ORAL MANIFESTATIONS IN RENAL TRANSPLANT RECIPIENTS IN SULAIMANI CITY, KURDISTAN REGION, IRAQ

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ABSTRACT

Background

Renal transplant is the treatment of choice for patients with end-stage renal disease. To prevent graft rejection, recipients are receiving a combination of immunosuppressive medications. Among common side effects of the therapy, many oral manifestations are found either as a direct effect of the drugs or due to suppression of the immune system.

Objectives

This study aimed to investigate oral problems and their relation to the oral hygiene status of the recipients.

Patients and methods

This cross-sectional study was performed on 150 renal transplant recipients in Sulaimani city, Kurdistan Region, Iraq, from December 2018 to June 2019. Any existing condition was diagnosed on a clinical basis. Additional data including a questionnaire of demographic, pharmacologic, and transplant duration were also collected.

Results

The 150 transplant recipients included 103 males and 47 females (mean age 40.5 years). A total of 22.1% had at least one oral lesion. The most common lesion was gingival hyperplasia in 16.7% of cases who received cyclosporine A as the primary immunosuppressive medication, followed by candida infection 4.7%, which were mostly in patients with a transplant duration of less than 3 months.

Conclusion

In this study, we reported a lower incidence of oral lesions compared to other studies published in the literature. Improvement of oral hygiene status of the recipients is associated with reduced oral manifestation specifically gingival hyperplasia. Also, using prophylactic antifungal and antiviral agents during the first few months of transplant has a direct effect on reducing the number and frequency of viral and fungal infections.

Keywords: *Renal transplant; Immunosuppression; Oral hygiene; Oral lesions.*

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INTRODUCTION

Solid-organ transplantation has increased the survival and improved the quality of life of patients with end-stage organ failure. Historically, the first successful kidney transplantation began with Dr. Murray and his team in 1954 with the transplantation of a kidney between the identical twin Herrick brothers. Since then, kidney transplantations are considered globally as conventional procedures for patients with irreversible kidney failure for restoring a healthy and productive life. It is considered as the treatment of choice which has shown to increase the survival rate as compared to patients on dialysis [1, 2].

One of the significant concerns after transplantation is the risk of rejection. To decrease or eliminate the risks of acute and chronic rejection of kidney transplants, patients receive immunosuppressive therapy at the highest level in the early period (induction phase) and reduced for maintenance therapy. Currently, conventional immunosuppressive protocols consist of triple therapy: a calcineurin inhibitor, an adjunctive agent, and corticosteroids [3].

These medications affect various components of the immune system. Corticosteroids have specific action, which causes inhibition of the dendritic cells, transcription of cytokines genes, and all the stages of the T-cell activation. The nonspecific effects are lymphopenia. Calcineurin inhibitors [Cyclosporine A (CsA) and Tacrolimus] suppress the activation of T lymphocytes. The third agent in the protocol is Anti-proliferative agents [Azathioprine and mycophenolate mofetil (MMF)] provide additive effects, but less essential than the calcineurin inhibitor and corticosteroid component. Azathioprine is a purine analog that inhibits DNA replication and suppresses B and T cell proliferation. MMF produces cytostatic effects on T and B cells [3,4].

Kidney allograft recipients also have significant comorbidities since prior to the kidney transplantation, the majority of the patients have undergone dialysis for varying periods [5]. Besides systemic problems, transplant recipients are also liable to orofacial complications, mainly due to the effects of immunosuppressive drugs[6]. One of the most common complications is gingival enlargement, which is associated with the use of a Calcineurin inhibitor. The condition may be exaggerated by the co-administration of a calcium channel blocker used in hypertensive patients in this population [7, 8].

The oral hygiene status of the transplant recipients has a significant effect on the degree of oral manifestations and their severity, especially gingival hyperplasia [9].

Depressed immune response in this group of patients is associated with an increased risk of oral infection and other associated complications, including fungal infections. These have different presentations. As an example, oral candidiasis may present as pseudomembranous, atrophic, and hyperplastic [10, 11, 7].

