative route of excretion by the body in compromised renal function state [8]. Hence, saliva is a multi-constituent biologic fluid secreted by salivary glands with hundreds of components serving to detect systemic diseases and provide biomarkers of health and disease status [10].

The aim of this study was to quantitatively estimate the amount of urea and creatinine present in the serum and saliva of the CKD, diabetic and hypertensive subjects and objectives were to compare and correlate the serum and salivary parameters with age and sex matched controls and to determine the advantages of non-invasive method for the estimation of CKD.

MATERIALS AND METHODS

A cross- sectional study was conducted in Hitkarini Dental College and Hospital, Jabalpur, Madhya Pradesh, India for 2.5 years duration on 120 subjects of either sex aged between 30 to 70 years. An ethical clearance was obtained from the ethical committee of the college and hospital.

Subjects included in the study were divided into four groups:

- Group I: 30 subjects with CKD
- Group II: 30 subjects with diabetes
- Group III: 30 subjects with hypertension
- Group IV: 30 subjects healthy adults as controls (age and sex matched).

Subjects with diagnosed CKD, type II diabetes mellitus and hypertension were included in the study and patients with other diseases that affect the water and electrolyte balance, patients under medication (other than insulin and anti hypertensive) that could affect saliva production, smokers, alcoholics, pregnant women, subjects with recent history of hospitalization, infusions and trauma, subjects known to have any salivary gland or oral diseases, subjects who are critically ill or unconscious, subjects not willing to participate and approve the informed consent were excluded from the study.

Sample Collection: Under aseptic conditions 2ml of the patient's intra-venous blood was obtained and centrifuged at 4000rpm for 8-10 minutes. The spitting method was used for collection of unstimulated whole saliva sample and was immediately subjected to analysis, to avoid deterioration due to incubation and to avoid enzymatic alteration of urea and creatinine in saliva. Approximately 3ml of saliva was collected in a sterile graduated tube with the subjects in a seated position after a minimum of 5 minutes. Saliva collection was done between 9.00 a.m. to 12 noon to avoid diurnal variations and saliva was taken into a disposable test tube and centrifuged at 2000rpm for 2-3 minutes. With the help of a micro-pipette 1ml of the urea and creatinine reagents were taken in four different test tubes. Total 10μl of the supernatant centrifuged serum and saliva samples were obtained and added to the urea and creatinine reagents. This was then kept in a temperature controlled water bath at 37°C for 10 minutes. The color change of solution was noted and the Optical Density (OD) was measured in a photocalorimeter for urea (Berthelot-urease method enzymatic colorimetric method) and for creatinine (alkaline picrate, Jaffe's method) based on the principle of enzymatic calori metry.

STATISTICAL ANALYSIS

Entire data obtained from this study was entered in a master chart and then tabulated. Frequency, percentage, means, Standard Deviation (SD), median, minimum and maximum values of variables was calculated. Kruskal Wallis test and Mann Whitney U test were used for comparison between different groups. Correlations between serum and salivary parameters were evaluated by applying Spearman's correlation test. The p-value<0.05 was considered statistically significant. Data analysis was done using Statistical Package for Social Sciences (SPSS) version 1 for windows.

RESULTS

There were a total of 120 subjects with a median age of 54 years and there were 64 males (53.3%) and 56 females (46.7%) with no significant difference observed among groups with respect to age and gender (p > 0.05). The comparison of serum urea values with salivary urea values showed that in all the groups serum urea values were significantly higher than salivary urea values with p-value = 0.000 (<0.001) [Table/Fig-1]. The comparison of serum creatinine values with salivary creatinine showed that in all the groups serum creatinine values were significantly higher than salivary creatinine p- value = 0.000 (<0.001) [Table/Fig-2]. Among all groups' serum and salivary urea and creatinine levels were highest increase in CKD subjects followed by diabetics then hypertensives and least in controls. The overall (n=120) correlation coefficient for serum urea and salivary urea was 0.977 and for serum creatinine and salivary creatinine was 0.976, which showed very strong positive

