ORIGINAL RESEARCH ARTICLE

ESTIMATION OF SALIVARY pH, BUFFERING CAPACITY, FLOW RATE, CARIES PREVALENCE AND ORAL MANIFESTATION IN CHRONIC RENAL FAILURE PATIENTS UNDERGOING DIALYSIS

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ABSTRACT

Background: Renal failure is a process that expresses a loss of functional capacity of the nephrons, independently of its etiology. Although acute renal failure is reversible in the majority of cases, chronic renal failure presents a progressive course towards terminal renal failure. Hemodialysis is the most widely used technique leading to systemic alterations, oral complications and variations in the flow and composition of the saliva. The purpose of this study was to estimate salivary pH, buffering capacity, flow rate in chronic renal failure patients undergoing hemodialysis with its oral manifestation and caries prevalence.

Methods: Saliva samples were collected from 40 patients with chronic renal failure undergoing dialysis and 40 healthy subjects after taking the informed consent. Saliva samples were then taken to the lab for processing. Salivary pH, buffering capacity and flow rate was estimated. DMFT was calculated. The statistical analysis was done using SPSS version 23.

Results: A statistically significant rise in salivary pH, buffering capacity with decrease in flow rate was noted in chronic renal failure patients undergoing dialysis compared to controls. Furthermore, decrease in DMFT value was noted in CRF group despite of poor oral hygiene of the patient. We could also observe different oral manifestations in CRF group among which uremic fetor being the commonest.

Conclusions: Our report suggest that saliva is noninvasive tool which act as an adjunct in diagnosing oral lesions and manifestations in CRF patients whose oral hygiene is often neglected with their reluctance in long term dental appointment in the middle of regular hemodialysis schedule.

INTRODUCTION

Chronic renal failure is progressive decline of glomerular filtration rate which ultimately leads to an increase in serum creatinine and blood uric nitrogen level.[1] Uremic patient must receive dialysis or renal transplant to maintain their normal body mechanism. Such treatment may cause systemic and oral changes, complication and alteration in salivary composition and flow rate.[2] Causes of chronic renal failure are hypertension, diabetes mellitus, chronic glomerulonephritis and autoimmune disease. It occurs when glomerular filtration rate is around 5-10 %.[3] Incidence of renal disease is increasing worldwide.[4] Chronic renal failure patients may suffer from number of medical problems along with the changes in oral cavity.[3]

A wide-ranging variety of oral manifestations have been reported in end stage renal disease (ESRD) patients including gingivitis, xerostomia, ammonia-like smell, mucosal pallor, tooth mobility and an increased risk of dental erosion due to frequent regurgitation.[5,6] One of the significant protective factors of saliva is its buffering capacity and flow rate. In comparison to the normal people, chronic renal failure patients in dialysis have periodontal disease and low caries incidence with low salivary pH and buffering capacity.[3]

Despite numerous reports on this matter, it has received little attention. The purpose of this study was to estimate salivary pH, buffering capacity, flow rate, oral manifestation and caries prevalence in chronic renal failure patient undergoing dialysis and to correlate these factors with normal healthy individuals. In this study, an attempt was made to estimate salivary changes and its relationship with caries prevalence in renal failure patient undergoing dialysis.

METHODS

This is a cross-sectional study conducted in Dialysis center of Kantipur Dental College from August 2015 to July 2017. Ethical approval was obtained from the Institutional Review Committee of Kantipur Dental College prior to the study. The study included two groups: first group comprising of 40 individuals with chronic renal failure undergoing dialysis and second group comprising of 40 healthy individuals with no major illness in past.

