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Original Article

Prevalence of Oral Findings in Adult Patients with Chronic Kidney Disease: A Cross-sectional Study

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Abstract

Aim: The study assesses the prevalence of oral findings among a sample of Egyptian population with chronic kidney disease and analyze the oral findings at pre-dialysis and end stage renal disease.
Subjects and methods: 225 participants were interviewed filling out a questionnaire followed by an oral examination and the findings were reported. The data were statistically analyzed; continuous variables were expressed by mean ± standard deviation & median (range), the categorical variables were expressed by number (percentage)
Results: Prevalence of oral findings was 95.1% across all patients. The highest was detected in G5 undergoing dialysis (98.6%). The most recorded findings were tongue coating (78.7%), dry fissured lip (24.9%), then purpura (16.4%). Patients under hemodialysis were at risk of being HCV infected.
Conclusion: Egyptian CKD patients are prone to oral problems according to the disease stage, medications used and dialysis status. The findings are attributed to uremia, xerostomia and medications. Besides of poor oral hygiene was detected in all the study participants.

Keywords: Oral findings; Chronic kidney disease; Dialysis; Oral mucosal lesions

Introduction

Chronic kidney disease (CKD) is considered a major health problem worldwide. It is defined by the National Kidney Foundation (NKF) as "Abnormalities of kidney structure or function, present for more than 3 months, with implications for health"(Stevens *et al.*, 2024).

The filtering power of the kidney is best expressed by the glomerular filtration rate (GFR). CKD occurs when there is a fall in the total GFR below <60ml/min/1.73m^2 denoting the functional decline of the kidney. The disease advances in 5 progressive stages: from G1 to G5; based on the decrease in GFR levels. At the initial stages of the disease (G1 and G2), there is a slight drop in GFR (GFR 60-89ml/min/1.73m2) where the patient is usually asymptomatic due to the renal reserve capacity. This is followed by gradual functional decrease through G3 stage (GFR 30-60ml/min/1.73m^2) and G4 stage (GFR 15-29ml/min/1.73m$^{2)}$ The final phase G5 (GFR <15ml/min/1.73m^2) denotes the total loss of kidney function; known as End Stage Renal Disease (Filipska *et al.*, 2021).

Having the disease progressed into ESRD, the patient becomes in an essential need for renal replacement therapy (Levin *et al.*, 2017). Moreover, the burden of CKD further extends to amplify the risks of all non-communicable diseases, as cardiovascular-related disorders; thereby, causing higher mortality rates and poor quality of life)(Francis *et al.*, 2024)**.**

On the global level, the prevalence and death rates of CKD show rising figures throughout the years. It was reported to have reached 13% across different parts of the world (Hill *et al.*, 2016). In 2017, the Global Burden of Disease (GBD) study ranked CKD as 12th leading cause of death worldwide. In addition, 7.6% of all CVD deaths (1.4 million) could be attributed to impaired kidney function (Bikbov *et al.*, 2020).

According to the Egyptian Renal Data System (ERDS), Egypt had the second highest prevalence of CKD in Africa after Tunisia by 669 per million patients and 713 per million patients respectively (Hassaballa *et al.*, 2022)

The oral cavity is the mirror reflection of the general health condition. It is highly inflicted by many systemic diseases such as diabetes mellitus, cardiovascular and autoimmune disorders. CKD has negative impacts on oral health either due to the disease itself or the related therapeutics (Mainali and Chettri, 2020).

Persistently decreased glomerular filtration rate leads to accumulation of nitrogenous wastes; as urea in the blood, causing a state of uraemia. Both the uraemia and therapeutic measures, which include fluid restrictions, dietary changes, side effects of systemic therapy, dialysis and/or kidney transplantation, can alter the oral mucosa leading to wide clinical findings such as increased tongue coating, candidiasis, uremic stomatitis and renal osteodystrophy (Gupta, Gupta and Abhishek, 2015)**.**

The oral mucosal injuries may negatively impact the patient's overall quality of life. Consequently, there is an urgent need to describe the oral signs and complaints aiming to improve the oral wellbeing for CKD population and provide them with the optimum medical services.

Subjects and Methods

A total sample of 225 adult patients diagnosed with CKD attending at the Nephrology Department at Kasr Al-Ainy Cairo University Hospital were enrolled in the study as follows:

Group I (Predialysis group): 125 patients enrolled from the out-patient clinic of King Fahd's Nephrology unit with GFR stages G2, G3 and G4.