Groups	Urea (mg/dl)				Mann Whitney U test value	p-value
	Serum Urea		Salivary Urea			
	Mean ± SD	Median	Mean ± SD	Median		
Chronic Kidney Disease (n=30)	112.66 ± 43.52	107.90	46.17 ± 11.41	43.11	16.000	p=0.000 (<0.001) Significant difference
Diabetes (n=30)	55.13 ± 19.42	48.44	32.80 ± 9.59	31.71	101.000	p=0.000 (<0.001) Significant difference
Hypertension (n=30)	43.41 ± 8.00	42.70	26.16 ± 7.18	27.80	48.000	p=0.000 (<0.001) Significant difference
Controls (n=30)	26.74 ± 3.91	27.50	12.59 ± 0.66	12.17	465.000	p=0.000 (<0.001) Significant difference

[Table/Fig-1]: Comparison of mean and standard deviation of serum and salivary urea values in study groups.

Groups	Creatinine (mg/dl)				Mann Whitney U test value	p-value
	Serum Creatinine		Salivary Creatinine			
	Mean ± SD	Median	Mean ± SD	Median		
Chronic Kidney Disease (n=30)	7.19 ± 4.77	5.65	1.33 ± 0.94	1.01	23.000	p=0.000 (<0.001) Significant difference
Diabetes (n=30)	1.79 ± 0.46	1.65	0.31 ± 0.19	0.23	465.000	p=0.000 (<0.001) Significant difference
Hypertension (n=30)	1.62 ± 0.22	1.60	0.28 ± 0.24	0.20	465.000	p=0.000 (<0.001) Significant difference
Controls (n=30)	0.94 ± 0.20	0.97	0.08 ± 0.03	0.06	465.000	p=0.000 (<0.001) Significant difference

[Table/Fig-2]: Comparison of mean and standard deviation of serum and salivary creatinine values in study groups.

Groups	Correlation between	Correlation Coefficient (Spearman's rho)	p-value
Chronic Kidney Disease (n=30)	Serum urea and salivary urea	0.958 Very strong positive relationship	0.000 (<0.001) Significant correlation
	Serum creatinine and salivary creatinine	0.931 Very strong positive relationship	0.000 (<0.001) Significant correlation
Diabetes (n=30)	Serum urea and salivary urea	0.957 Very strong positive relationship	0.000 (<0.001) Significant correlation
	Serum creatinine and salivary creatinine	0.920 Very strong positive relationship	0.000 (<0.001) Significant correlation
Hypertension (n=30)	Serum urea and salivary urea	0.905 Very strong positive relationship	0.000 (<0.001) Significant correlation
	Serum creatinine and salivary creatinine	0.960 Very strong positive relationship	0.000 (<0.001) Significant correlation
Controls (n=30)	Serum urea and salivary urea	0.931 Very strong positive relationship	0.000 (<0.001) Significant correlation
	Serum creatinine and salivary creatinine	0.896 Very strong positive relationship	0.000 (<0.001) Significant correlation
Over all (n=120)	Serum urea and salivary urea	0.977 Very strong positive relationship	0.000 (<0.001) Significant correlation
	Serum creatinine and salivary creatinine	0.976 Very strong positive relationship	0.000 (<0.001) Significant correlation

[Table/Fig-3]: Overall correlation between serum and salivary urea and creatinine in study groups.

relationship with p-value = 0.000 (<0.001) which is a highly significant correlation [Table/Fig-3]. It means as serum urea and creatinine value increases, salivary urea and creatinine value also increases and vice versa.

