Oral and salivary changes among renal patients undergoing hemodialysis: A cross-sectional study

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ABSTRACT

We wanted to assess oral and salivary changes in end stage renal disease (ESRD) patients undergoing hemodialysis (HD) and to understand the correlation of such changes with renal insufficiency. The cross-sectional study was performed among 100 ESRD patients undergoing HD. Among these, 25 patients were randomly selected to assess the salivary changes and compared with 25 apparently healthy individuals who formed the control group. Total duration of the study was 15 months. Oral malodor, dry mouth, taste change, increased caries incidence, calculus formation, and gingival bleeding were the common oral manifestations. The flow rates of both unstimulated as well as stimulated whole saliva were decreased in the study group. The pH and buffer capacity of unstimulated whole saliva was increased in the study group, but stimulated whole saliva did not show any difference. ESRD patients undergoing HD require special considerations during dental treatment because of the various conditions inherent to the disease, their multiple oral manifestations and the treatment side-effects.

Key words: Hemodialysis, oral manifestations, renal diseases, salivary changes

Introduction

The incidence of renal diseases continues to rise worldwide and as a consequence, increasing number of renal patients will probably require oral healthcare. The oral clinicians need to understand the multiple organ systems that can be affected, the compromised renal clearance, and the adverse side-effects of multiple drugs therapy usually prescribed to these patients.[1] Hence, the present study was performed to assess oral and salivary changes (flow rate, pH, and buffer capacity) in end stage renal disease (ESRD) patients undergoing hemodialysis (HD).

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Materials and Methods

A total of 100 patients with ESRD on HD in M S Ramaiah Group of Hospitals, Bangalore formed the study group [Table 1]. Patients with early stages of kidney diseases not requiring HD and patients with kidney transplantation were not included. Among the 100 study subjects, 25 were randomly selected to assess the salivary changes. Twenty-five healthy individuals without history of any serious illness and who were not under any medication known to affect salivary flow rate formed the control group for salivary changes.

Oral examination

The clinical examination was carried out by the method suggested by Kerr *et al.*,[2] Oral hygiene index simplified was used to assess the clinical levels of debris and calculus, decayed missing filled tooth index (DMFT Index) for prevalence of dental caries, and Periodontal disease index for gingival and periodontal status.

Salivary collection

Salivary samples were collected from the study group and the control group after obtaining the informed consent and the various salivary variables were analyzed.

Salivary flow rate

Samples from patients (a day after dialysis visit) and control group were collected between 8:00 AM and 11:00 AM to minimize effects of the diurnal variability in salivary composition. Samples were collected before meals or at least 2 h after meals. During the time of collection, smoking, eating and talking were prohibited. Unstimulated whole saliva was collected for 10 min by spitting method. Stimulated whole saliva was collected for 5 min from each subject with the aid of standard weight Paraffin-Wax chewing method. The collection was timed, so that flow rate (mL/min) could be measured.[3]

Salivary pH

Following saliva collection, pH was measured immediately using the narrow range pH strip system (Merck). One drop of the collected saliva (unstimulated and stimulated) was placed on the test strip and its color change reflected the pH of saliva.

Salivary buffer capacity

Salivary buffer capacity was measured according to the standard method of Ericsson.[4] The final pH of the solution was assessed in the way similar to determine salivary pH and taken as an expression of the buffer capacity of the salivary samples.

Statistics

Continuous variables such as age, flow rate, pH, and buffer capacity were analyzed using mean and standard deviation. Independent Students' *t* test was used to compare mean values of the salivary parameters between the study and the control group. Level of significance was fixed at 0.5%.

Results

Sixty-five (65%) of the 100 study subjects showed at least one oral manifestation. Oral malodor, dry mouth, and taste change were the common subjective symptoms.

Table 1: Demographic data of the study group included for oral examination

	Number of patients	Mean age (years)	Mean duration of HD (months)
Males	61	44.30±8.03	26.39±12.07
Females	39	44.62±6.82	26.15±10.71
Total	100	44.42±7.53	26.30±11.50

SD: Standard deviation

Increased caries incidence, calculus formation, and gingival bleeding were common objective signs [Graph 1].

