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PREVALENCE OF ORAL LESIONS AND SALIVARY CHANGES AMONG RENAL PATIENTS UNDERGOING HEMODIALYSIS IN A SAMPLE OF EGYPTIAN POPULATION CROSS- SECTIONAL STUDY

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PREVALENCE OF ORAL LESIONS AND SALIVARY CHANGES AMONG RENAL PATIENTS UNDERGOING HEMODIALYSIS IN A SAMPLE OF EGYPTIAN POPULATION CROSS- SECTIONAL STUDY

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ABSTRACT

Chronic kidney failure (CRF) is becoming a major public health problem worldwide particularly in developed countries with a higher prevalence of the renal disease. Hemodialysis is the most widely used treatment of nephropathy. Both the disease and the treatment could influence the patient's oral status as well as alterations in salivary flow and salivary pH. There are guidelines for oral health care in patients with systemic diseases; additionally, a significant improvement in the underlying systemic diseases has been reported following treatment of the associated oral lesions

Materials and Methods: 114 patients of each gender with age vary from 30 to 60 years diagnosed with end-stage renal disease undergoing hemodialysis from 6 months up to 2 years were involved in this study from the Nephrology department at Benha University. Patients with a history of any serious sickness as malignancy or who undergo kidney transplants or those that take medication that would cause oral manifestations and smokers were excluded in our study. Oral examinations were done according to the modified WHO oral health survey 2013 criteria. Saliva was collected to measure the rate of flow and pH.

Results: Oral changes were present in all 114 (100%) CRF patients. Chronic periodontitis was the most frequently seen disease in (81.6%) CRF patients. Alternative findings were xerostomia, burning mouth, uremic breath, petechial lesions, and pallor. In our study, we found an association between xerostomia and salivary flow rate. We also found that patients with lip pigmentation showed statistically significantly low mean blood urea levels.

Keywords: renal patients, oral findings, salivary flow, hemodialysis

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INTRODUCTION

As technology and medicine advances, oral health care professionals have to attain a full approach to the management of patients with complex medical problems. Amongst all the systemic disorders, diseases of the renal system pose a chief cause of morbidity and mortality globally as the kidneys are vital organs for maintaining a stable internal environment ***(Greenberg et al., 2008).***

Chronic renal failure (CRF) is a process that expresses a loss of functional capacity of the nephrons, independently of its etiology and has the usual irreversible and progressive nature, which leads to end-stage renal disease (ESRD). The most widely used technique to combat renal failure is either hemodialysis or transplantation. ***(Abdallah et al., 2012; Shetty et al., 2018).***

Oral health status is of interest from both a medical and dental point of view as patients with CRF, especially who undergo dialysis or renal transplants are susceptible to several infections, because of the depression of the immune functions and masking of the classical signs of inflammation and infection**.** Chronic Renal failure can give rise to a large spectrum of oral manifestations, affecting the hard or soft tissues of the mouth ***(Borawski et al., 2007; Kuravatti, et al., 2016).***

In developed countries, inadequate attention has been given to oral health care needs in this group of patients which has further worsened the prognosis of the underlying disease. Realizing the relation between oral health and general health has been widely acknowledged during the past two decades, and evidence backing up a link between oral and general health is rapidly growing. Intervention studies were also found to institute the link between dental treatments including its impact on such medical conditions; this is an indicator of the significance of oral health care in the management of systemic diseases ***(Peter et al., 2012; YuYH et al., 2015).***

Saliva is known to play an important role in maintaining oral health as the saliva sample represents a revolution in diagnostic and therapeutic monitoring strategies in CRF patients **(*Blicharz et al., 2008).***

Many alterations happen during hemodialysis and this would have an effect on the flow rate and chemical composition of saliva **.**In addition to changes in the composition of the saliva and the rate of flow of saliva which in the broader sense can result in xerostomia, bad breath, changes in the oral mucosa like increased tongue coating, mucosal petechiae, ecchymosis, oral ulceration and high incidence of periodontitis. Also abnormal pigmentation has been reported in uremic patients ***(Proctor et al., 2005; Khanum et al., 2017).***

