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Original Article

Oral Findings in a Group of Egyptian Pediatric Patients at End Stage Renal Disease Either On Haemodialysis Or After Kidney Transplantation: A Cross-Sectional Study

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Abstract:

Objectives: To assess the oral findings among a group of Egyptian pediatric patients at End-Stage Renal Disease either on haemodialysis or after kidney transplantation.

Subjects and Methods: A total number of 84 pediatric patients from April 2019 till October 2019 were recruited. A comprehensive oral examination was performed for both soft and hard oral tissues and the following outcomes were assessed: dental caries, enamel hypoplasia, oral candidiasis, and gingival hyperplasia. Patients were classified into: group I represents the haemodialysis group and group II represents the kidney transplantation group.

Results: In both groups, 17 were caries affected (20 %) and 67 were caries-free (80%). The percentage of enamel hypoplasia was reported in 25% of both groups. The percentage of gingival enlargement among group I was 3.4 % while 16.7 % in group II. Oral candidiasis was not encountered in all study participants.

Conclusion: End-Stage Renal Disease patients are in an essential need for an awareness program to encourage maintenance of oral hygiene and other measures such as a balanced diet and proper hydration.

Keywords: Chronic Kidney; Dental Caries; pediatric; Oral manifestations.

Introduction

The National Kidney Foundation (NKF) defined chronic kidney disease (CKD) as "abnormalities of kidney structure or function, present for more than three months, with implications for health". The structural abnormalities are the changes in the integrity of the kidney that is detected by imaging such as ultrasound and computed tomography. While, functional abnormalities include markers as albuminuria and urinary sediment abnormalities. Kidney disorders are classified into acute, sub-acute, and Chronic Kidney Disease (CKD), based on its onset. Although acute renal failure is reversible in most cases CKD shows a progressive course until the total failure of kidney functions termed as End-Stage Renal Disease (ESRD). Treatment of CKD involves dietary

changes, correction of systemic complications, and dialysis or renal transplantation at ESRD. [1-2]

Chronic Kidney Disease can lead to a series of oral complications, affecting the hard or soft tissues due to the disease itself and the underlying therapy. Apart from systemic changes, kidney disease patients with renal therapy may have oral problems due to immunological response impairment, and drug therapy masking of signs and symptoms. The immune deficiency condition in CKD predisposes renal patients to opportunistic infections caused by fungi. The most prevalent oral finding is pallor of oral mucosa due to anemia. While periodontal disease is common due to poor oral hygiene. Disturbed calcium and phosphate metabolism may result in enamel opacities, loss of lamina dura, loosening of teeth, and bone fractures. Chronic Kidney Disease is associated with a reduced incidence of caries. Gingival hyperplasia occurs secondary to medication used in renal transplantation such as cyclosporine or calcium blockers in dialysis patients, gingival margins of the lingual or palatal surface may get affected with hyperplasia. [3-4]

Although CKD is relatively uncommon in pediatrics, it is a devastating illness with many long-term serious complications. The mortality rate for children receiving dialysis therapy is 30–150 times more than in the general pediatric population. The expected lifetime for a child undergoing dialysis is approximately 50 years less than a healthy child. While renal transplantation is considered to be the best therapeutic choice for ESRD, most clinical complications dramatically affect patients' health before the complete loss of renal function. [5-6] In Egypt, few studies were performed on the prevalence of oral findings so this study was conducted to investigate the oral findings among a group of pediatric patients at end-stage renal disease either on haemodialysis or after kidney transplantation.

Subjects and methods

Ethical approval:

Ethical approval was obtained before the start of the study from the Research Ethics Committee, Faculty of Dentistry. Consent was obtained by the respective hospital in-charge of the patients. The purpose of the study was clearly explained to the patients/legal guardian and verbal assent was obtained before participation in this study.

The study was registered with ClinicalTrials.gov **(Identifier: NCT03590067)**

Sample Size Calculation

Convenient consecutive sampling was applied; it included all patients at end-stage renal disease fulfilling inclusion criteria attending El- Mounira children's hospital (Abu El Rish Hospital) over six months' period from April till October 2019. The patients were recruited in the study randomly in consecutive order to minimize the selection bias. The sample size was calculated and approved by the Evidence-Based Committee of Faculty of Dentistry, Cairo University.

Subjects

This cross-sectional study was performed on 60 patients undergoing dialysis during their hemodialysis session and 24 patients who received transplant during their monthly follow up, according to eligibility criteria which included pediatric patients from two to fourteen years old with a diagnosis of ESRD "stage V" with GFR <15, both genders were included, parental or guardian and children verbal acceptance for participation in the study.