Viral infections are another common problem. Herpes simplex virus (HSV) and other types of herpes viruses are the most common viral pathogens. Varicella-zoster virus (VZV) and Epstein Barr Virus (EBV), as well as cytomegalovirus (CMV), have been involved in oral diseases [7].

These infectious agents have different presentations in immunosuppressed patients in comparison to immunocompetent individuals. The medications increase the risk of invasive or disseminated infections which are potentially life-threatening and considered as an important cause of morbidity and mortality. The highest number of infections occurs during the early period after transplantation especially the first month. The incidence of these infections can be reduced by the use of prophylactic medications [12].

The knowledge of oral lesions due to immunosuppressive medication in renal transplant recipients is essential to improve the quality of life in this population [13]. Therefore; the current study aimed to investigate oral lesions in a group of renal transplant recipients, analyze the association with the use of medications and oral hygiene status of this group of patients.

PATIENTS AND METHODS

Study design

This cross-sectional study was performed on 150 renal transplant recipients in the private clinic of a Nephrologist during their routine follow-up visits from December 2018 to June 2019. The study was reviewed and approved by the Ethical Committee of the Kurdistan Board for Medical Specialties, and all the participants signed an informed consent designed for this study.

The participants were recruited randomly. Patients above the age of 18 years who had received a renal transplant were included. While the exclusion criteria were those recipients in the state of acute rejection or chronic rejection who were receiving dialysis. Details of gender, age, history of dialysis, duration of transplant, immunosuppressive treatment with their

dose and duration, co-existing systemic disease, and use of concomitant agents were also collected.

Clinical Assessment

A single investigator examined all participants in this study. Oral and mucosal lesions were diagnosed clinically.

The coated tongue was diagnosed through visual inspection of the dorsal surface of the tongue when protruded and assessed by the Index of Kojima et al (1985) as well as a modified index that assesses the location of the coating rather than its thickness and color.

The scores are as follows:[14, 15]

0 -No coating (visual)

1 - A thin coating of less than one-third of the back of the tongue

2 - A thin coating of less than two-thirds of the tongue or less than one third covered with a thick coating

3 - More than two-thirds covered with a thin coating on tongue less than two-thirds covered with a thick tongue coating on the tongue

4 - More than two-thirds of the tongue is covered with a thick coating

The degree of gingival enlargement was also scored following the Carranzas' (2006) classification, which included:[16]

• Grade 0: No signs of gingival enlargement.

• Grade I: Enlargement of interdental papilla.

• Grade II: Enlargement of the papilla and extends to involve marginal gingiva.

• Grade III: Enlargement covering three quarters or more of the crown.

Oral candidiasis was diagnosed depending on the characteristic clinical feature and classified to pseudomembranous candidiasis, erythematous candidiasis, angular cheilitis, and median rhomboid glossitis [17].

Herpes simplex infection is diagnosed as erosions and ulcerations or crust preceded by blisters. [18]

Halitosis was assessed by organoleptic measurement and scaled from 0- to 5-point (0: no odor, 1: barely noticeable, 2: slight but noticeable, 3: moderate, 4: strong, and 5: extremely strong) [19].

Subjective assessment of xerostomia was performed using the Fox et al questionnaire. Positive responses to all the questions, regarded as low saliva flow rates. [20,21]

The questionnaire included:

- Does the amount of saliva in the patient's mouth seem to be too little, too much, or is it not noticeable?
- Does the patient have any difficulty in swallowing?
- Does the patient feel the dryness of the mouth when having a meal?
- Do the patient sip liquids to aid in swallowing dry food?

The oral hygiene status of the patient was assessed using the Simplified Oral Hygiene Index, designed by Greene and Vermillion (1964). The examination included six tooth surfaces (minimum of 2) including four posterior teeth and two anterior teeth. The amount of both debris and calculus was recorded and OHI was calculated using a specifically modified equation. The values range from 0-6 and accordingly defined as good(0-1.2), fair (1.3-3) and poor (3.1-6) [22].