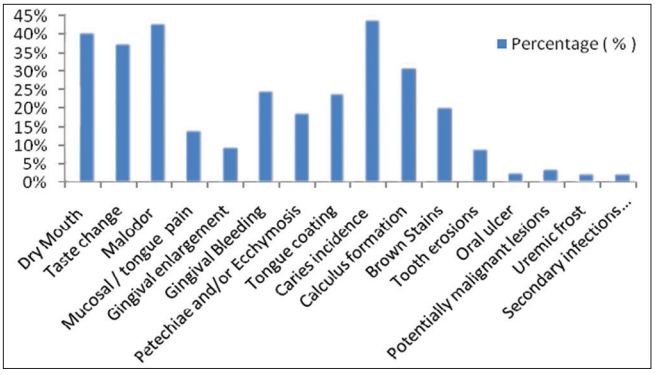
The mean flow rate of unstimulated and stimulated whole saliva was significantly lower in the ESRD patients compared to the controls. The pH and buffer capacity of the unstimulated whole saliva in ESRD patients was significantly higher than the controls. The pH and buffer capacity of the stimulated whole saliva of ESRD patients did not show any significant differences compared to the controls [Table 2].

Discussion

Uremic fetor, an ammoniacal odor typical of uremic patients is caused by high concentration of urea in the saliva which is broken down to ammonia by urease.[5,6] in addition, oral malodor can also result from neglected oral health due to the chronic nature of the illness.

Dry mouth (xerostomia) can be observed in renal patients due to restriction in fluid intake, the side effects of drugs (fundamentally antihypertensive agents), possible salivary gland alteration and oral breathing secondary to lung perfusion problems.[7] The significantly reduced mean flow rate of unstimulated as well as stimulated whole saliva in ESRD patients can be a contributory factor to xerostomia.

ESRD can give rise to altered taste sensation, and some patients may complain of an unpleasant and metallic taste. High levels of urea and dimethyl and trimethyl amines, and low level of zinc might be associated with



Graph 1: Oral manifestations among the study group

Table 2: Changes in unstimulated and stimulated whole saliva from the study and control group

	Number of patients (*n*=25)		Number of controls (*n*=25)		Significance	
	UWS	SWS	UWS	SWS	UWS	SWS
Flow rate (ml/min)	0.31±0.01	0.66±0.02	0.52±0.06	1.16±0.11	*P*<0.001	*P*<0.001
pH	7.24±0.25	7.28±0.25	6.60±0.32	7.24±0.25	*P*<0.001	NS
Buffer capacity	7.02±0.33	7.18±0.35	5.25±0.25	7.16±0.27	*P*<0.001	NS

UWS: Unstimulated whole saliva, SWS: Stimulated whole saliva, NS: Not significant

decreased taste perception in uremic patients.[3] These taste disturbances could also be caused by metabolic disturbances, the use of medication, a diminished number of taste buds, and changes in salivary flow rate and composition. Sour and sweet tastes can be more seriously affected than bitter and salty tastes.[8]

Reduced caries prevalence has been reported in ESRD patients. This is attributed to the protective effect of metabolism of urea in saliva, which inhibits bacterial growth and neutralizes bacterial plaque acids.[9,10] In the current study, DMFT index has revealed an increased prevalence of caries which can be correlated to poor oral hygiene, diminished saliva production, and an increase in the number of cariogenic *Streptococcus mutans*.[11]

Gingival enlargement secondary to drug treatment is one of the most widely documented oral manifestations in patients with renal failure. Such enlargement can be induced by cyclosporine, which is used as immunosuppressant in transplant patients, and/or calcium channel blockers (nifedipine, amlodipine, diltiazem, verapamil) used in pre-dialyzed and dialyzed patients for management of hypertension.[7,12] The condition in turn is aggravated by the deficient oral hygiene [Figure 1].

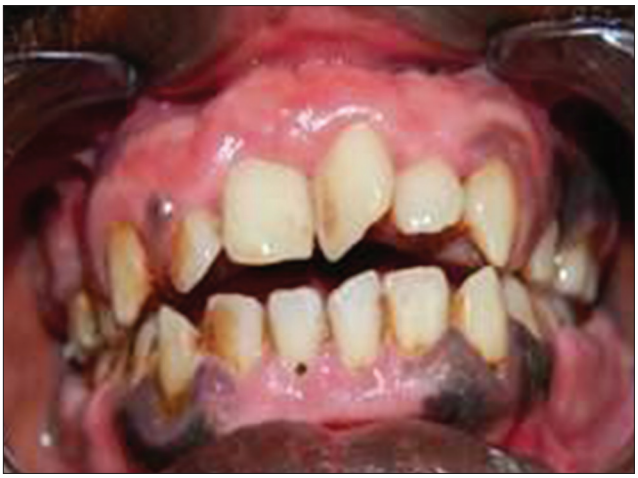


Figure 1: Gingival enlargement following cyclosporine therapy

A great majority of ESRD patients present with dental calculus possibly due to high salivary urea and phosphate levels. Other important risk factors for the development of dental calculus and dark brown staining of teeth are the ingestion of large quantities of calcium carbonate (used as a phosphate binder to maintain phosphorus homeostasis), extrinsic staining secondary to liquid ferrous sulfate therapy given for the management of anemia and deficient oral hygiene.[6,13,14] Diminished cleansing action due to reduced salivary production can also lead to greater incidence of calculus formation [Figure 2].

