

Oral Manifestations in Chronic Renal Failure Patients Attending Two Hospitals in North Karnataka, India

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Abstract

Aim: To determine the nature, incidence, and severity of oral manifestations that occur in chronic renal failure (CRF) in patients attending two hospitals in North Karnataka, in comparison with healthy, disease-free controls.

Methods: The study was carried out with 200 individuals (100 CRF patients and 100 controls). The case group was randomly selected from a population of CRF patients whose glomerular filtration rate (GFR) values were between 15-30 mL/min; the control group was selected in the same age group with normal GFR and was apparently disease free. The patients were asked about dry mouth, taste and halitosis, and mucosal pain, and were examined for oral changes such as tongue coating, pallor, ulceration and enamel hypoplasia. The results obtained from the study were then compared with various other similar studies.

Results: The most common oral findings in the CRF patients were dry mouth (91%), pallor (87%), altered taste (42%), and halitosis (34%). CRF patients showed significantly more oral changes than those in the control group. These changes could be attributed to metabolic disturbances due to renal failure.

Conclusion: In the patients studied, the impact of CRF on the oral cavity was evidenced by significant oral changes, which pointed to an inter-relationship between oral health and CRF. Further studies are required to relate the extent of such changes with disease progression.

Key Words: Chronic Renal Failure, Dry Mouth, Haemodialysis, Oral Health, Oral Manifestations, Pallor

Introduction

Mankind is affected by several diseases with diverse aetiological factors. Irrespective of the organ system involved, changes frequently occur in the oral cavity reflecting disease elsewhere in the body. Chronic renal failure (CRF) is an irreversible deterioration in renal function, which classically develops over a period of years due to reduction in functional nephrons [1]. It constitutes a low glomerular filtration rate persisting over a period of three or more months. The incidence of CRF is known to be increasing globally [2]. Improper kidney function is reflected in every organ system of body, showing various signs and symptoms. About 90% of renal failure patients have oral symptoms,

which may be consequences of dialysis and renal transplantation and aetiological factors causing chronic renal failure [3].

CRF patients are more susceptible to infection because of general debilitation and depression of their immunologic response [4]. Both oral diseases and dental manipulation create bacteraemias that may lead to significant morbidity and potential mortality in patients with renal failure who are receiving dialysis. Periodontal diseases, pulpal pathology, oral ulcers, and dental procedures all lead to microorganisms in the blood stream.

Thorough knowledge of the oral changes in CRF patients is essential to diagnose the underlying disease and to take precautions to avoid the bacteraemia and prevent complications.

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Aim

To determine the nature, incidence, and severity of oral manifestations that occur in chronic renal failure (CRF) in patients attending two hospitals in North Karnataka, in comparison with healthy, disease-free controls.

Methods

This study was designed as an observational, case control, cross-sectional study. Ethical clearance to undertake the study was obtained from the Institutional Ethical Committee of the two hospitals concerned. The study population was randomly selected from the CRF patients regularly attending the nephrology department of two medical colleges in north Karnataka, India. Regardless of the aetiology of the condition, a total of 100 patients (77 male and 23 female) with CRF were recruited. They were from 18 years to 78 years of age and were patients with a glomerular filtration rate (GFR) of between 15-30 mL/min for more than three months. The following patients were excluded from the study: those suffering from any systemic disease that could affect their GFR and/or the oral health status and those who were receiving any type of drugs that could affect their oral health status.

The control group population was recruited from the Department of Oral Medicine and

Radiology, PMNM Dental College and Hospital, Bagalkot, India, from systemically healthy people, with no history of kidney disease, or any other chronic debilitating illness, or habit of smoking or drinking, and/or not receiving any medication that could affect oral health, but who were seeking treatment due to dental problems. This group matched exactly the test group such that it comprised 100 individuals, of whom 77 were male and 23 were female, and were aged 18 years to 78 years. The study was carried out over a six-month period. The demographic data of individuals who took part in the study are shown in *Table 1*.