Furthermore, a consultation is needed for the CRF patients with the nephrologist to identify the stage of the disease, the drugs prescribed, and the homeostasis state of these patients ***(Martí Alamo et al., 2011).***

In Egypt, the prevalence of dialysis patients is presumed to be increasing ***(Buiten et al., 2014).*** So it is necessary to have a thorough knowledge of oral manifestations in hemodialysis patients to take necessary precautions. ESRD patients on hemodialysis treatment need special attention during dental treatment. The present study aimed to estimate the prevalence of the oral lesions and salivary changes as a primary objective and correlate the blood urea, salivary pH and salivary flow rate to the oral diseases as a secondary objective.

METHODOLOGY:

A cross-sectional study was done on 114 patients with ESRD from the outpatient clinic of the Nephrology department at the Faculty of Medicine, Benha University. Both gender with age range from 30 t0 60 years were selected while patients with a history of any serious sickness as malignancy or who undergo kidney transplants or those that take

medication that would cause oral manifestations as steroids and smokers were excluded in our study .The proposal was reviewed by the faculty of Dentistry, Ain Shams University Research Ethics Committee **(FDASU-REC).** Salivary and blood samples have not been used for any other purposes and individual patient's results have been kept confidential. Patients who met the eligibility criteria were subjected to comprehensive oral assessment using a designed chart adapted from the World Health Organization oral health assessment form for adults, 2013 and scored ***(OHS WHO 2013).*** The edentulous patients were asked to remove their denture(s) (if any) to examine the underlying tissues more accurately. Data was collected through a structured questionnaire and oral examination.

The form included mainly history taking (Per-sonal history, demographic data, medical and drug history). Extraoral examination included (general appraisal, skin, eyes, face cervical lymph nodes and TMJ examination). Intraoral examination was done using 2 plain mouth mirrors, explorer under artifi-cial light. Oral mucosal changes were divided into two main categories: Normal variations and patho-logical changes. The lesions, in turn, were catego-rized into six subgroups: (White lesions, mixed red and white lesions, vesicular ulcerative, ulcerative, exophytic and pigmented lesions). All the oral le-sions that were found were recorded then types and distribution and frequencies were calculated.

Fig. (1): Pseudomembranous candidiasis.

Fig. (2): Erythema multiforme.

The Tongue Coating Index (TCI) used to evaluate tongue-coating status: ***(Shimizu et al., 2007)*** recorded as: **Score 0:** Coating of the tongue not apparent. **Score 1**: coating of the tongue thin, papillae is apparent. **Score 2**: coating of the tongue very thick, papillae are not apparent.

Salivary flow rate: Samples from patients (a day of dialysis visit) were collected by the spitting method ***(Navazesh and Kumar, 2008).*** The collection was timed, so that the flow rate (mL/5min) could be measured and evaluated ***(Shetty et al., 2018).***

Salivary pH was measured immediately using the narrow range pH strip system (universal indicator paper).

Blood urea was measured by taking a (2.5 ml) of blood from the patient on the same day of dialysis.

RESULTS

Oral manifestations:

Forty subjects (35.1%) had altered taste sensation, while Thirty-seven subjects (32.5%) had burning mouth. Xerostomia was detected in Seventy-nine subjects (69.3%), Uremic breath was smelled in Fifty-two subjects (45.6%). Forty-four subjects (38.6%) had petechial lesions. Lip pigmentation was seen in Thirty-six subjects (31.6%) while Twenty-eight subjects (24.6%) had intra-oral pigmentation.

Distribution for periodontal status is presented in Table (1). The most frequent periodontal condition was chronic periodontitis (81.6%) followed by gingivitis (12.3%). Seven subjects (6.1%) were completely edentulous.

TABLE (1) Frequencies (n) and percentages (%) for periodontal status of the study participants (n = 114)

Periodontal status	N	%
Chronic periodontitis	93/114	81.6
Gingivitis	14/114	12.3
Completely edentulous	7/114	6.1

Twenty-four subjects (21.1%) had normal tongue coating; thirty subjects (26.3%) had decreased tongue coating while sixty subjects (52.6%) had increased tongue coating. Keratosis was detected in seven subjects (6.1%) keratosis.