Stage 5 patients (n=100) were included into 2 groups depending on the dialysis status:

Group II (Stage G5-on dialysis): 72 patients were receiving dialysis and selected from the Dialysis Units of CKD.

Group III (Stage G5-not on dialysis): 28 patients were not receiving dialysis and were recruited from the out- patient clinic of King Fahd's Nephrology unit.

Inclusion and exclusion criteria:

Inclusion criteria:

-Adult patients more than 18 years old.

-Patients diagnosed with CKD at stages G2, G3, G4 and G5.

-Patients with available records for GFR, BUN and serum creatinine.

-For dialysis patients should have laboratory investigations for HCV

-Recorded data of PT, INR and platelets count for patients reporting oral purpura

Exclusion criteria:

-End stage renal disease patients undergoing peritoneal dialysis.

-Patients not physically able to participate in oral examination.

-Patients who undergo kidney transplantation.

-Patients undergoing renal dialysis for reasons other than chronic kidney disease.

Methods of data collection

1- The questionnaire was filled up through an interview with the study subjects followed by a comprehensive intra-oral examination**.** The questionnaire included four partitions:

- Demographic data

- Medical history including recorded data of serum creatinine, BUN, GFR estimated by CKD-EPI-equation, systemic diseases, history of dialysis therapy, initial cause of nephropathy and medications.

- Personal history: smoking, alcohol, spicy, hot food.

- Dental history: history of previous oral health care, oral hygiene practices and patients' self-report of oral and dental complaints.

2- Clinical oral examination was performed using basic dental instruments to record any oral findings/lesions. For haemodialysis patients, all examinations were performed by the bedside during the haemodialysis session. Findings were recorded for each patient.

Primary outcome:

-Prevalence of oral mucosal lesions: Presence of oral mucosal lesions was assessed by clinical picture as a dichotomous outcome (Yes/No).

The scores used in case of the presence of any oral finding:

- Tongue coating using the Index (Kojima's index) (Panov, Krasteva and Nikolov, 2017)
- Clinical oral dryness using oral dryness score system by "Kings College London Dental Institute Guy's & St Thomas" (Das and Challacombe, 2016)
- Uremic stomatitis: Yes /No, type and site
- Gingival enlargement using the Angelopoulos and Goaz index (Angelopoulos and Goaz, 1972) .
- Dry fissured lip: Yes/ No
- Aphthous-like ulcer: Yes/No, number, type
- Purpura using the immune thrombocytopenic purpura bleeding score assessment (Page *et al.*, 2007)**.**
- Lichenoid reaction: Yes/No, type
- Oral candidiasis: Yes/No, type
- Other oral findings:Yes/No, type (patients may present with more than one type)

Secondary outcomes:

-Periodontal condition using basic periodontal examination (Dowell and Chapple, 2002) (*Scoring Codes Pockets <3.5mm*, 2019)**.** It was expressed in the form of scores.

-For patients at dialysis stage, HCV infection: HCV infection following dialysis was assessed by the presence or absence of HCV antibodies in blood. They were sub-grouped into HCV+ and HCV-.

Statistical analysis:

Data were coded and entered using the statistical package for the Social Sciences (SPSS) version 26 (IBM Corp., Armonk, NY, USA). Data was summarized using mean, standard deviation, median, minimum and maximum for quantitative variables and frequencies (number of cases) and relative frequencies (percentages) for categorical variables. Comparisons between groups were done using analysis of variance (ANOVA) with multiple comparisons post hoc test or unpaired t test in normally distributed quantitative variables while non-parametric Kruskal-Walli's test and Mann-Whitney test were used for non-normally distributed quantitative variables (Chan, 2003a). For comparing categorical data, Chi square (□2) test was performed. Exact test was used instead when the expected frequency is less than 5 (Chan, 2003b). Logistic regression was done with

HCV as dependent variable and periodontal score as independent predictor (Chan, 2004). P-values less than 0.05 were considered statistically significant**.**

Results

The baseline demographic data of the 3 study groups showed roughly equal distribution of gender. The mean age of the included participants was 55±5 years. The age of the majority of group I patients ranged between 36 to 40 years old, while stage G5 patients (group II and III) ranged between 55 to 65 years old.

Prevalence of oral mucosal findings was 95.1% in all the included CKD patients. The prevalence differed among the 3 study groups where the lowest prevalence was in group III (92.9%), followed by group I (93.6%), and the highest was in group II (98.6%).