DISCUSSION

During the past three decades, the incidence and prevalence of End Stage Renal Disease (ESRD) has risen progressively [11]. Most important reasons for rapid increase in CKD patients are rapidly increasing worldwide incidence of diabetes and hypertension [12]. According to a recent estimate, approximately 285 million people worldwide (6.6%) in the 20-79 years age group had diabetes in 2010 and by 2030, 438 million people (7.8%) of the adult population are expected to develop diabetes [13]. In India alone, the prevalence of diabetes is expected to increase from 31.7 million in 2000 to 79.4 million in 2030 [14]. About 1/3rd of those affected will eventually have progressive deterioration of renal function [15]. As suggested by a worldwide data on the global burden of hypertension, 20.6% of Indian men and 20.9% of Indian women were suffering from hypertension in 2005 and it is expected that by 2025 the rates of hypertension are expected to go up to 22.9% and 23.6% for Indian men and women respectively [16]. Adequate blood pressure control is widely recognized as an essential factor in slowing the progression of CKD and preventing its main sequel, ESRD and cardiovascular disease [17]. As kidneys are the main target of organ damage in hypertension and long term exposure to elevations in blood pressure even within normotensives can induce early renal damage [18].

High blood sugar levels damage millions of nephrons resulting in inability of kidneys to maintain fluid and electrolyte homeostasis. Creatinine is filtered by glomerulus and thus, serum creatinine level is considered as an indirect measure of glomerular filtration. Diminishing of glomerluar filtration rate results in rise of plasma concentrations of serum creatinine and urea. This rise indicates progression of kidney disease and thus serum creatinine has greater prognostic ability compared with urea for predicting the

adverse outcomes [15]. An elevated serum creatinine level is also a late sign of renal damage in essential hypertension with frankly elevated serum creatinine values predict a poor prognosis in patients with hypertension [18]. Creatinine due to its physical properties in a healthy state under normal conditions is unable to diffuse easily across the cells and tight intercellular junction of the salivary gland. But in diseased state, its value increases in saliva possibly due to an alteration in the permeability of salivary gland cells and the increased 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 [19].

Whenever there is an increase in the blood urea there is concomitant increase in salivary urea also because the kidneys are unable to excrete urea in 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 30-40mg/dl where as normal salivary urea is 12-70mg/dl [8]. Therefore, salivary creatinine and urea levels correlate well with the serum creatinine and urea respectively so that saliva can be used as a non-invasive diagnostic tool [2].

This study supported that there was a significant linear relationship between serum urea and creatinine and salivary urea and creatinine levels respectively. The correlation coefficient for serum urea and salivary urea was 'r' = 0.977 and for serum creatinine and salivary creatinine was 'r'= 0.976 which is statistically very highly significant (p = 0.001). Comparison of results of present study with other studies is compared in [Table/Fig-4].

Present study conclusion for CKD Group	Comparative studies
A statistically highly significant difference was observed for serum urea and creatinine values between groups (p = 0.000) with CKD group subjects showing highest range of serum urea followed by diabetic group then hypertensive group as compared to controls.	1. Mittal A et al., also demonstrated almost similar results on 440 patients with a significant increase in mean serum creatinine and urea in kidney disease patients with diabetes mellitus. In non-diabetic kidney disease patients mean value of serum creatinine and urea were also moderately raised as compared to controls [15].
Present study conclusion for diabetic group	**Comparative studies**
Raised serum urea and creatinine in almost all diabetic patients with normal values of serum urea and creatinine in almost all controls.	1. Similar results were seen in studies done by Shrestha S et al., [20].
	2. Kamal A demonstrated that urea and creatinine levels deflects corresponding to increase blood glucose level indicating a reduction in kidney function in diabetic patients [21].
	3. Findings were also similar to the studies done by Deepa K et al., [22] and Rohitash K et al., [23].
Present study conclusion for hypertensive group	**Comparative studies**
1. Serum urea and creatinine values were significantly increased in hypertensive group when compared to controls 2. Mean of serum creatinine level in hypertensive subjects was significantly higher (1.62 mg/dl) than control (0.94 mg/dl)	1. AL-Hamdani IH conducted a study on 82 hypertensive patients and 43 healthy volunteers and found a significant increase in mean values of serum urea and creatinine concentration in hypertensive patients in comparison to controls [24]. 2. Similar results were obtained by study conducted by Yadav R et al., demonstrating a positive correlation in blood urea and creatinine levels with severity of renal dysfunction in hypertensive patients [25]. 3. Results of our study were consistent with the results of study conducted by Pooja and Mittal Y where the mean serum creatinine level of hypertensive cases was significantly higher as compared to controls [26].