All the examinations were carried out by one author (oral medicine specialist). Before recording the clinical parameters, the examiner and another author, who is a specialist in oral pathology, calibrated the clinical examination. The examiner could not be "blind" to the subjects' general systemic condition, because they were examined in a hospital. On the other hand, the examiner was "blind" to the subgroup (type) of renal failure from which each test group patient suffered.

Patients were asked about dry mouth, taste and halitosis, mucosal pain, bleeding tendencies, burning sensation, and were examined for oral changes such as tongue coating, pallor, ulceration, red and/or white lesion, and enamel hypoplasia. Information relating to the blood chemistry of each

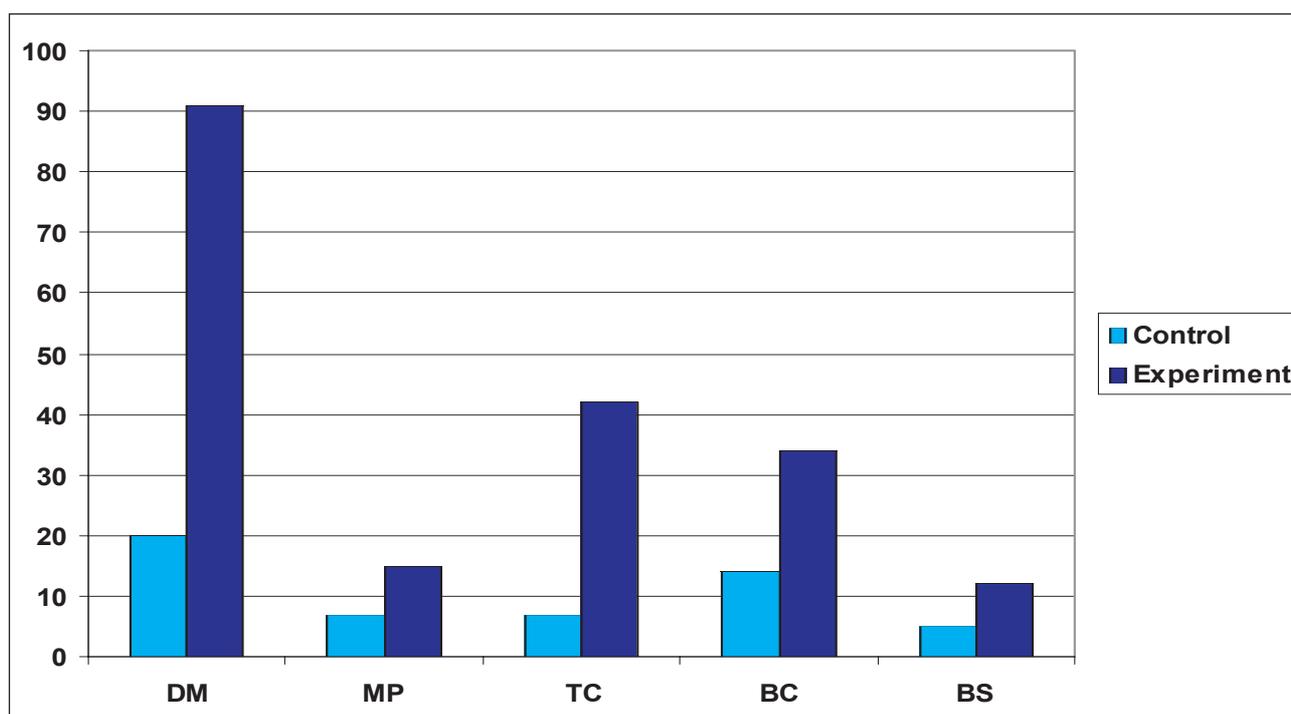


Figure 1. Percentage distribution of subjects by various symptoms present.