Statistical analysis

After data collection and before data entry and analysis, the questions of the study were coded. Data entry was performed using an excel spreadsheet then the statistical analysis was performed by the SPSS program, version 21 (IBM SPSS Statistical Package for the Social Sciences). Data were presented in tabular forms showing frequency and relative frequency distributions of different variables and means and standard deviations were used to describe the quantitative variables. Compliance of quantitative random variables with the Gaussian curve (normal distribution) was analyzed using the Kolmogorov-Smirnov test. The variables which shown to be normally distributed quantitative continuous variables were described by mean and SD (standard deviation). Statistical significance of differences between two groups was assessed using an independent sample t-test, while between more than two groups, ANOVA test was used.

Some variables were not distributed normally as oral hygiene scores. Median and mean rank was used for description besides arithmetic means and standard deviations. Differences in mean ranks between the 2 groups were assessed by non-parametric tests (Mann-Whitney), and for variables that divided the data into several groups Kruskal Wallis test was used for

comparing the medians and mean ranks among these groups.

For finding the risk of certain variables as the duration of transplant and regimens of immunosuppressant medications on oral outcomes as gingival hyperplasia and halitosis crude odd ratio were used and then multivariate analysis was used to find the adjusted odds ratio. The *p*-values of 0.05 or less were used as cut-off points for the significance of the statistical test.

RESULTS

A total of One hundred and fifty (150) renal transplant recipients were examined. The mean age was 40.5 ± (range 19 to 65), with male predilection (68.7%). The duration of the transplant ranged between 0.3 and 189.3 months. The most common associated systemic disease were hypertension and diabetes mellitus with a range of 45.3% and 27.3% respectively. The majority of the patients underwent hemodialysis, before the transplant ; mostly two sessions per week, Table 1.

Table 2 presents a summary of the oral problems that were observed during the period of the study. The most common lesion was gingival hyperplasia which was found in 16.7% of participants mostly Grade 1, followed by candida infection (4.7%). The majority of the patients presented with halitosis and coated tongue (64.7% and 62.7% respectively), while the complaint of dry mouth was reported only in 13 patients (8.7%). Furthermore, the oral examination included evaluation of oral hygiene status; 35.3% of the participant had good, 28% fair, and 36.7% poor oral hygiene.

All transplant recipients were receiving triple immunosuppressive therapy, among which 77 patients (51.3%) were taking (Prednisolone, Tacrolimus, and Mycophenolate mofetil); 69 patients (46%) were taking a combination of (Prednisolone, Cyclosporin A, and Mycophenolate mofetil) whereas 44 patients (29.3%) with the duration of transplant less than 3 months were receiving prophylactic medication. Other immunosuppressive regimens and mean dose of drugs with standard deviation, Table 3.

Table 4 reveals the association of the observed findings with oral hygiene score. Statistical analysis showed a direct association of oral hygiene status with gingival hyperplasia (p= 0.006), coated tongue (p= 0.001), and halitosis (p=0.001).

To evaluate the impact of transplant duration, patients were divided into two groups; a group of patients with a duration equal and less than three months (≤ 3 months), and the second group included patients who had transplant surgery for more than three months (> 3 Months). Gingival hyperplasia was more significant in patients with a duration of more than three months with a P-value of 0.16, Table 5.

Table 6 is showing the odds ratio (OR) and 95% confidence interval (CI) for multiple logistic regression. Gingival hyperplasia was chosen first for the drug regimen, second for the duration of transplant, and third for the use of calcium channel blocker antihypertensive drug. The use of Cyclosporine was a significant predictor of gingival hyperplasia (OR=8.04) when compared with patients using Tacrolimus, while the increased duration of the transplant was significantly associated with the increased risk of gingival hyperplasia (OR=3.71). Moreover, the use of calcium channel blockers was also associated with an increased risk of gingival hyperplasia (OR=3.16).

We also calculated the effect of concomitant use of Ca channel blocker with immunosuppressive medications on gingival hyperplasia. The comparison was made between the group of patients receiving CsA or tacrolimus as the main immunosuppressant. The combination of CsA with Ca channel blocker increases the risk of gingival hyperplasia (OR =3.29)., Table 7.