Methods

All the participants were subjected to a questionnaire (Appendix 1) and comprehensive oral examination that was based on the criteria suggested by the World Health Organization (WHO) for oral health surveys.[7] Demographic data were recorded in the form of age, sex and address and the medical records were screened

for etiology, duration of dialysis or since transplantation and their screening tests.

The questionnaire consisted of three sections; *first section* included personal history of the patient and his guardian, *second section* included medical history of the patient and the *third section* included dental history and clinical examination.

Regarding the dental history, patients were asked about their oral hygiene practice (how often did they clean their mouths, tool used for cleaning, frequency of brushing if a tooth brush was used) and the guardians were asked about their children's oral hygiene practice. Also, they were asked about any dental visits in the last year and if there were any current oral and dental complaints. In case of the presence of serious oral and/or dental conditions that required treatment the patient was referred to a specialist with an attached referral form (Appendix 2).

Oral examination was performed for both oral (soft tissue) and dental (hard) tissues while the patients were laying on their beds with their heads at an appropriate height for his or her convenience using the room fluorescent light aided by mobile flash. The primary and secondary outcomes were assessed: dental caries, enamel hypoplasia, oral candidiasis and gingival hyperplasia.

Dental caries indices were recorded using dmft index for primary teeth and DMFT index for permanent teeth which is the number of decayed, missing, and filled teeth.[8] For children in the mixed dentition period two indices were used which are two indices were used which are DMFT index for permanent dentition and deft index for dentition during this period. [9]

Enamel hypoplasia was recorded using the modified developmental defects of the enamel (DDE) index. [9,10] If dental caries is present no matter whether there was a developmental defect originally, the score is 4.[10] if there were two distinct DDEs on the same surface of the same tooth, the most severe lesion was scored. [11]

Oral candidiasis assessment was based on Lehner oral candidiasis classification 1967.[12] Modifications were made in Lehner Oral candidiasis classification to fit children.

Gingival hyperplasia was visually assessed as the proportion of the labial face of the tooth crown which was overlapped by gingival tissue, and recorded as normal (Score 0), covering up to one-third (Score 1), covering up to two-third or half of the crown (Score 2), more than two-thirds or as completely obscuring the natural tooth crown (Score 3)**.**[13]

Statistical analysis

Statistical analysis was performed using a commercially available software program (SPSS 19; SPSS, Chicago, IL, USA).

Qualitative values were presented as numbers and percentages. A Chi-square test was used to compare categorical data**.**

Quantitative values were expressed as mean and standard deviation and were compared between groups using independent t-test.

Results

Regarding the results of this study concerning the most common cause of Chronic Kidney Disease among all the study participants was familial /metabolic diseases by 33.3% and 37.5% in haemodialysis and kidney transplantation respectively. The mean age for dialysis patients was 9.2±3.07, while for kidney transplantation was 11.75 ±2.48. The majority of the participants were males (60% males : 40% females) and the most prevalent cause was familial/metabolic diseases. Oral hygiene negligence was the most common finding in almost all study participants. 51.7% of group I

and 41.7% in group II never brushed their teeth. Among the dialysis patients, 90% never visited the dentist in the last year, in comparison to 83.3% in the transplantation group, with no significant difference (p=0.645). The prevalence of dental caries in the present study was low in both groups. The mean DMFT score in the dialysis group was 2.25, in comparison to 2.33 in the transplantation group. The mean dmft score in the dialysis group was 4.57. The mean deft score in the dialysis group was 2.8, in comparison to 2.4 in the transplantation group (Table 1). Regarding enamel hypoplasia among the dialysis patients, 75% were normal, while 6.8% had demarcated opacity, 5% had diffuse opacity and 13.6 % had hypoplasia. In comparison, 70.8% in the transplantation group were normal, while 12.5% had demarcated opacity, 4.2% had diffuse opacity and 8.3 % had hypoplasia. No incidence of acute or chronic candidiasis in both groups. The urea level was 10.28±2.56 in group I, while the level of BUN in group II was 33.83± (19.88). Regarding Gingival hyperplasia among the dialysis patients, 96.6% had recorded score 0, while 1.7% had score 1 and 1.7 % had score 2. In comparison, 83.3% in the transplantation group had Score 0, while 12.5% had score 1 and 4.2 % score 3 (Table 2)**.**