Present study conclusion for salivary urea and creatinine values	Comparative studies
1. A statistically highly significant difference was observed for salivary urea values between groups (p = 0.000) with CKD group subjects which showed highest range of salivary urea followed by diabetic group then hypertensive group as compared to controls. 2. A statistically significant difference for salivary creatinine values between groups with CKD group patients showed highest increase followed by equal increased values in both diabetic and hypertensive groups as compared to controls.	1. Tomas I et al., conducted a study on 50 CRF (chronic renal failure) patients with 22 M-S CRF (moderate-severe chronic renal failure) and 28 TRF (terminal renal failure) patients and 64 healthy controls. Results revealed that salivary urea level of TRF patients was significantly higher than that of M-S CRF patients [27].
Present study conclusion on group wise comparison of salivary and serum values	**Comparative studies**
1. In all the groups serum urea and serum creatinine values were significantly higher than salivary urea and creatinine p-value = 0.000 (<0.001).	1. These findings were contradictory with the findings of Suresh G et al., in their study on 45 hemodialysis patients, 15 transplant group patients and 10 healthy controls which suggested that salivary urea levels were slightly higher than blood urea levels in all study groups. In hemodialysis group, mean blood urea level was 71.75 mg/dl and mean salivary urea level was 97.15 mg/dl and in transplant group mean blood urea and salivary urea levels were 56.8 mg/dl and 71.53 mg/dl [8]. 2. Similar findings were also obtained by study done by Ali SP et al., demonstrating that mean salivary urea levels (107.52 mg/dl) were higher than mean blood urea levels (103.57 mg/dl) in hemodialysis patients [28].
Present study conclusion on over all correlation between serum and salivary urea values	**Comparative studies**
1. Overall correlations (n=120) were significant between serum urea and salivary urea in all the groups and demonstrated that as serum urea value increases, salivary urea value also increases and vice versa.	1. Similar results were obtained by Cardoso EML et al., concluding that salivary urea estimation is a harmless and useful diagnostic tool [29].
Present study conclusion on over all correlation between serum and salivary creatinine values	**Comparative studies**
1. Overall correlations (n=120) were significant between serum creatinine and salivary creatinine and demonstrated that as serum creatinine value increases, salivary creatinine value also increases and vice versa.	1. Lloyd JE et al., conducted a study on 26 renal disease patients and 23 healthy volunteers and found a statistically significant relationship between salivary and serum creatinine concentrations for the patients and salivary creatinine concentrations are 10-15% of those in blood [30].
Present study correlation between serum and salivary values	**Comparative studies**
1. In CKD subjects Spearman's rho correlation coefficient for serum urea and salivary urea was 0.958 and for serum creatinine and salivary creatinine was 0.931, which showed very strong positive relationship with p value = 0.000 (<0.001) which is a highly significant correlation.	1.Similar results were obtained by Venkatapathy R et al., [1] Seethalakshmi C et al., [10].

[Table/Fig-4]: Comparison of results of present study with other studies.

Clinical Implications and Future Perspectives of the Study: Eliminating repeated blood withdrawal for investigation and application of non-invasive useful fluid saliva as an adjunct diagnostic fluid in renal function assessment.

In future saliva can not only act as adjunct but can be applied on daily basis for investigations of urea and creatinine due to its high

success rate in expressing accurate urea and creatinine levels as found in serum.

LIMITATION

Blood has always remained as one of the most frequent and effective marker to assess renal status and rise in salivary values, even though, correlated with serum values could not always accurately predict exact alteration in renal status and there could also be variations in salivary flow and method of collection which could have affected the results.