Table 1. Demographic data of individuals who participated in the study

		Study group	Control group
No of individuals (n)		100	100
Gender	Male	77	77
	Female	23	23
Age range (years)		18-78	18-78
Mean \pm SD (years)		48.02 \pm 15.15	49.49 \pm 16.45
Smoker		0	0
Alcoholic		0	0
CRF		100	0

patient of study group was obtained from the patient's records. A standardised pro forma was used and all the relevant information for each patient was recorded after informed consent.

For patient convenience, all examinations were done at the bedside with simple instruments. Because all CRF patients were examined in their beds, it was not feasible to examine their periodontal tissues with a periodontal probe or to take radiographs of their teeth. This severely limited any assessment of periodontal status and dental caries, and these diseases were not recorded.

Statistical analysis

The null hypothesis was that there would be no difference in the frequency of oral changes between the study (CRF) and control (healthy) groups.

A statistical software program (Statistical

Package for the Social Sciences; SPSS Inc, Chicago, USA) was used for statistical analysis. Chi-square analysis was used to examine the significance of the differences in means and distribution of categorical variables between groups. The level of significance was set at $P < 0.05$.

Results

Symptoms

Dry mouth was present in 91% of patients in the study group and 20% of patients in the control group ($P < 0.00001$, which was highly significant). Mucosal pain was present in 15% of patients in the study group and 2% of patients in the control group ($P < 0.001$, which was highly significant). Altered taste sensation was present in 42% of patients in the study group and 7% of patients in the control group ($P < 0.0001$, which was highly significant), while halitosis was present in 34% of patients in the study group and 14% of patients in the control group ($P < 0.001$, which was highly significant). An oral burning sensation was present in 12% of patients in the study group and 5% of patients in the control group ($P < 0.08$, which was not statistically significant) (Table 2). There were no statistically significant differences between the study and the control groups for nasal bleeding or loss of appetite (Table 2 and Figure 1).

Altogether in the study group, 91% had dry mouth, 42% had taste change, 34% had halitosis, 15% had mucosal pain, 12% had burning sensation and 3% had other symptoms (Figure 1).

Table 2. Distribution of various symptoms in control and study group

Symptoms		Study group (100)	Control group (100)	Statistical analysis
Dry mouth	Present	91	20	Chi-square = 102.0550, df=1, $P < 0.0001$, S
	Absent	9	80	
Mucosal pain	Present	15	2	Chi-square = 10.8650, df=1, $P < 0.001$, S
	Absent	85	98	
Taste change	Present	42	7	Chi-square = 33.1130, df=1, $P < 0.0001$, S
	Absent	58	93	
Halitosis	Present	34	14	Chi-square = 10.9650, df=1, $P < 0.001$, S
	Absent	66	86	
Burning sensation	Present	12	5	Chi-square = 3.1500, df=1, $P < 0.08$, NS
	Absent	88	95	
Other	Nasal bleeding	1	0	Chi-square = 1.0204, df=2, $P > 0.6$, NS
	Loss of appetite	2	1	
	Total present	3	1	
	Total absent	97	99	