Discussion

Kidney disease is a global public health problem, with increasing incidence and prevalence, high cost, and poor outcomes. It causes the loss of functional capacity of the nephrons, regardless of its etiology. Oral cavity is the mirror of systemic health. More than 90% of CKD patients present with oral symptoms that are related to the disease itself and the therapeutic intervention. End-stage renal disease patients complain more than other stages from oral problems because they rely on dialysis centers and neglect their oral health. However, with the aid of the dialysis therapy and the filtration of the blood from all the waste products, many of the oral manifestations of CKD and uremia are less commonly seen. The oral changes include mucosal and glandular tissues, the gingival, and the periodontal apparatus, the maxillary, and mandibular bone, and finally the dental status**.** [14-15]

Previous studies investigated the oral findings among ESRD pediatric patients receiving haemodialysis only. Up to the authors' knowledge, the present study is the first cross-sectional study in Egypt that investigates the oral findings among ESRD pediatric patients receiving kidney transplantation as well.

In the present study, the mean age for haemodialysis patients was 9.2±3.07, while for the kidney transplantation was 11.75 ±2.48. In the current study, only participants with age ranging from 2 to 14 years were enrolled. That is because, El- Mounira children's hospital (Abu El Rish Hospital) referred patients above 14 years to El-Kasr El Ainy hospital. Only Egyptian children were included in this study to minimize variables that could affect the results due to different environmental and ethnic factors.[16] The percentage of males was higher than females in both haemodialysis and transplantation groups this was consistent with the results from various geographic areas.[17-20] The top cause of pediatric Chronic Kidney Disease in almost all CKD registries is congenital anomalies of the kidney and urinary tracts(CAKUT) at approximately

Table (1): Caries indices in both groups and comparison between dialysis and transplantation groups (independent t-test)

Mean		Dialysis	Transplantation	t	P
DMFT	**Number of patients**	41	23	--	--
	DMFT=0	29=70.7%	14=60.9%	0.65	0.42ns
	D	2.17±2.01	1.89±1.86	1.09	0.162ns
	M	0.08±0.07	0.11±0.09	0.84	0.23ns
	F	0±0	0.33±0.26	Not computed	
	DMFT	2.25±2.13	2.33±2.28	0.61	0.72ns
dmft	**Number of patients**	14	1	--	--
	dmft=0	7=50%	1=100%	--	---
	d	3.7±3.65	0	--	--
	m	0.43±0.84	0	--	---
	f	0.43±0.84	0	--	--
	dmft	4.57±3.78	0	--	---
deft	**Number of patients**	39	13	--	--
	deft=0	24=61.5%	3=23.1%	0.578	0.016*
	d	1.67±1.59	1.5±2.32	0.98	0.42ns
	e	0.87±0.73	0.9±0.74	0.36	0.89ns
	f	0.27±0.32	0±0	Not computed	
	deft	2.8± 2.64	2.4±2.17	1.09	0.36ns

Significance level p≤0.05, * significant, ns=non-significant

Table (2): Gingival hyperplasia scores in both groups and comparison between dialysis and transplantation groups (chi-square test)

Gingival hyperplasia	Dialysis group (n=60)	Transplantation group (n=24)	X^2	P
Score 0	58 (96.6%)	20 (83.3%)	7.45	0.058**ns**
Score 1	1 (1.7%)	3 (12.5%)		
Score 2	1 (1.7%)	0		
Score 3	0	1 (4.2%)		

Significance level p≤0.05, ns=non-significant

50% and it varies by age, gender, and race. Children under 12 years are more likely to have congenital defects with more risk of males.[21] That is because males are more prone to urinary tract obstructive malformations and this can justify the higher percentage of males in the current study. [22-24]

Regarding the results of this study concerning the most common cause of Chronic Kidney Disease among all the study participants was familial /metabolic diseases by 33.3% and 37.5% in haemodialysis and kidney transplantation respectively. This result agreed with another studies which reported CAKUT as the most prevalent etiology of Chronic Kidney Disease by a 28.4%, 34.5%, and 21.2% respectively. [25-27] That was consistent with the retrospective study which concluded that CAKUT was the most common cause of ESRD followed by glomerular diseases by 31.1% and (18.9%) respectively.[28] In this study, the parents of participants with familial/metabolic diseases reported consanguineous marriages which predispose to the development of congenital anomalies. This result goes in agreement with another studies .[19,29]

Oral hygiene negligence was the most common finding in almost all study participants. Irregular brushing was observed in group I as well as group II by 48.3% and 58.3% respectively. The results were consistent with other studies.[30-31] The proposed explanation was that oral hygiene negligence was due to the patients' poor level of education and low socioeconomic status. Also, renal haemodialysis is a time-consuming procedure and requires multiple sessions of prolonged duration which significantly compromises the patient's lifestyle .[32]