Table 1. Subject variable and demographic characteristics.

Age		
19 - 30 Years	35	23.3%
31 - 40 Years	39	26.0%
41 - 50 Years	51	34.0%
51 - 65 Years	25	16.7%
Mean ± SD	40.5 ± 11.4	
Gender		
Male	103	68.7%
Female	47	31.3%
History of dialysis	120	80.0%
Number of dialysis per week		
One	1	0.7%
Two	77	51.3%
Three	42	28.0%
Duration of transplant (months)		
Minimum – Maximum	0.3 – 189.3	
Mean (Standard deviation)	16.29 (22.80)	
Diabetes Mellitus	41	27.3%
Hypertension	68	45.3%
Thyroid problem		
Hypothyroid	11	7.3%
Thyrotoxicosis	1	0.7%
Connective tissue disease	1	0.7%

Table 2. Oral problems in renal transplant recipients.

Oral problems	Frequency	%
Oral hygiene status		
Good (0.0 – 1.2)	53	35.3%
Fair (1.3 – 3.0)	42	28.0%
Poor (3.1 – 6.0)	55	36.7%
Halitosis	97	64.7%
Barely	25	16.7%
Slight	32	21.3%
Moderate	25	16.7%
Strong	15	10.0%
Coated tongue (score)	94	62.7%
One	63	42.0%
Two	18	12.0%
Three	10	6.7%
Four	3	2.0%
Gingival hyperplasia (grade)	25	16.7%
One	19	12.7%
Two	5	3.3%
Three	1	0.7%
Dry mouth	13	8.7%
Candidal infection	7	4.7%
Pseudo-membranous candidiasis	3	2.0%
Erythematous candidiasis	2	1.3%
Angular cheilitis	2	1.3%
Geographic tongue	1	0.7%
Hairy tongue	1	0.7%

Table 3. Medications and immunosuppressive regimens.

Medications used by patients	Frequency	%	The dose	
			Mean	Standard_ Deviation
Prednisolone	150	100.0%	10.13	7.185
Cs A	71	47.3%	194.51	104.414
Tacrolimus	78	52.0%	3.63	2.705
Azathioprine	3	2.0%	83.33	28.868
MMF	147	98.0%	1986.39	100.437
Sirolimus	1	0.7%	0.25	
Prophylactic agents	44	29.3%		
Valganciclovir	41	27.3%	779.27	201.859
INH	41	27.3%	226.83	90.206
Trimoxazole	40	26.7%	852.00	202.993
Miconazol gel	36	24.0%		
Antihypertensive drugs	67	44.7%		
Amilodipine	60	40.0%	8.50	2.807
Diltiazem	2	1.3%	105.00	21.213
Metoprolol	25	16.7%	60.00	20.400
Immunosuppressant Regimens				
Pridnisolone + Cs A + MMF	69	46.0%		
Pridnisolone + Tacrolimus + MMF	77	51.3%		
Pridnisolone + Azathioprine + Tacrolimus	2	1.3%		
Pridnisolone + Cs A + Azathioprine	1	0.7%		
Pridnisolone + Sirolimus + MMF	1	0.7%		

MMF: Mycophenolate mofetil, INH: Isoniazid, CsA: Cyclosporin A

Table 4. Association of oral hygiene status and oral problems.