S = significant, NS = non significant

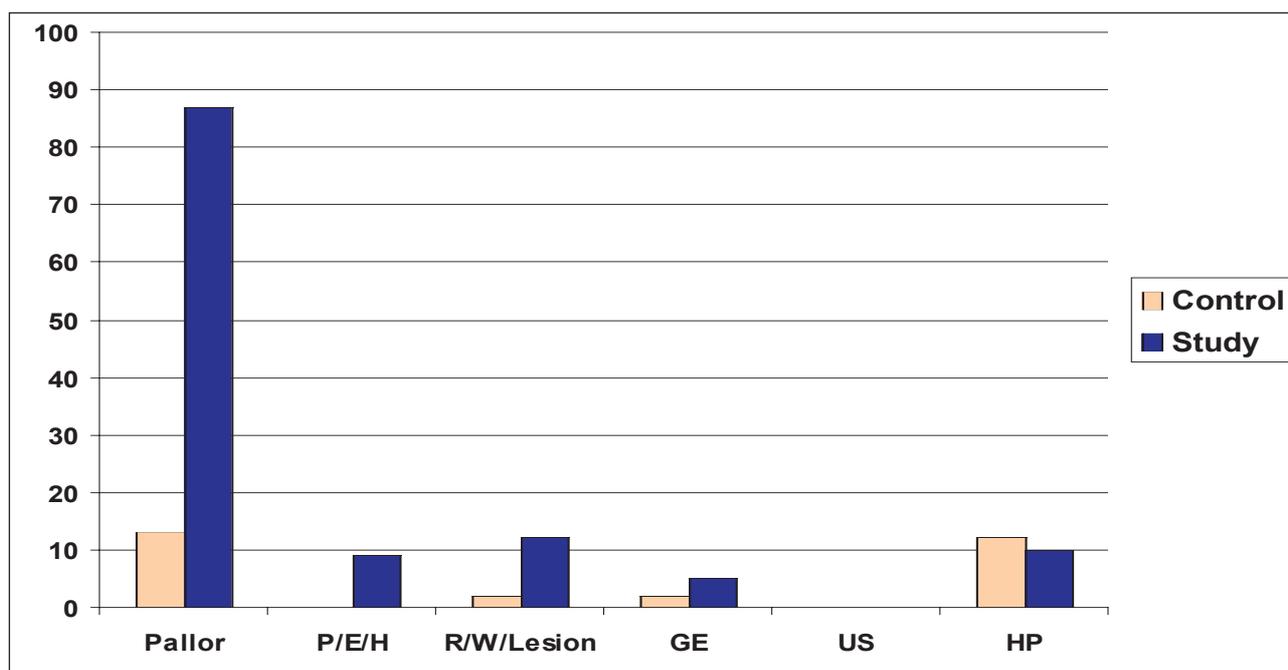


Figure 2. Percentage distribution of subjects by various signs present.

(Key: P/E/H = petechiae/ecchymosis/haematoma, R/W/Lesion = red/white lesions, GE = gingival enlargement, US = uraemic stomatitis, HP = hypoplasia)

Table 3. Distribution of various signs in control and study group

Signs		Study group (100)	Control group (100)	Statistical analysis
Pallor	Present	87	13	Chi-square = 109.5200, df=1, $P < 0.00001$, S
	Absent	13	87	
Petechiae/ Ecchymosis/ Haematoma	Present	9	0	Chi-square = 9.4240, df=2, $P > 0.02$, S
	Absent	99	100	
Red/white lesion	Present	12	2	Chi-square = 8.8230, df=3, $P > 0.03$, S
	Absent	88	98	
Enamel hypoplasia	Present	10	12	Chi-square = 0.2060, df=1, $P > 0.6$, NS
	Absent	90	88	

S = significant, NS = non significant

Signs

Mucosal pallor was seen in 87% of patients in the study group and 13% of patients in the control group ($P < 0.00001$, which was statistically highly significant). The distribution of petechiae, ecchymosis and haematoma in the study and control group was as follows. The petechiae were present in 8% of patients and ecchymosis was present in 1% of patients in the study group and not found in the control group ($P > 0.02$, which was statistically significant). Intra-oral ulceration was seen in about 6% of CRF patients, but none of the control group patients had ulceration. No haematoma was seen in either the study or the control group. In the study group, red lesions were present in 6% of patients, white lesions were present in 6% of patients, and both red and white lesions were present in one

patient's mouth, whereas in the control group, no patient had red lesions but 2% patients had white lesions ($P > 0.03$, which was statistically significant).

The percentage distribution of various signs in the study and control group are shown in *Figure 2*. In the study group, 87% of patients had pallor, 9% of patients had petechiae and ecchymosis, and 12% of patients had red and white lesion. In the control group, 13% of patients had pallor, 2% of patients had red and white lesions, and 12% of patients had enamel hypoplasia.