Sample size was calculated using the reference article by

Kaushik A et al.[4] ,
Mean salivary pH (μ_1) for renal failure patients: 7.24
Standard deviation of pH for chronic renal failure patients (σ_1): 0.25

Mean salivary pH (μ_2) for healthy controls: 6.60

Standard deviation of pH for healthy controls (σ_2) :0.32

$$\sigma = \sigma_1 - \sigma_2/2$$

Calculation of effect size (ES) using formula ES$= \mu_1 - \mu_2/\sigma$ = 2.245

Taking level of significance (α)= 5%

Taking power of the study (1- β) = 90%

Value of Z $_{1-\alpha/2}$ = 1.96

Value of Z $_{1-\beta}$ = 1.282

Applying all the values in the following formula for estimation of sample size:

$$n_i = 2\left(\frac{Z_{1-\alpha/2} + Z_{1-\beta}}{ES}\right)^2$$

The calculated sample size is 5 in each group. Since, the calculated sample size is too small, we followed the assumption of normal distribution of central limit theorem for sampling distribution of mean and planned to take sample size of 30 in each group. Amplifying the sample size by 10% for processing errors and another 10% for non-response errors, the final sample size became 30 + 3+3 = 36.

Thus, we planned to take 40 samples in both the groups i.e. 40 healthy individuals and 40 patients with chronic renal failure undergoing dialysis.

Inclusion and exclusion criteria include known cases of chronic renal failure and individuals suffering from any other systemic disease, with regular history of drugs intake, individual with physical limitation, individuals with any significant oral and soft tissue pathology based on visual examination and un co-operative individual respectively.

After obtaining verbal and written consent from the patients, detail history was taken, and all the information was documented in a proforma. Saliva sample was collected in the morning hours considering the circadian rhythm. For collection of unstimulated saliva each patient was seated comfortably. Subjects who were able to spit were instructed to spit in a sterile plastic container for approximately every 20 seconds for 5 minutes and those individual who were unable to spit, sample was collected by a plastic syringe measuring 5ml.[7] Saliva was collected and taken to biochemistry lab within 2 hours.[8] Samples were collected before meal or at least 2 hours after

meal. During the time of collection, smoking, eating, and talking were prohibited. The data was then transferred to SPSS version 23 for further analysis. The comparison of mean values of continuous variables i.e. salivary pH, buffering capacity, flow rate and DMFT scores between both the groups was done with the help of independent sample t test. The difference of proportions of oral manifestations between the groups was tested with the help of a Chi-square test. The level of significance was set at 5% with the confidence level of 95%.

RESULTS

The present study included total of 80 individuals out of which 40 were clinically diagnosed cases of chronic renal failure undergoing dialysis and 40 were healthy controls. Out of 40 cases 25% (n=10) belonged to the age group 50-59 similarly 25% (n=10) were above 60 years. In the study 17.5% (n=7) cases were between the age group of 20-29 years who suffered from chronic renal failure (Table 1).

Table 1: Comparison of age between the case and control (n=40+40)

Age range	Case (n)	Control (n)
20-29	17.5 (7)	17.5 (7)
30-39	15 (6)	25 (10)
40-49	17.5 (7)	10 (4)
50-59	25 (10)	27.5 (11)
>=60	25 (10)	20 (8)

Regarding the gender distribution, our study comprised of 76.25% (n=61) males and 23.75% (n=19) females in total. There were 82.5% (n=33) of male participant among the case whereas only a small portion of female, 17.5% (n=7) were undergoing hemodialysis.

CRF patient undergoing hemodialysis had various oral manifestations as shown in Table 2 among which 90% (n=36) of the individual complained of uremic fetor and only 32.5% (n=26) had the history of burning tongue. Whereas 75% (n=30) of total cases complained of xerostomia.

Table 2: Comparison of oral manifestation between the case and control (n=40+40)

Oral Manifestation	Case (n)	Control (n)
Uremic fetor	90 (36)	0
Unpleasant taste	42.5 (17)	0
Thirst	50 (20)	5 (2)
Xerostomia	75 (30)	10 (4)
Burning tongue	32.5 (13)	2.5 (1)
Dry fissured lips	52.5 (21)	0
Pale mucosa	40 (16)	5 (2)

One third of the total case, 67% (n=27) in our study gave the positive history of consumption of alcohol and/or tobacco. Among them 40% (n=16) have or had history of alcohol

consumption.