Among the CKD included patients, the most common causes of nephropathy have been hypertension (24.9%), obstructive uropathy (20.4%), diabetes mellitus (9.7%). The most recorded oral mucosal finding among the 3 groups was tongue coating (78.7%), followed by dry fissured lip (24.9%), then purpura (16.4%) as shown in table 1. When these oral findings were correlated to the etiological causes of nephropathy, most of them were associated with hypertension and obstructive uropathy.

Regarding the tongue coating, the most common indices were index 2 and 3 in the 3 groups with roughly equal prevalence/group (27.2% and 26.4% in group I, vs 26.4% and 26.4% in group II, vs 25% and 25% in group III) with no statistical significance across the three groups. Index 4 was higher in the G5 groups (II and III) (12.5% and 25 % respectively) if compared to group I (3.2%) with the presence of intergroup statistical significance (<0.05) between group I and II (3.2% and 12.5% respectively) and group I and III (3.2% and 25% respectively).

Among the oral findings detected was clinical oral dryness. The highest score was attributed to group II (1.6±0.84) followed by group III (0.96±0.83) and lastly, group I (0.77±1.23)**.** The differences between the 3 groups were statistically significant (P <0.001). Furthermore, the general periodontal score for the 3 study groups reflected a poor periodontal condition with loss of attachment (2.4±1.6). The 3 study groups showed almost similar results with no statistically significant differences (2.44±1.23) in group I, vs (2.38±1.02) in group II, followed by (2.32±1.25) in group III p value (<0.861). The purpura was found to be in group I (20.8%), followed by group III (17.9%), then group II (8.3%) with no statistical significance across all groups.

This was followed by the oral lichen planus (OLP) and oral lichenoid group. They were mainly examined in group I patients (14.4%) with minimal appearance in group III (3.6%) then group II (2.8%) with significant statistical difference between groups (I and III) and groups (II and III).

Among group II patients, namely stage G5 patients on dialysis, 40.3% contracted HCV following dialysis.

Discussion

Chronic kidney disease is a progressive asymptomatic disease with high mortality rate (Kakitapalli *et al.*, 2020). Although various oral findings are detected secondary to CKD, there are no distinct oral signs or symptoms. Oral alterations are mostly related to therapeutic interventions, the restriction in fluid consumption, immunological imbalance and renal osteodystrophy (Gupta, Gupta and Abhishek, 2015). A systematic review by Ruospo et al. (2014) concluded that the spectrum of oral changes shows great diversity among various geographic areas. Thus, the present study aimed to investigate the prevalence and types of oral findings among adult Egyptian population having CKD.

The current study examined the oral findings among 225 patients branched into: group I included stages G2, G3, and G4, group II comprised stage G5 under dialysis and group III was stage G5 not receiving dialysis. Stage I was not included as in this stage, the GFR is normal or slightly high, rather than low, with no significant clinical influences (Fraser and Blakeman, 2016). On the other hand, stages G2, G3 and G4 were gathered in one study group as the GFR level is lower than normal, yet the kidney is still functioning (Chen, Knicely and Grams, 2019).

Patients of stage G5 suffer from renal failure with extremely deteriorated GFR levels. Thus, stage G5 was not statistically combined with the previous stages. Furthermore, patients of stage G5 were further grouped based on their dialysis treatment status into stage G5 with dialysis (Group II) and stage G5 not undergoing dialysis (Group III). This was based on the difference between the two groups of patients in the levels of uraemia, which is a major risk factor for the oral and clinical manifestations (Dioguardi *et al.*, 2016a).

The age of the majority of group I patients ranged between 36 to 40 years old, while stage G5 patients (group II and III) ranged between 55 to 65 years old. After the age of 30 years, GFR decreases by 1 mL/min/1.73 m2 per year (Cusumano et al., 2022).Regarding the gender, the included participants showed roughly equal distribution of males and females in all groups., These results may be attributed to the roughly equal gender distribution of the main CKD etiological causes (hypertension and diabetes mellitus) in the Egyptian population (Zain *et al.*, 2019).