Oral problems		Oral hygiene score			
		Frequency	Median	Mean rank	P-value
Candidal infection	No candida infection	143	1.8	74.7	0.74 [b]
	Pseudo-membranous candidiasis	3	2.8	91.8	
	Erythematous candidiasis	2	3.3	102.5	
	Angular cheilitis	2	2.1	79.0	
Gingival hyperplasia grade	Zero	125	1.8	70.2	0.006 [b]
	One	19	4.3	106.0	
	Two	5	2.0	82.5	
	Three	1	4.2	118.0	
Coated tongue score	Zero	56	1.0	51.5	< 0.001 [b]
	One	63	2.8	82.7	
	Two	18	3.4	99.9	
	Three	10	4.6	108.4	
	Four	3	4.2	115.3	
Halitosis	No Odor	53	0.8	34.9	< 0.001 [b]
	Barely	25	1.8	72.9	
	Slight	32	3.3	94.5	
	Moderate	25	4.0	113.8	
	Strong	15	4.6	118.9	
Dry mouth	Yes	13	2.4	85.4	0.39 [a]
	No	137	1.8	74.6	
Geographic tongue	Yes	1	1.8	71.0	0.92 [a]
	No	149	1.9	75.5	
Hairy tongue	Yes	1	1.8	71.0	0.92 [a]
	No	149	1.9	75.5	

Mann- Whitney U test [a]
Kruskal Wallis test [b]

Table 5. Association of oral problems and duration of transplantation.

Oral problems		Duration of transplantation (months)		P value
		≤ 3 months	> 3 Months	
Candidal infection				
	Pseudo-membranous candidiasis	3	0	0.04
	Erythematous candidiasis	1	1	
	Angular cheilitis	0	2	
	No candida infection	41	102	
Gingival hyperplasia grade				
	Zero	42	83.0	0.16
	One	3	16	
	Two	0	5	
	Three	0	1	
Coated tongue score				
	Zero	16	40	0.62
	One	21	42	
	Two	4	14	
	Three	4	6	
	Four	0	3	
Halitosis	No Odor	17	36	0.50
	Barely	9	16	
	Slight	8	24	
	Moderate	9	16	
	Strong	2	13	
Dry mouth	Yes	3	10	0.57
	No	42	95	
Geographic tongue	Yes	0	1	0.51
	No	45	104	
Hairy tongue	Yes	1	0	0.13
	No	44	105	

Table 6. Odds ratio (OR) and confidence interval (CI) for multiple logistic regression.

		Gingival hyperplasia			
		Crude OR (95% CI)	**P- value**	**Adjusted OR**	**p-value**
Treatment regimen	Cyclosporine A	8.04 (2.6 - 24.8)	< 0.001	8.87 (2.74 - 28.76)	< 0.001
	Tacrolimus	1			
Transplant duration	> 3months	3.71 (1.05 - 13.11)	0.04	4.28 (1.11 - 16.56)	0.035
	≤ 3 months	1			
Ca channel blocker	Yes	3.16 (1.29 - 7.73)	0.01	3.72 (1.38 - 10.0)	0.01
	No	1			

- **Cyclosporine A and Tacrolimus were chosen as the main immunosuppressive drugs.**
- **One case which was receiving Sirolimus was excluded.**
- **Calcium channel blocker was used in 41.3% of the total number of participants; Amlodipine in 40% (mean dose of 8.5mg), Diltiazem 1.3% (mean dose of 105 mg)**

Table 7. Effect of concomitant use of Ca channel blocker.

	Gingival hyperplasia	
	Odds Ratio (95% CI)	**P value**
Cyclosporine A and Ca Channel blocker	3.29 (1.15 - 9.41)	0.03
Cyclosporine A Alone	1	
Tacrolimus and Ca Channel blocker	2.52 (0.40 - 16.0)	0.33
Tacrolimus Alone	1	

DISCUSSION

The survival rate of renal transplant recipients has increased due to the improvements in the selection of donor and recipient, study process, modified surgical techniques, immunosuppressive medication and protocols, and better management of complications and associated medical problems [23]. Renal transplant recipients are receiving life-long immunosuppression to prevent allograft rejection, which either starts before surgery or immediately after the surgery. Usually, the highest doses of medications are administered during the first few months which are then lowered to the maintenance dose. The protocol for immunosuppression commonly consists of combination treatment with a calcineurin inhibitor, an anti-proliferative agent, and a corticosteroid [1, 24].

In our study, different immunosuppressive regimens were applied. The most frequently used immunosuppressive drugs were Tacrolimus with prednisolone and MMF which was comparable with the Lopez –Pintor (2010) study, while previous studies by King et al and de la Rosa et al used prednisolone with azathioprine and cyclosporine as an immune suppressant treatment.