Chi square test was applied to compare the difference in distributions of categorical variables among case and healthy controls. Table 3 shows the comparison between case and control having uremic fetor where in 90% (n=36) of the case while none of the healthy control manifested this symptom. 50% (n=20) of case complained of thirst whereas only 5% (n=2) among the healthy control had feeling of thirst. Similarly, manifestations like xerostomia, burning tongue and dry fissured lips were compared which shared statistically significant difference between the two groups (p<0.001*) (Table 3).

In our study the different salivary parameters were measured in the cases as well as controls (Table 4). The salivary flow rate among cases was 1.73 with SD ± 1.01 ml as compared to 3.89 with SD ± 0.81 among controls and mean buffering capacity of saliva in cases was 4.09 with SD ± 1.13 whereas the buffering capacity in controls was 2.27 with SD ± 0.75. Similarly mean pH of saliva among cases was 7.21 with SD ± 1.29 whereas it was 5.48 with SD ± 1.20 in controls. The comparison of mean difference of flow rate, buffering capacity and pH of saliva between the cases and controls showed statistically significant difference (p<0.001*).

Table 3: Comparison of Oral Manifestations between case and control (n=80)

Oral Manifestation	Response	case	%	control	%	Total	χ^2	p
Uremic fetor	No	4	10.00%	40	100.00%	44	65.455	<0.001*
	Yes	36	90.00%	0		36		
	Total	40	100.00%	40	100.00%	80		
Thirst	No	20	50.00%	38	95.00%	58	20.313	<0.001*
	Yes	20	50.00%	2	5.00%	22		
	Total	40	100.00%	40	100.00%	80		
Xerostomia	No	10	25.00%	36	90.00%	46	34.578	<0.001*
	Yes	30	75.00%	4	10.00%	34		
	Total	40	100.00%	40	100.00%	80		
Burning Tongue	No	27	67.50%	39	97.50%	66	12.468	<0.001*
	Yes	13	32.50%	1	2.50%	14		
	Total	40	100.00%	40	100.00%	80		
Dry fissured Lip	No	19	47.50%	40	100.00%	59	28.475	<0.001*
	Yes	21	52.50%	0		21		
	Total	40	100.00%	40	100.00%	80		
Pale mucosa	No	24	60.00%	38	95.00%	62	14.05	<0.001*
	Yes	16	40.00%	2	5.00%	18		
	Total	40	100.00%	40	100.00%	80		

Statistically significant

Table 4: Comparison of mean salivary parameters between case and control (n=80)

Salivary parameters	Case		Control		t-test	p-value
	Mean	SD	Mean	SD		
Flow rate	1.73	1.01	3.89	0.81	-10.59	<0.001*
Buffering capacity	4.09	1.13	2.27	0.75	8.46	<0.001*
pH level	7.21	1.29	5.48	1.2	6.23	<0.001*

Statistically significant

Table 5 shows comparison of mean decayed teeth among case and control with statistically significant result (p<0.001*). It also highlights the comparison of mean missing and filled teeth which do not showed statistically significant result. Although

there is decrease in salivary flow rate leading to xerostomia and rise in salivary pH, mean number of decayed teeth in case (0.65) is lower than that of the healthy individuals (1.68); which focuses that despite the poor oral health status and increase salivary pH and decrease salivary flow rate hemodialysis patients have low caries prevalence.