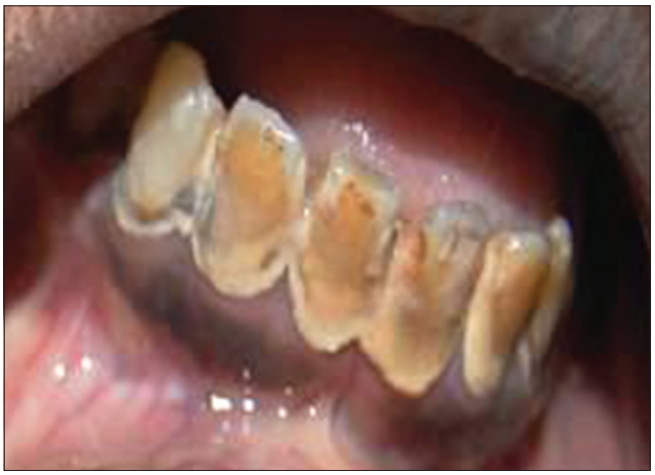


Figure 2: Calculus formation and dark brown staining of teeth

Gingival bleeding, petechiae, and/or ecchymosis can result from platelet dysfunction and the effects of anticoagulants like heparin used to maintain the patency of AV fistulae required for regular vascular access. Uremic toxins and anemia can also play a role [Figure 3].[3,15]

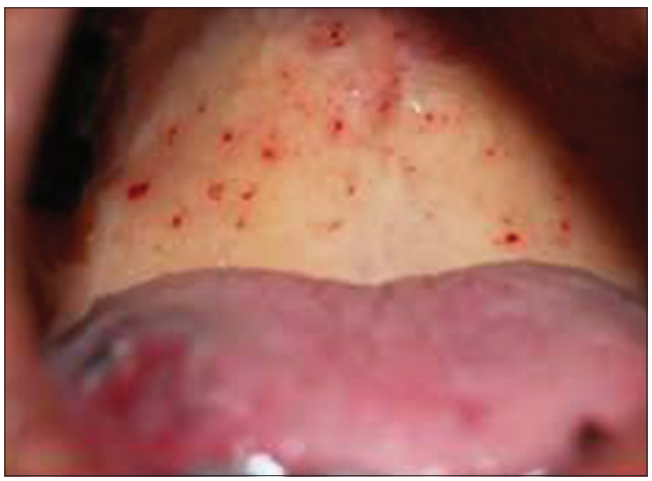


Figure 3: Petechiae present at hard and soft palate

The accumulation of ammonia might irritate the oral mucosa, resulting in mucosal inflammation. A decrease in the salivary mucin coating over the oral mucosa makes it vulnerable to infections, inflammation, and tissue damage leading to tongue and mucosal pain.[3,16]

Uremic frost, an uncommon clinical observation associated to azotemia and uremia may occasionally be present in the renal patients. Uremic frost is a condition when urea and urea derivatives are secreted through the saliva in oral cavity and sweat in skin, which evaporates away and may leave solid uric compounds, resembling a frost [Figure 4].[16,17]

Candidiasis and increased vulnerability to human herpes virus 8 is common among hemodialyzed as well as transplant patients due to longer durations of immunosuppression.[1,18,19] Due to diminished salivary flow, the salivary defense can be compromised in these patients, and a shift in the composition of the oral microflora can occur toward more virulent gram-negative species [Figure 5]. Mucosal lesions, particularly white lesions have been reported in ESRD patients. Common observations are drug induced lichenoid lesions, an increased susceptibility to epithelial dysplasia and carcinoma of the lip. The increased risk of malignization in ESRD patients probably reflects the effects of iatrogenic immune suppression [Figure 6].[1,17,18]