Additionally, all the patients in the early periods of transplantation in our study received prophylactic Trimethoprim-Sulphamethoxazole, Isoniazid, Valganciclovir, and Miconazole oral gel that was prescribed depending on KDIGO clinical practice guideline for the care of kidney transplant recipients [25] .This prophylactic regimen, which has been applied during the first three months, was not mentioned in other published researches [23, 26, 27, 18, 28]. It is well known that different oral problems occur in patients with renal transplantation, mainly as a direct consequence of drug-induced immunosuppression. In the literature a wide discrepancy in the presentation of oral problems reported by several authors. These discrepancies might be due to changes in the immunosuppressive therapy regimen with increased usage of induction agents and the replacement of azathioprine by mycophenolate mofetil. Also in recent years, the use of tacrolimus has

been increased from 13% to 79 %, while the use of cyclosporine A has reduced from 76% to 15% [29].

Our research included an examination of 150 renal transplant patients; among them, 22.1% had at least one oral lesion, and the most frequent lesion was gingival hyperplasia in 16.7%. The study by King et al included 159 renal transplant recipients, and the prevalence of oral lesions of 54.7% was reported with the most common lesion being gingival hyperplasia [26]. While Al-Mohaya et al investigated oral lesions in 58 renal transplant recipients compared to 52 HC subjects. A total of 97 oral lesions were found in transplant recipients. In this study, gingival hyperplasia was also the most frequently encountered lesion. The second most frequent oral lesion in renal transplant recipients was erythematous candidiasis [27].

On the other hand, a very high proportion of oral lesions (60%) were reported in the study published by Rosa et al in which 90 patients participated in the research. Again the most frequent lesion was gingival hyperplasia [23]. Similar results were published by In Spolidorio et al in which 155 renal transplant recipients were recruited for the study. The oral hygiene status of the patients was also examined. Gingival hyperplasia was manifested in 68 recipients, herpes simplex virus infection in 10 cases, and squamous cell carcinoma in 3 cases [28]. Interestingly the study by Lopez-Pintor et al involved 500 RTP and 501 healthy control. Although the study excluded gingival hyperplasia, however, 40% of RTP presented with oral problems, the most frequent lesion was candidiasis [18].

In Vescovi et al the study was conducted on 121 renal transplant patients that were receiving CsA. A proportion of 48.4% of the patients had gingival hyperplasia. The duration of immunosuppressive treatment and the prevalence of gingival lesions were significantly associated with the screening group. An association between oral hygiene scores and the degree of gingival hyperplasia was also demonstrated [30].

In general, the prevalence of gingival hyperplasia in patients with renal transplantation among CsA users ranges between 20% and 45%, being exacerbated by combining with calcium channel blockers (CCB) [31]. We reported a lower frequency of gingival hyperplasia when compared to other studies, which were 25 cases (16.7%). In King et al., the frequency was 35 cases (22%). In Al Mohaya et al a much higher percentage has reported a total of 43 (74.1%) of all patients had gingival hyperplasia. In Rosa et al study, 44 patients (48.9%) were reported. In the study by Spolidorio et al, the number of cases suffering from gingival hyperplasia were 68 patients, of which 54 renal recipients were treated with CsA and CCB, and 14 patients were treated with CsA alone.

In this study, we also assessed the association between gingival hyperplasia and several variables that have influenced the presence and the degree of gingival hyperplasia. In particular, we found that there was a low prevalence of gingival hyperplasia during the first three months of therapy, and patients treated with CsA had a high level of gingival hyperplasia. These findings are in agreement with the study reported by Vescovi et al (2005) indicating that periods of transplantation will enhance gingival hyperplasia when the patients receiving CsA medication. Spolidorio et al. suggested that renal transplant recipients on CsA are more susceptible to develop oral complications than those who receive Tacrolimus [28].