Table 5: Comparison of DMFT between case and control (n=80)

DMFT	Case		Control		t-test value	p-value
	Mean	SD	Mean	SD		
Decayed	0.65	0.8	1.68	1.4	-4.01	<0.001*
Missing	0.9	1.01	0.38	0.7	2.7	0.008
Filled	0.5	0.91	0.68	0.83	-0.9	0.37

Statistically significant

DISCUSSION

Renal failure is a process that expresses a loss of functional capacity of the nephrons, independently of its etiology. Although acute renal failure is reversible in the majority of cases, chronic renal failure (CRF) presents a progressive course towards terminal renal failure, even if the cause of the initial nephropathy disappears. When the glomerular filtration rate (GFR) is <15 ml/min (TRF), it is necessary to start hemodialysis or renal replacement therapy to avoid the serious complications which can lead to the death of the patient.[9]

Patients with chronic kidney disease (CKD) often present systemic complications such as anemia, coagulation and platelet function disorders. Some of them manifest oral symptoms and signs. It has been proven that more than 90% of the patient with CKD have soft tissue changes.[1] Besides these soft tissue changes, patient also has increased risk of caries which is considered to be multifactorial disease.[10]

In the present study we observed the mean age of people suffering from CRF was 48.2 ± 16.12 years and more than two-third of the cases were males which highlights the fact that renal failure is prevalent in male population. In a study done by Ghimire et al.[11] majority of patients of CKD were at their late 40s which was consistent with our study. The male preponderance seen in our study is consistent with several other studies and this may be due to more consumption of alcohol and smoking.

Evidence supports a direct, acute nephrotoxic effect of alcohol on the kidney. Chronic use may result in alcohol induced hypertension, indirectly increasing the risk of CKD;[12] supporting this fact, our study also showed more than 40% of our cases gave the history of chronic alcohol consumption along with smoking.

The current study also explored the oral symptoms manifested by group undergoing hemodialysis. We observed seven different oral manifestations. Out of which uremic fetor was present in 90% of the total cases studied. Similarly, 75% suffered from xerostomia and 50% complained of thirst and dry lips. Diminished function of the kidneys results in an increase in the levels of urea in the blood and also in the saliva, where it will turn into ammonia. For this reason, uremic individuals have characteristic halitosis (uremic fetor) which was found in more than two-third of the hemodialyzed patients in our study.[13] Additional possible cause for uremic fetor also includes increase phosphate and protein concentration as well as increase in salivary pH resulting in unpleasant taste which was observed in our study.[14]

Sensation of unpleasant taste was also the major complaint of the individuals undergoing dialysis in our case. Near about half of the study group had the unpleasant taste sensation. According to Kho et al.[15] more than 30 oral signs and symptoms of patients with CKD have been reported. In our study 73.2% subjects showed oral signs and symptoms, and in most cases,

these were dry mouth, taste change and uremic odor. Burning tongue, pale mucosa were also the symptoms in our study. Larato reported that accumulation of ammonia might irritate the oral mucosa, resulting in glossitis and stomatitis and that, oral mucosal changes might be only a phase of a generalized mucosal breakdown. He also mentioned oral bleeding as a result of the use of anticoagulants and quantitative and qualitative changes of platelets in these patients is well known.[16]

Pale mucosa was observed in 40% of the total cases in our study. According to Alamo decrease in salivary secretion occurs as a consequence of liquid intake restrictions, secondary effects of medication mainly hypertensive drugs, atrophy of minor salivary glands and mouth breathing which is associated with loss of taste perception. Sometimes these individuals are affected by anemia mainly due to decrease in the synthesis of erythropoietin which can be clinically observed as paleness in mucosa as well as in skin.[13]

In this study, an attempt to estimate salivary parameters and its relationship with caries prevalence was done. Estimation of mean salivary pH for case with difference in mean pH among case and control group was found to be statistically significant.