The majority of the study subjects were caries-free, although they were under a carbohydrate-rich diet, hidden sugars in long–term medicated syrups and presented with bad oral hygiene. Moreover, the urea level was in the normal range (10.28±2.56) which would not induce a change in the pH of saliva. In this study, the low caries was attributed to the use of medications containing calcium and vitamin D. 86.7% of participants receiving haemodialysis were under calcium-containing drug (calcimate) and 51.24% under vitamin D supplements (one alpha). Calcium and vitamin D supplementation are from the protocol of management of ESRD patients either under haemodialysis or waiting for kidney transplantation. The effect of vitamin D and calcium medications on the risk of caries has been highlighted by a systematic review which concluded that the percentage of caries decreases in the population under these drugs by 47% .[33] That is because vitamin D assists in the absorption of calcium and phosphorus from the intestine, which in turn increases the degree of mineralization of teeth.[34] Additionally, all the study participants have not presented with xerostomia that is one of the main contributing factors of dental caries.

Gingival hyperplasia was not encountered in almost all study groups, only 3.4% in the haemodialysis group and 16.8% in the transplantation group showed gingival overgrowth. The reported gingival enlargement was due to local factors as poor oral hygiene, bacterial plaque accumulation, and medications like azathioprine (Imuran). Also, the stage of mixed dentition is associated with a slight alteration in the gingiva contour as the result of the permanent teeth eruption. Eruption gingivitis may be induced by a greater risk of plaque accumulation in areas of shedding primary teeth and erupting permanent teeth since oral hygiene will be difficult to perform. The inflammatory changes accentuate the normal prominence of the gingival margin and create the impression of a marked gingival enlargement in normal conditions.[35] In the present study, the low

percentage of gingival hyperplasia is assigned to the use of tacrolimus instead of other immunosuppressive drugs (like cyclosporine) that cause gingival overgrowth. Almost all the participants were taking tacrolimus (prograf); only 2 patients were given azathioprine (Imuran). This result was in accordance with another study.[36] whom gingival enlargement was described only in children under Imuran.

Enamel hypoplasia was only detected in a small percentage of patients at both groups as 25% in the haemodialysis group (15 patients) and 29.2% in the transplantation group (seven patients)**.** Different severity was detected as eight participants under haemodialysis were with hypoplasia, while at the transplantation group, three patients showed demarcated hypoplasia. The same results were concluded in similar studies**.** [37-38] The severity of hypoplasia is related to the age, the onset of the disease, and the duration under haemodialysis therapy.

Oral candidiasis was not reported in the present study as the patients were not suffering from severe uremia (elevated urea and BUN >150mg/dl) that predisposes to candida infection. The urea level was within the normal range 10.28±2.56 in group I, while the level of BUN in group II was 33.83± (19.88). Lack of oral candidiasis in the dialysis group can be explained due to the filtration of the blood from urea by renal dialysis procedure. While concerning the transplantation group, the study subjects were under a low maintenance dose of immunosuppressive therapy that does not alter the immune system and doesn't predispose to candida infection**.** [39]

Conclusions

1. The majority of patients in both groups never visited the dentist in the last year that is mainly because of the lack of awareness; the oral problems (caries, enamel hypoplasia and gingival hyperplasia) were not a major concern for those patients, which could indicate the adaptation to impaired oral health or a change of health priorities.
2. The medications associated with ESRD have highly affected the oral cavity as vitamin D supplements decrease the risk of dental caries.
3. The substitution of cyclosporine with tacrolimus reduces the potential of gingival enlargement in renal transplantation patients.
4. The oral health status is not considered a priority to ESRD patients due to the chronic nature of their disease, frequent hospitalization and restricted diet and fluid regimen.

Recommendations

Long term studies are recommended to investigate the effect of vitamin D and calcium medications on tooth decay. Increasing the awareness among dialysis patients about the importance of the need for primary dental prevention. The incorporation of dental service into the medical program and oral hygiene care is necessary because children undergoing strict treatment routines have got less time for preventive or treatment procedures regarding their oral complaints.

Limitations of the study:

This study is a cross-sectional study at a certain time point so the long-term effect of the disease or medications on the oral findings weren't detected.

Clinical examination wasn't performed on dental units and was inconvenient for both the researcher and the patients.

Conflict of interest

The authors declare no conflict of interest.

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