CONCLUSION

Literature showed very few studies demonstrating the correlation between the serum and salivary parameters, no other studies were found to demonstrate the serum and salivary urea and creatinine estimation in CKD, diabetic and hypertensive groups together. Based on the observations from the present study it can be inferred that serum and salivary urea and creatinine levels were significantly higher in CKD subjects followed by diabetic then hypertensive subjects. Increased amount of salivary urea and creatinine levels were seen only in CKD subjects, diabetic and hypertensive subjects and no difference was seen in controls. Thus, it can be recommend that salivary urea and creatinine values can be used for screening of renal status in CKD, diabetic and hypertensive subjects. The present study substantiated that saliva can also be employed as an alternative potent non-invasive inexpensive diagnostic tool thus, preventing the unnecessary and periodic withdrawal of blood which is not only cumbersome but also comes with an added risk of infection. The use of urea and creatinine to diagnose kidney health is an established practice that translates well into the development of a salivary assay. Thus, saliva is a stepping stone and has the potential to revolutionize the diagnostic protocol for patients with renal diseases.

REFERENCES

[1] Venktapathy R, Govindarajan V, Oza N, Parameswaran S, Dhanasekaran BP, Prashad KV. Salivary creatinine estimation as an alternative to serum creatinine in chronic kidney disease patnties. *IJN*. 2014 (2014), Article ID 742724, 6 pages.

[2] Abdulla HI, Al-Kotany MY, Mahdi KA. Assessment of oral manifestations of patients with renal failure undergoing hemodialysis by serum and salivary biomarkers. *MDJ*. 2012;9(1):118-29.

[3] Narula AS. Chronic kidney disease. The looming threat. *MJAFI*. 2008;64(1):2-3.

[4] Anupama YJ, Uma G. Prevalence of chronic kidney disease among adults in a rural community in South India: Results from the kidney disease screening (KIDS) project. *IJN*. 2014;24(4):214-21.

[5] Thomas R, Kanso A, Sedor JR. Chronic kidney disease and its complications. *Prim Care*. 2008;35(2):1-15.

[6] Gowda S, Desai PB, Kulkarni SS, Hull VV, Math AAK, Vernekar SN. Markers of renal function tests. *N Am J Med Sci*. 2010;2(4):170-73.

[7] Kamal A. Estimation of blood urea (BUN) and serum creatinine level in patients of renal disorder. *IJFALS*. 2014;4(4):199-202.

[8] Suresh G, Ravi Kiran A, Samata Y, Naik P, Kumar V. Analysis of blood and salivary urea levels in patients undergoing haemodialysis and kidney transplant. *J Clin Diagn Res*. 2014;8(7):ZC18-20.

[9] Madalli VB, Basavaraddi SM, Burde K, Horatti P. Saliva- A diagnostic tool. *JDMS*. 2013;11(6):96-99.

[10] Seethalakshmi C, Koteeswaran D, Chiranjeevi V. Correlation of serum and salivary biochemical parameters in end stage renal disease patients undergoing hemodialysis in pre and post- dialysis state. *J Clin Diagn Res*. 2014;8(12):CC12-14.

[11] Schoolwerth A, Engelgau MM, Hostetter TH, Rufo KH, Chianchiano D, McClellan WM, et al., Chronic kidney disease: A public health problem that needs a public health action plan. *PCD*. 2006;3(2):1-6.

[12] Singh AK, Farag YMK, Mittal BV, Subramanian KK, Reddy SRK, Acharya VN, et al., Epidemiology and risk factors of chronic kidney disease in India – Results from SEEK (screening and early evaluation of kidney disease) study. *BMC Nephrol*. 2013;14(114):1-10.

[13] Ramchandran A, Das AK, Joshi SR, Yajnik CS, Shah S, Kumar KMP. Current status of diabetes in India and need for novel therapeutic agents. JAPI. 2010;58:7-9.

[14] Olokoba AB, Obateru OA, Olokoba LB. Type 2 diabetes mellitus: A review of current trends. *OMJ*. 2012;27(4):269-73.

[15] Mittal A, Sathian B, Kumar A, Chandrasekharan N, Sunka A. Diabetes mellitus as a potential risk factor for renal disease among napalese: A hospital based case control study. *NJE*. 2010;1(1):22-25.