Saliva has a pH normal range of 6.2-7.6 with 6.7 being the average pH. Resting pH of mouth does not fall below 6.3. In the oral cavity, the pH is maintained near neutrality (6.7-7.3) by saliva. The saliva contributes to maintenance of the pH by two mechanisms. First, the flow of saliva eliminates carbohydrates that could be metabolized by bacteria and removes acids produced by bacteria. Second, acidity from drinks and foods, as well as from bacterial activity, is neutralized by the buffering activity of saliva.[17]

Increase in the salivary pH is a constant finding in the CRF patients. According to Bots et al.[18] saliva has a crucial role. Changes in the flow of saliva, pH values and biochemical composition are reflected on the oral clinical findings.[18] This rise in salivary pH in CKD can be contributed to a higher concentration of ammonia in saliva due to the hydrolysis of urea by the enzyme urease.[4] Similar study by Bayratktar et al.[19] also showed rise in pH of saliva in patients undergoing dialysis. Several studies claim that higher concentration of ammonia as a result of urea hydrolysis is the only cause for elevated pH.[20]

A study by Kaushik et al.[4] on oral and salivary changes among renal failure patients undergoing hemodialysis shows consistent result with our study. They suggested that elevated buffering capacity is due to elevated phosphate concentration. But in their study, they could not find out significant difference in buffering capacity of stimulated and unstimulated saliva as stimulation itself increases the concentration of bicarbonate leading to higher buffering capacity.

Phosphate values are significantly increased in the dialysis patient. In part at least, this elevation is a reflection of reduced flow rate since salivary phosphate concentration is inversely related to flow rate. Dialysis patients often exhibit a hyper-

phosphatemia, however and this also may be a factor in the elevated salivary level.[21]

Our study shows decrease in salivary flow rate among the group undergoing dialysis resulting in xerostomia. Kaushik et al.[4] in their study also demonstrated significant decrease in flow rate of both stimulated and unstimulated saliva and also observed its contribution to xerostomia.

In the study by Kho et al.[15] mean flow rate of unstimulated whole saliva was significantly lower in the cases than in controls which was consistent with our study. Lower flow rates of both stimulated and unstimulated saliva reflected a higher prevalence of dry mouth in the case group. Similar result was also reported by Bayraktar et al.[19] where salivary flow rate in hemodialysis patient was below the hyposalivation limit (0.8ml/min).

Several reports attributed the reduced salivary flow rate in CKD patients to fluid restriction, dehydration, electrolyte imbalance and possibly the effect of overwhelming infection observed in CKD patients on salivary glands.

Estimating all the parameters and observing the manifestation, this study also correlates salivary parameters with DMFT index. Increase concentration of salivary pH and rise in salivary phosphate would partially contribute to higher buffering capacity of saliva of patients with CKD. These salivary changes can explain the low caries incidence that is reported in these patients despite their poor oral hygiene and high incidence of enamel hypoplasia. As in our study mean decayed teeth in our cases was almost half than of control which was consistent with the findings by Yahya et al.[22] wherein they have concluded that there was significantly greater proportion of cases who were caries free.

Bayraktar also reported a tendency towards lower prevalence of caries in CKD group.[23] Consistent with this study Jaffe et al.[24] examined DMFT index and reported a significant difference in DMFT index between CRF and healthy controls. They also explained the lower prevalence of caries in CKD patients with an increased salivary urea concentration, which split to form ammonia and may raise the pH above the critical level that causes demineralization of dental enamel. It has also been suggested that high level of salivary urea produces anticariogenic effect by inhibiting growth of microorganism and neutralizing acid formed in dental plaque.[24]

Thus, in the present study we have observed a consistent rise in salivary pH and buffering capacity and decrease in salivary flow rate in renal failure patients undergoing dialysis. We also observed decrease in DMFT index in comparison to healthy control group despite of neglected oral hygiene and reduction in salivary flow rate. Critical oral manifestations like uremic fetor, xerostomia and burning tongue could be noted during their treatment procedure.

CONCLUSION

Based on our observation and previous reports, we suggest that estimation of pH, buffering capacity and flow rate of saliva is non-invasive procedure which may prove to be primary adjunctive tool in screening oral lesions in huge mass and spreading awareness regarding the consequences of dialysis in oral mucosa

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