Hypertension, diabetes mellitus and recurrent urinary tract infection are regarded as modifiable risk factors of CKD (Mallamaci and Tripepi, 2024). Interestingly, in the present study, the top 3 etiological factors are hypertension (24.9%), obstructive uropathy (20.4%) and diabetes mellitus (9.7%). That is consistent with the study by Ephraim et al. (2015)that demonstrated both hypertension and diabetes were the principal factors in the etiology of CKD. Also, the cross-sectional study by El-Ballat, El-Sayed and Emam (2019) in Egypt reported the same results as hypertension, diabetes and obstructive uropathy were the most common causes of CKD.

The primary outcome of the present study; namely the prevalence of oral findings, was 95.1% in all the included CKD patients. Similarly, Afroozi et al. (2017) reported a higher percentage (78%) of oral manifestations in CKD population. The systematic review by Ruospo et al. (2014) stated that the poor oral condition is common in CKD patients due to the lack of awareness and oral facilities. While the study conducted by (Nylund *et al.*, 2018) in Finland showed low prevalence of oral lesions among CKD (28%). The is attributed to the better oral maintenance program and the increased awareness of the disease.

In the present study, tongue coating was the most frequent finding in all groups by a percentage of 76.8% in group I, 79.2% group II and 85.7% in group III. The observational study by Muhamed (2015) demonstrated that the most prevalent oral features in patients under haemodialysis are dry mouth and coated tongue by a percentage 76.1 and 73.4 respectively. The highest prevalence of index 1 was attributed to group I and index 4 was the highest in group III. Oral results are understandable in the light of knowing that with the worsening of CKD condition, oral hygiene becomes more neglected, together with higher levels of xerostomia. These factors contribute to the increase in tongue coating (Egbring *et al.*, 2023).

Concerning the clinical oral dryness, it showed statistically significant difference among the means of the 3 groups; where it was 0.77±1.23 in group I, 1.61 ± 0.84 in group II and 0.96±0.83 in group III. Oral dryness is a common symptom secondary to restriction of fluid intake, side effects of the therapeutic interventions and salivary gland disorder due to

uraemia in ESRD (Dioguardi *et al.*, 2016b).On the other hand, the subjective reporting of xerostomia by the patients was described by about 39.2% in group I, 38.9% in group II and 42.9% in group III. That agrees with Kareem, Ameena and Diajil (2018) who found that 36.6% of CKD patients on conservative treatment and 46.6% of the patients receiving haemodialysis reported dry mouth.

In reference to oral purpura, it was documented in 20.8% of group I, 8.3% of group II and 17.9% of group III. Similar data was reported by Yadav et al. (2015) that noticed petechiae and ecchymosis in 2.2% of dialysis patients. Unlike De La et al. (2006) who reported 15.2% cases of purpura in diabetic patients undergoing dialysis versus 0.8% not undergoing dialysis. The prevalence of oral purpura in this study is related to contributing factors such as cardiovascular disease, anticoagulant therapy and liver problems. In the present study, the higher level of purpura detected in group I and III in comparison to group II can be attributed to the higher levels of circulating uremic toxins adversely impacting the function of the platelets and the coagulation factors (Kuravatti and Priscilla David, 2016).

In the current study, lichenoid reaction was reported in 14.4 % of group I, while 2.8% of group II and 3.6% of group III. The atrophic type OLP was the most encountered type. Gautam et al. (2014)reported a similar percentage in dialysis patients (1.9%). Unfortunately, few studies mentioned lichenoid reaction as oral finding in CKD. The drugs used in management of CKD can induce lichenoid reaction as antihypertensive, hypoglycaemics and antibiotics (Thongprasom, 2018). The high percentage of group I patients (71.2%) administering antihypertensives would be explanatory to the significantly high prevalence of oral lichenoid among group I patients; especially when compared to the lower administration of antihypertensives among group II (54.2%) and III (67.9%) patients.

The mean periodontal score was 2.4± (1.2) in group I, 2.3± (1.02) in group II and 2.3± (1.2) in group III. The mean periodontal score did not differ significantly across different stages of CKD. Bad oral hygiene, smoking and systemic diseases such as diabetes were the main contributing factors in worsening of the periodontal condition. These findings are in accordance with findings reported in the longitudinal study held by Nylund et al. (2018).

Regarding the last outcome of the study, the prevalence of HCV in participants who contracted HCV after haemodialysis is 40.3%. The results are close to the 53% reported by Jakupi et al. (2018). Based on a recent survey among Egyptian patients undergoing haemodialysis, the percentage of HCV was found to be 34.8% (Kerollos *et al.*, 2020). These high percentages may be attributed to the cross-contamination from the dialysis circuits. This was corroborated by a meta-analysis performed in 2015 by El-Ghitany et al.. It illustrated that blood transfusion and haemodialysis were the top risk factors of HCV infection in Egypt.