Discussion

More than 30 oral signs and symptoms in patients with chronic renal failure have been reported, some of which commonly seen are calculus, high urea

concentration in saliva, ammonia-like smell, xerostomia, oral bleeding, stomatitis, pale gingivae, drug-induced gingival hyperplasia, loss of lamina dura, maxillary and mandibular radiolucent lesions, abnormal bone remodelling after extraction, enamel hypoplasia, delayed tooth eruption pattern, low caries prevalence, dental erosion, sensitivity to percussion and mastication, tooth mobility and malocclusion [5,6]. In the present study, all 100 CRF patients showed changes in the oral cavity, some of them being a cause of the disease itself and others resulting from the treatment of the pathology [3]. Dry mouth (91%), pallor (87%), taste change (42%), and halitosis (34%) were some of the common findings. Several reports of gingival haemorrhage, change of taste acuity, and dry mouth in CRF patients have been presented in the literature [5,7,8]. The present study supports the previous findings of these oral changes in CRF patients to a lesser or greater extent.

In the present study, statistically highly significant values were obtained when the occurrence of dry mouth was compared between the CRF (91%) and control group (20%). A comparatively lower percentage of dry mouth was found in previous studies [5,9], which reported 32.9% and 56% respectively in CRF patients. Some authors suggest possible reasons for this finding are as a result of a glandular involvement (atrophy of minor salivary glands' parenchyma), chemical inflammation, decrease in salivary secretion (as a consequence of liquid intake restrictions), secondary effects of medication (mainly anti-hypertensives), and mouth breathing. This manifestation is associated with the loss of taste perception [3].

In this study, mucosal pallor was one of the most common oral findings and was seen in 87% of CRF patients. Its occurrence was statistically significant when compared to the control group (13%). This observation has also been reported by DeRossi and Glick (1996) [3]. Pallor is seen in the oral mucosa secondary to anaemia in CRF patients, which may occur mainly due to decreased production of erythropoietin by the kidneys, renal loss of red blood cells, marrow fibrosis, and increased red cell fragility with subsequent early destruction [10].

About 34% of study group patients complained of halitosis, which was in the form of ureniferous odour, compared to 14% in the control group. A statistically significant difference was noted between these two groups. Our result was in accordance with the findings of a previous study [5],

which reported halitosis in 34% of CRF patients, but was inconsistent with the results of another study [11], which reported halitosis in 24% of CRF patients. Most of the CRF patients had taste-sensitive disturbances, such as altered taste sensations (especially for sweet and acid flavours). This may be due to the high levels of urea or the presence of dimethyl- and trimethyl-amines, or low zinc levels (due to the malabsorption derived from gastrointestinal disorders). This uraemic fetor, an ammoniacal odour, is caused by a high concentration of urea in saliva, which is broken down into ammonia [12]. The diminished function of the kidneys results in an increase in the levels of urea in the blood and also in the saliva, where it turns into ammonia. For this reason, uraemic individuals have a characteristic halitosis. This halitosis is related to another manifestation: the perception of an unpleasant, metallic taste. Interestingly, in the present study significant alteration in taste was noted in patients with CRF (42%) when compared with the control group (7%) whereas previous studies have reported taste changes in 31% [11] and 31.7% [5] of CRF patients. Apart from urea, other factors that may be implicated are the increase in the concentration of phosphates and proteins and changes in the pH of saliva [7,13].

In the present study, petechiae and/or ecchymosis were seen in 9% of CRF patients but in none in the control group. A statistically significant difference was noted between these two groups. This finding was similar to that of a previous study [5] that found petechiae and ecchymosis in 12.2% of CRF patients. These findings may reflect the underlying increased capillary fragility, decreased platelet adhesion, increased prostacyclin activity, decreased availability of platelet factor 3 and renal anaemia (secondary to deficient erythropoiesis) and relate to dialysis, which diminishes platelet count due to mechanical damage and heparin anticoagulation during this process. For this reason, it can be concluded that haemodialysis predisposes to ecchymosis, petechiae and haemorrhage in the oral mucosa [3,5,14,15].