Candida infection was present in seven subjects (6.1%) Figure (1). Eighty-seven subjects (76.3%) had pallor although eighteen subjects (15.8%) had other manifestations. Distribution for these manifestations is presented in Table (2) and Figure (2). The most frequent other manifestation was fissured tongue, hairy tongue and uremic frost (1.8% for each manifestation).

Saliva assessment: The mean (SD) values for pH were 7 (0.8) with a minimum of 6 and a maximum of 9. While The mean (SD) values for salivary flow rate were 1.7 (1.2) mL/5min with a minimum of 0.1 and a maximum of 5 mL/5min.

Blood urea (mg/dL): The mean (SD) values for blood urea were 141 (40.9) mg/dL with a minimum of 59 and a maximum of 271 mg/dL.

There was no statistically significant correlation between blood urea, salivary pH, salivary flow rate, dialysis duration, age , and Hemoglobin level but there was a statistically significant correlation btween salivary pH and salivary flow rate (Correlation coefficient = 0.284, *P*-value = 0.002), An increase in salivary pH is associated with an increase in salivary flow rate and vice versa.

TABLE (2) Distrubution of Oral menifestation

Other manifestations	N	%
Fissured tongue	2/114	1.8
Hairy tongue	2/114	1.8
Uremic frost	2/114	1.8
Angular cheilitis	1/114	0.9
Erosive Lichen Planus	1/114	0.9
Erythema multiforme	1/114	0.9
Geographic tongue	1/114	0.9
Herpes Labialis	1/114	0.9
Tongue ulcer	1/114	0.9
Fissured lower lip	1/114	0.9
Palatal papillary swelling	1/114	0.9
Ulcer at hard palate	1/114	0.9
Speckled Leukoplakia	1/114	0.9
Traumatic ulcer	1/114	0.9
No other manifestations	96/114	84.2

Association between blood urea level and oral manifestations:

Subjects with lip pigmentation showed statistically significantly lower mean blood urea levels than normal subjects (*P*-value = 0.004, Effect size = 0.592) as shown in Figure (3) .There was no statistically significant difference between mean blood urea levels in subjects with and without altered taste sensation (*P*-value = 0.908, Effect size = 0.022), burning mouth (*P*-value = 0.236, Effect size = 0.238), xerostomia (*P*-value = 0.085, Effect size = 0.353), uremic breath (*P*-value = 0.105, Effect size = 0.308), intra-oral pigmentation (*P*-value = 0.995, Effect size = 0.000), keratosis

(*P*-value = 0.670, Effect size = 0.166), candida infection (*P*-value = 0.655, Effect size = 0.176) and pallor (*P*-value = 0.853, Effect size = 0.041). There was also no statistically significant difference between mean blood urea levels of subjects with decreased and increased tongue coating (*P*-value = 0.507, Effect size = 0.149).There was no statistically significant correlation between blood urea level and number of petechial lesions (Correlation coefficient = -0.086, *P*-value = 0.362).

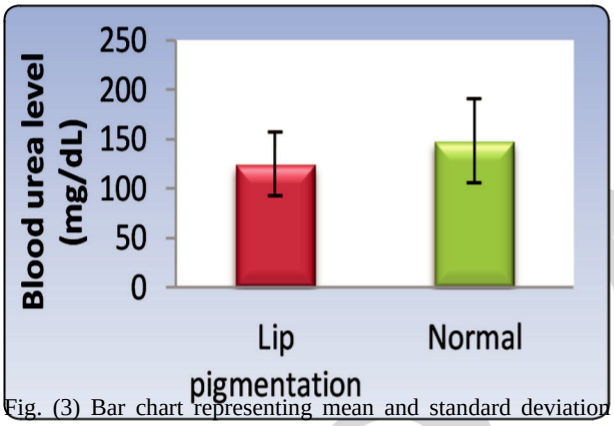

Fig. (3) Bar chart representing mean and standard deviation values for blood urea levels in subjects with lip pigmentation and normal subjects

Association between salivary pH level and oral manifestations:

There was no statistically significant difference between mean salivary pH levels in subjects with and without altered taste sensation (*P*-value = 0.990, Effect size = 0.012), burning mouth (*P*-value = 0.995, Effect size = 0.000), xerostomia (*P*-value = 0.820, Effect size = 0.047), uremic breath (*P*-value = 0.315, Effect size = 0.197), lip pigmentation (*P*-value = 0.990, Effect size = 0.012), intra-oral pigmentation (*P*-value = 0.737, Effect size = 0.073), keratosis (*P*-value = 0.387, Effect size = 0.343), Candida infection (*P*-value = 0.387, Effect size = 0.343) and pallor (*P*-value = 0.646, Effect size = 0.110).

There was also no statistically significant difference between mean salivary pH levels of subjects with decreased and increased tongue coating (*P*-value = 0.462, Effect size = 0.172).There was no statistically significant correlation between salivary pH level and number of petechial lesions (Correlation coefficient = 0.010, *P*-value = 0.915).

Association between salivary flow rate and oral manifestations:

Subjects with xerostomia showed statistically significantly lower mean salivary flow rate than normal subjects (*P*-value <0.001, Effect size = 0.694).There was no statistically significant difference between mean salivary flow rate in subjects with and without altered taste sensation (*P*-value = 0.376, Effect size = 0.165), burning mouth (*P*-value = 0.774, Effect size = 0.053), uremic breath (*P*-value = 0.325, Effect size = 0.183), lip pigmentation (*P*-value = 0.409, Effect size = 0.153), intra-oral pigmentation (*P*-value = 0.765, Effect size = 0.056), keratosis (*P*-value = 0.738, Effect size = 0.062), candida infection (*P*-value = 0.197, Effect size = 0.241) and pallor (*P*-value= 0.936, Effect size = 0.015). There was also no statistically significant difference between mean salivary flow rates of subjects with decreased and increased tongue coating (*P*-value = 0.131, Effect size = 0.282).

Association between tongue coating and Xerostomia: There was no statistically significant association between tongue coating and Xerostomia (*P*-value = 0.312, Effect size = 0.143).

Association between Hemoglobin level and oral manifestations

Subjects with pallor showed statistically significantly lower mean Hemoglobin levels than normal subjects (P-value <0.001, Effect size = 1.759) as shown in Figure (4). There was no statistically significant difference between mean

Hemoglobin levels in subjects with and without altered taste sensation (P-value = 0.371, Effect size = 0.175), burning mouth (P-value = 0.054, Effect size = 0.694), xerostomia (P-value = 0.498, Effect size = 0.135), uremic breath (P-value = 0.379, Effect size = 0.169), lip pigmentation (P-value = 0.523, Effect size = 0.130), intra-oral pigmentation (P-value = 0.626, Effect size = 0.107), keratosis (P-value = 0.241, Effect size = 0.464) and candida infection (P-value = 0.592, Effect size = 0.213).There was no statistically significant correlation between Hemoglobin level and number of petechial lesions (Correlation coefficient = -0.068, P-value = 0.475).

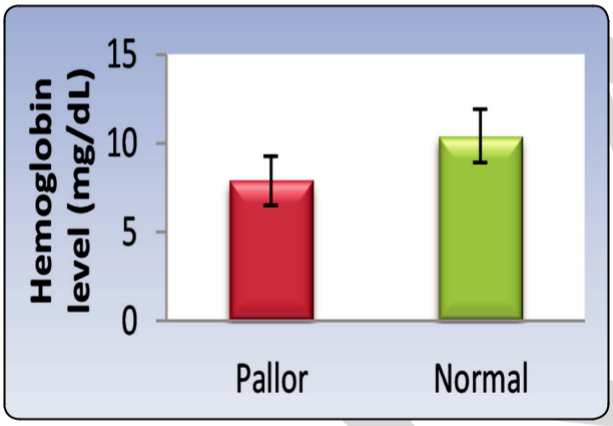

Fig. (4) Bar chart representing mean and standard deviation values for Hemoglobin levels in subjects with pallor and normal subjects.