The lower flow rates of both unstimulated and stimulated whole saliva can be attributed to direct uremic involvement of the salivary glands leading to decreased parenchymatous and excretory functions, and as a result of dehydration due to restriction in fluid intake. Acute stress levels in these patients may also possibly reduce the salivary flow rate.[3,19]

The higher pH of unstimulated whole saliva in ESRD patients can be contributed to a higher concentration of ammonia in saliva due to the hydrolysis of urea by the enzyme urease.[20] pH of stimulated whole saliva does not reveal any significant difference because sodium and bicarbonate concentrations increase with increased flow rates, resulting in a higher salivary pH. This effect might mask the changes that are due to the disease condition.[21]

The higher buffer capacity of unstimulated whole saliva in ESRD patients can be correlated to the elevated salivary phosphate concentration.[3,20] No significant difference is observed in buffer capacity of stimulated whole saliva as stimulation itself increases concentration of bicarbonates in parotid saliva, leading to a higher buffer capacity.[21,22]

Conclusion

ESRD patients undergoing HD show apparent oral and salivary changes. These patients require special considerations in relation to dental treatment, not only because of the conditions inherent to the disease and its multiple oral manifestations, but also because of the side-effects and characteristics of the treatments they receive. The untreated dental infection in immunosuppressed renal patients can potentially contribute to morbidity and future transplant rejection. Thus, there is a need for detailed assessment and provision of good oral care following the diagnosis of ESRD.

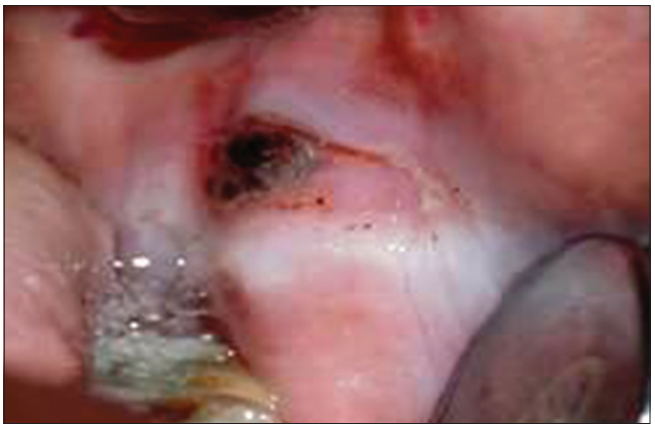


Figure 4: Uremic frost involving left buccal mucosa

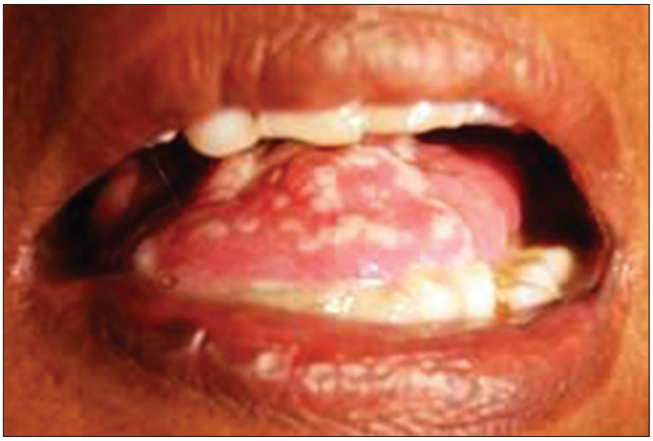


Figure 5: Psuedomembranous candidiasis affecting tongue

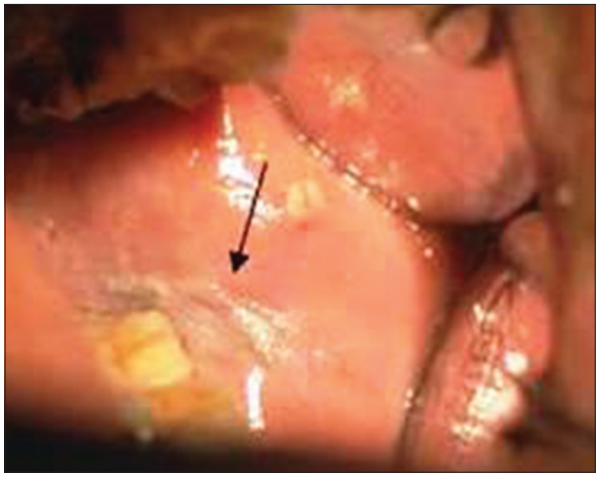


Figure 6: Homogenous leukolplakia involving left buccal mucosa (Smoking related)

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