Uraemic stomatitis is an oral complication of unknown aetiology and it is relatively uncommon [14], usually seen in patients with an end stage or untreated renal disease [3,15,16]. Clinically, it is characterised by the presence of erythematous lesions, which are localised or generalised. These lesions are covered by pseudo-membranous exudates that can be removed, leaving an intact or

ulcerated mucosa [7]. As there are no histological pathognomonic signs of this manifestation, the definitive diagnosis is made by combining clinical findings and excluding other diseases with the histopathology [14]. It does not require a specific treatment and an involution will usually occur after uraemia is restored [3]. In order to assist lesion healing, 10% hydrogen peroxide gargles (1:1 in water), four times a day, can be recommended [7].

The occurrence of mucosal pain was seen in 15% of CRF patients, which was significantly higher than in the control group (2%). This finding was fairly similar to that of a previous study which reported that 12.2% of CRF patients had mucosal pain [5]. This problem may be due to irritation of the oral mucosa due to accumulation of ammonia leading to stomatitis and glossitis [16].

In the current study, intra-oral ulceration was seen in about 6% of CRF patients, but none of control group patients had ulceration. This finding was similar to that of another study [9], which reported ulceration in 6% of CRF patients, but differed from the findings of two other studies which reported ulcers in 1% [11] and 1.2% [5] of CRF patients. The rarity of uraemic stomatitis and intra-oral ulceration in the present study may be attributed to the proper medical care given to the patients.

A previous study [17] in which the oral mucosa of individuals with chronic renal failure was assessed reported several mucosal lesions, uraemic stomatitis and *Candida* infections in 37% of those patients who were examined. In the current study, white lesions were seen in 5% of CRF patients and in 2% of the control group. These were lower percentages than those reported in a previous study, which found white lesions in 11% of CRF patients [11]. The white lesions in the current study were lichen planus-like lesions, which may be developed secondary to the medications taken by patients. Also in the current study, only one CRF patient showed asymptomatic enlargement of left submandibular gland. Salivary gland enlargement can be an occasional complication for CRF patients. A previous study [18] described a CRF patient with enlarged submaxillary salivary gland, which led to a massive neck swelling. Various authors have suggested that there will be involvement of salivary glands in patients with chronic renal failure due to direct gland involvement, chemical inflammation, and dehydration [3,19,20].

In the present study, enamel hypoplasia was seen to be slightly more common in the control

group (12%) when compared to the study group (10%). This was perhaps a little surprising as it has been suggested that if uraemia is present during the development of dentition, it results in teeth with enamel hypoplasia and brownish discoloration [21]. Thus it might have been expected that more CRF than control group patients would have had these problems.

The early evaluation of the oral health status of renal patients is essential to eliminate potential infection foci from the oral cavity [22]. The need for prophylactic antibiotic therapy before operative dental procedures to prevent local or distant infection, the patient's ability to tolerate dental treatment, the coagulation profile, and the severity of cardiac arrhythmias should also be assessed [23].

In summary, in the current study in almost every CRF patient, changes to the oral soft tissues were present and were a potential source of active infection in these medically compromised individuals and, as such, potentially contribute to morbidity and mortality. Thus, there is need for dental practitioners to be aware of distinctive oral characteristics related to individuals with CRF. Findings from the present study may aid clinicians' understanding and, therefore, early identification of oral manifestations in individuals with CRF. Maintenance of ideal oral health could have a positive effect on this high-risk group of patients. Because the CRF patients were in bed, this study was limited to an investigation of the oral soft tissues. Dental caries and periodontal health were not assessed. It would be desirable to assess these aspects in a future study.

Conclusions

In the patients studied, the impact of CRF on the oral cavity was evidenced by significant changes to the soft tissues, which pointed to an inter-relationship between oral health and CRF. Further studies are required to relate the extent of such changes to disease progression.

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Contributions of each author

- SP designed the study.
- SK assisted in data collection.
- BD compiled the clinical data.
- FR carried out editing of the manuscript.

- SK coordinated all aspects of this study and assisted in proof reading.

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Statement of conflict of interest

As far as the authors are aware, there is no conflict of interests.