DISCUSSION:

To our knowledge this is the first study in Egypt in this field, investigating oral manifestations in CKD patients undergoing hemodialysis. Based on the findings from this study as we expected a high prevalence of oral symptoms and lesions were recorded. We believe this result came out because hemodialysis patients are not very suitable for routine dental treatment, their dependence on dialysis centers and also because of their lack of motivation and less priority to maintain oral health contrary to the severity of their primary disease.

In the present study, there was a higher prevalence of males (61.4%) than females (38.6 %) among the participants. This was compatible with earlier studies ***(Kaushik et al., 2013; Oyetola et al., 2015; Marieh et al., 2017)***. This may be related to the predilection of chronic kidney disease in males than in females ***(Proctor et al., 2005).***

Periodontitis was the most prevalent oral change observed in our CKD patients 81.6 % which was in accordance with what was reported by ***Oyetola et al., 2015.*** A study reported by ***Bayraktar et al., 2004*** has shown that dental care in patients undergoing hemodialysis is neglected and that they brush and floss infrequently. This high prevalence of the periodontal disease is observed in patients with the kidney disease in both early and end stages, The aspect of complications present in the oral cavity requires detailed research because conflicting data are presenting poor oral health and periodontitis As patients undergoing hemodialysis generally have a poor objective periodontal status ***(Gerritsen et al., 2010; Akar et al., 2011; Teratani et al., 2013).***

Pallor of the oral mucosa has commonly observed among most of the CKD participants 76.3 % and this is close to results reported by ***(Belazelkovsk et al., 2013)***. The appearance of pale mucosa in renal patients explained by anemia that mainly developed following the inability of the failing kidneys to secrete erythropoietin, loss of red blood cells through dialysis, the brittle red blood cells and the early destruction of them and in some cases, from malnutrition. This was confirmed by low hemoglobin count from the patient's last records as the mean (SD) values for Hemoglobin level were 8.5 (1.8) g/dl in all participants.

Xerostomia was a symptom present in 79 out of 114 patients (69.3 %) and this finding was in agreement with findings in other earlier studies (***Dirschnabel et al.2011; Belazelkovska et al., 2013; Popovaska et al., 2013).*** We think that xerostomia in hemodialysis patients appears as a

result of the fluid restriction implemented to prevent fluid overload between dialysis sessions, and as a consequence of the present hyposalivation. Also, it has been hypothesized that this may be due to direct damage to the glands ***(Proctor et al., 2005).*** In our study, we found an association between xerostomia and salivary flow rate as patients with xerostomia showed a statistically significantly lower mean salivary flow rate than patients without xerostomia and these results consistent with previous studies ***(Kaushik et al., 2013; Shetty et al., 2018).***

Twenty-Four patients (21.1%) with normal tongue coating, 30 patients (26.3%) had decreased tongue coating while 60 patients (52.6%) had increased tongue coating according to The Tongue Coating Index (TCI) ***(Shimizu et al., 2007).*** These results were inconsistent with ***(Belazelkovska et al., 2013).*** Retention of residues of food, desquamated epithelial cells and bacterial accumulation due to the filiform papillae enlargement, aggravated maintenance of oral hygiene and decreased amount of saliva, being all the main reasons for the appearance of this common oral manifestation***(Dirschnabel et al., 2011).***

Uremic breath was found at 52 patients out of 114 with a prevalence of 45.6% and this is close to results with earlier results ***(Belazelkovska et al., 2013; Kaushik et al., 2013; Marieh et al., 2017).*** This is caused by a high concentration of urea in the saliva which is broken down into ammonia by urease enzyme in people with kidney disease ***(Klassen and Krasko,2002).***

Petechiae was commonly found at 44 out of 114 patients with a prevalence 38.6% which is consistent with earlier studies***(Kerr et al.,2001),*** According to these authors, petechiae and ecchymoses are seen in patients with CKD most commonly, due to the platelet aggregation defiecnency in conditions of uremia.