[16] Raghupathy A, Kannuri NK, Pant H, Khan H, Oscar HF, Emanuele DA, et al., Hypertension in India: A systematic review and meta-analysis of prevalence, awareness, and control of hypertension. *J. Hypertens*. 2014;32(6):1170-77.

[17] Coresh J, Wei GL, McQuillan G, Brancati FL, Levey AS, Jones C, et al., Prevalence of high blood pressure and elevated serum creatinine level in the United States. *Arch Intern Med*. 2001;161:1207-16.

[18] Schillaci Giuseppe, Reboldi Gianpaolo, Verdecchia P. High-normal serum creatinine concentration is a predictor of cardiovascular risk in essential hypertension. *Arch Intern Med*. 2001;161:886-91.

[19] Wagle TJ. Genderwise comparison of serum creatinine and blood sugar levels in type-2 diabetic patients. *BHJ.* 2010;52(1):64-68.

[20] Shrestha S, Gyawali P, Shrestha R, Poudel B, Sigdel M, Regmi P, et al., Serum urea and creatinine in diabetic and non-diabetic subjects. *JNAMLS.* 2008;9(11):11-12.

[21] Kamal A. Impact of diabetes on renal function parameters. *IJFALS.*2014;4(3):411-416.

[22] Deepa K, Manjunatha GBK, Devi OS, Devaki RN, Nayal B, Prabhu A et al., Serum urea, creatinine in realtion to fasting plasma glucose levels in Type 2 diabetic patients. *IJPBS.* 2011;1(3):279-283.

[23] Rohitash K, Kumar R, Ranjana M, Jairam R. A study on renal function tests and its correlation with blood glucose and EGFR in freshly diagnosed Type-2 diabetes mellitus patients. *SAJB.* 2014;2(10):675-77.

[24] Al-Hamdani IH. Estimation of serum uric acid, urea and creatinine in essential hypertensive patients. *TMJ.* 2010;16(1):152-58.

[25] Yadav R, Bhartiya JP, Verma SK, Nandkeoliar MK. Evaluation of blood urea, creatinine and uric acid as markers of kidney functions in hypertensive patients: a prospective study. *IJBAMR.* 2014;3(2):682-89.

[26] Pooja, Mittal Y. Serum creatinine level in hypertensive patients: A study from Uttarakhand, India. *IJPSR.* 2014;5(7):2955-59.

[27] Tomas I, Marinho JS, Limeres J, Santos MJ, Araujo L, Diz P. Changes in salivary composition in patients with renal failure. *Arch Oral Biol.* 2008;53:528-532.

[28] Ali SP, Gupta J, Nagesh KS, Iyenger AR. Blood urea & salivary urea levels in end stage renal failure. *Ind Med Gaz*. 2013:373-75.

[29] Cardoso EML, Arregger AL, Tumilasci OR, Elbert A, Contreras LN. Assessment of salivary urea as a less invasive alternative to serum determinations. *Scand J Clin Lab Invest.* 2009;69(3):330-34.

[30] Lloyd JE, Broughton A, Selby C. Salivary creatinine assays as a potential screen for renal disease. *Ann Clin Biochem*. 1996;33:428-31.

PARTICULARS OF CONTRIBUTORS:
1. Postgraduate Student, Department of Oral Medicine and Radiology, Hitkarini Dental College and Hospital, Jabalpur, Madhya Pradesh, India.
2. Professor and HOD, Department of Oral Medicine and Radiology, Hitkarini Dental College and Hospital, Jabalpur, Madhya Pradesh, India.
3. Assistant Professor, Department of Preventive and Pediatric Dentisty, King Khalid University, Saudi Arabia.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Divya Pandya,
F-2 Atul Vihar II, SBI Colony Near Hathital Railway Crossing Gorakhpur Jabalpur-482001, Madhya Pradesh, India.
E-mail: divyapandya854@gmail.com

FINANCIAL OR OTHER COMPETING INTERESTS: None.