Conclusion

According to the overall study findings, adult Egyptian patients having CKD have an array of oral findings that differ according to the disease stage, medications used and dialysis status. The findings are mainly attributed to uraemia, xerostomia and the types of administered medications. Besides, a general finding of poor oral hygiene, together with poor periodontal condition, was detected in all the study participants.

Table (1) A table showing the comparison of oral mucosal findings of the three study groups

Oral mucosal findings		Group I (GFR>15)		Group II (GFR<15 on dialysis)		Group III (GFR<15 not dialysis)	
		Count	%	Count	%	Count	%
Tongue coating	**Index 0**	29_a	23.2%	15_a	20.8%	4_a	14.3%
	Index 1	25_a	20.0%	10_a	13.9%	3_a	10.7%
	Index 2	34_a	27.2%	19_a	26.4%	7_a	25.0%
	Index 3	33_a	26.4%	19_a	26.4%	7_a	25.0%
	Index 4	4_a	3.2%	9_b	12.5%	7_b	25.0%
Uremic stomatitis (all Ulcerative)		0	0.0%	0^1	0.0%	1_a	3.6%
Dry fissured lip		40_a	32.0%	6_b	8.3%	10_a	35.7%
Aphthous stomatitis (all minor)		2_a	1.6%	1_a	1.4%	0^1	0.0%
Purpura	**Score 0**	99_a	79.2%	66_a	91.7%	23_a	82.1%
	Score 1	25_a	20.0%	6_a	8.3%	5_a	17.9%
	Score 2	1_a	0.8%	0^1	0.0%	0^1	0.0%
OLP and OLL		18_a	14.4%	2_b	2.8%	$1_{a,\,b}$	3.6%
OLP and OLL type	**Reticular**	5_a	27.8%	2^1	100.0%	$0^{1,2}$	0.0%
	Atrophic	9_a	50.0%	0^1	0.0%	$0^{1,2}$	0.0%
	Plaque	3_a	16.7%	0^1	0.0%	$1^{1,2}$	100.0%
	Ulcerative	1_a	5.6%	0^1	0.0%	$0^{1,2}$	0.0%
Acute candidiasis		6_a	4.8%	1_a	1.4%	0^1	0.0%
Acute candidiasis type	**Pseudomembraneous candidiasis**	2_a	33.3%	$0^{1,2}$	0.0%	$0^{1,2}$	0.0%
	Acute atrophic candidiasis	4_a	66.7%	$1^{1,2}$	100.0%	$0^{1,2}$	0.0%
Chronic candidiasis		3_a	2.4%	0^1	0.0%	0^1	0.0%
Chronic candidiasis type	**Denture stomatitis**	1_a	33.3%	$0^{1,2}$	0.0%	$0^{1,2}$	0.0%
	Angular cheilitis	1_a	33.3%	$0^{1,2}$	0.0%	$0^{1,2}$	0.0%
	Median rhomboid glossitis	1_a	33.3%	$0^{1,2}$	0.0%	$0^{1,2}$	0.0%

Note: Values in the same row and sub table not sharing the same subscript are significantly different at $p< 0.05$ in the two-sided test of equality for column proportions. Cells with no subscript are not included in the test. Tests assume equal variances.[3]

1. This category is not used in comparisons because its column proportion is equal to zero or one.

2. This category is not used in comparisons because the sum of case weights is less than two.

3. Tests are adjusted for all pairwise comparisons within a row of each innermost sub table using the Bonferroni correction.

Conflict of Interest:

The authors declare no conflict of interest.

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Ethics:

This study protocol was approved by the ethical committee of the faculty of dentistry- Cairo university on: 24/4/2017, approval number: (17-4-15)

Data Availability:

Data will be available upon request

Clinical trial registration:

The protocol for this study was registered on clinicaltrials.gov, under ID: NCT03082365

CRediT statement:

Author 1: Conceptualization, Methodology, investigation, Resources, Writing - original draft, visualization.

Author 2: Data curation, formal analysis, Writing - review & editing.

Author3: Conceptualization, Project administration, Supervision, Methodology, Writing - review & editing.

Author 4: Methodology, Writing - review & editing, Supervision.

Author 5: Conceptualization, supervision, Methodology, Data curation, Writing - review & editing.

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