We suppose that this clinical finding refers to the impaired platelet aggregation as a consequence of the uremic syndrome and accumulation of inhibitory factors in blood that cannot be removed with the process of dialysis. It 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 ***(Kaushik et al., 2013).***

Altered taste has been commonly reported and was present in 40 out of 114 patients with prevalence 35.1 % which is close to results reported by ***(Belazelkovska et al., 2013; Kaushik et al., 2013; Marieh et al., 2017)***. The taste alteration may have several explanations such as increased levels of salivary urea and dimethyl and trimethylamine levels, metabolic disorders, taking medications, decreased number of taste buds, salivary flow rate and saliva composition alterations in uremic patients***(Oyetola et al., 2015).***

Burning mouth sensation which was significantly higher in our CKD patients 32.5% which was in accordance with what was reported by ***Belazelkovska et al., 2013***. While no association was found between the burning tongue and any of the oral manifestations, which is in agreement with the findings in a study reported by ***De la Rosa-Garcia et al., 2006.*** Predominant reasons for the appearance of burning tongue are dried oral mucosa, xerostomia due to most various etiologies, prolonged clearance of medications as well as vitamin deficit and damage to peripheral nerves by the uremic toxins ***(Leao et al., 2005).***

Abnormal lip pigmentation was present in 31.6% in our CKD patients and it was reported by only one study ***(Oyetola et al.,2015)***.In our study, we found that patients with lip pigmentation showed statistically significantly low mean blood urea levels.**Intraoral/ mucosal pigmentation** was found at (24.6%) in our

patients which was a much higher prevalence than a study done by ***(Oyetola et al.,2015)*** 12 %.

Oral and cutaneous hyperpigmentation in renal patients is due to the inability of the kidney to excrete excess beta melanocyte-stimulating hormone (b-MSH), the accumulation of which results in the stimulation of melanocyte at the basal layer of oral epithelium. Consequently, abnormal lip and face pigmentation constitutes a great aesthetic challenge to renal patients ***(Kauzman et al., 2004).***

Frictional Keratosis was reported in our CKD patients with a 6.1 % prevalence and wasn't reported among renal patients in the earlier studies before. **Oral candidiasis** was only found at 6.1 % of our CKD patients which is inconsistent with earlier studies ***(Belazelkovska et al., 2013; Oyetola et al.,2015)***. Nevertheless, these results in contrast to another study which reported a much higher prevalence of up to 37% ***(De la Rosa-Garcia et al., 2006).*** Environmental factors, possibly genetic variations, immune-suppressive medications and exclusion/ inclusion criteria like kidney transplantation may account for the little variation between our study and the above-mentioned studies.

Our research showed that salivary pH value was (7) in patients with chronic renal insufficiency which was in accordance with what was reported by***(Kaushik et al., 2013 ; Marieh et al., 2017).***

Increasesinureacompoundshavebeenmentioned as one of the findings in most studies carried out on renal patients ***(Davidovich et al., 2005; Anuradha et al., 2015).*** Based on this research, salivary pH values in hemodialysis patients were significantly high, and these results are in agreement with that found in research conducted by ***Al Nowaiser et al., 2003.*** Salivary urea is decomposed into ammonium ions and carbon dioxide by urease and, hence, may raise salivary pH to critical values. This effect might mask the changes that are due to the disease condition ***(Engelen et al., 2007; Marieh et al., 2017).***

Salivary flow rate mean values were (0.34 ml/ min) which is inconsistent with research reported by ***(Kaushik et al., 2013).***The diminished flow rates of unstimulated saliva can be due to direct influence of uremia on the salivary glands causing decreased parenchymatous and excretory functions, and as a result of dehydration due to the limited fluid intake. These patients exposed to many stresses that may also reduce the salivary flow rate ***(Kaushik et al., 2013).***

CONCLUSION

CKD patients require special attention to dental treatment, not only due to the disease and its multiple oral manifestations but also because of the side-effects and characteristics of the treatments they receive. The undiagnosed dental infection in immunosuppressed renal patients could lead to morbid-ity and transplantation rejection in the future. The dental management of patients with renal disease is complicated by systemic consequences of renal failure particularly anemia, bleeding, cardiovascular or endocrine diseases, the dental management in these patients can be effective and safe through a proper treatment protocol.Finally, a closer relationship between nephrologists and dentists is mandatory in the management of chronic renal patients to assure the best quality of life at all times.

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