Concerning the relationship between oral hygiene status and the observed oral findings in this study, we found a significant association between oral hygiene scores and the degree of gingival hyperplasia which was consistent with the findings by Vescovi et al. [30].

Candida infection was most significant among patients with recent renal transplants. In the current study, we reported 7 cases of candida infection (4.7%), which is regarded as a lower percentage when compared to previously published studies that shown a higher incidence of candida infection. In the study by King et al the prevalence of candidiasis in RTR was 10.1% (16 cases), while the research by Al-Mohaya et al showed that erythematous candidosis and Angular cheilitis were the prevalent types of oral candidiasis (15.5% and 1.7% respectively). Whereas the investigation by Lopez-Pintor et al revealed that the percentage of candidiasis was 7.4% in RTPs. This reduced frequency of oral candidiasis might be due to the use of miconazole oral gel as a prophylactic agent by the entire patients during the early postoperative period in the current study.

A coated tongue is another frequent finding in renal transplant recipient; 94 patients in our study had coated tongue (62.7%) which is relatively regarded as a higher prevalence number when compared to a study performed by Al-Mohaya et al [13 cases (22.4%)], and the study carried out by Rosa et al in which the number was 20 with the percentage of (22%).

Despite being a common infection among transplant recipients, no cases of herpes virus infection were reported in our study. The reported prevalence of oral HSV lesions in RTPs ranges from 0% to 11.3% [26, 23, 28]. The prevalence of oral HSV infection in the renal transplant recipients in the study performed by Lopez-Pintor et al was 2.6%. This could be due to the effect of antiviral medication which is prescribed prophylactically for all transplant recipients in our study during the early transplant period.

Xerostomia has not been subject of study in renal transplant recipients in most of the previously published articles. In Lopez-Pintor et al study xerostomia was more common in RTPs [7 cases(1.4%)] when compared to the healthy control. In our study subjective complaint of dry mouth was found in 13 cases (8.7%). We could not perform the salivary flow rate to confirm the existence of xerostomia due to the improper clinical setting for the accurate examination of participants.

None of the patients in the current study had hairy leukoplakia. In previous studies carried out by king et al (1994); Al-Mohaya et al (2009); Lopez-pintor et al (2010), Rosa et al (2005) (18 cases 11.3%, 5 cases 8.6 %, 7 cases 1.4%, and 11 cases 12.2%) were reported respectively.

We reported no cases of malignancy in this study even though organ transplant recipients have an enhanced risk of developing malignant tumors. The incidence of squamous cell carcinomas and basal cell carcinomas is progressively increased after transplantation from a cumulative risk of 10% after 10 years to a risk of 40% after 20 years of graft survival [32].

In conclusion, this study showed that renal transplant recipients are liable for a wide range of oral complications due to the administration of immunosuppressive medications depending on the type and duration of these agents. However, prophylactic medications that are prescribed during the first few months after transplant surgery had an essential role in reducing some of these complications such as herpes virus infection and also fungal infection which otherwise may be serious and life-threatening in this group of patients. Moreover, these complications are also directly affected by the oral hygiene status of the patient. Those recipients with good oral hygiene had a lower percentage and lesser severity of oral manifestations. This emphasizes applying various oral care programs to maintain good oral health status to improve the quality of life of this group of patients.

Conflict of Interest

The authors had nothing to declare, and they did not receive any fund from any source.

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REFERENCES

1. Black CK, Termanini KM, Aguirre O, Hawksworth JS, Sosin M. Solid-organ transplantation in the 21st century. Ann Transl Med. 2018; 6(20):409-409.

2. Sass DA, Doyle AM. Liver and Kidney Transplantation. Med Clin North Am. 2016; 100(3):435-448.

3. Muntean A, Lucan M. Immunosuppression In Kidney Transplantation. Clin Inst Urol Ren Transplant. 2013; 86(3):177-180.

4. Kalluri HV. The current state of renal transplant immunosuppression: Present and future. World J Transplant. 2012; 2(4):51-68.

5. Levarda-Hudolin K. Oral Lesions In Kidney Transplant Recipients. Acta Clin Croat. 2016; 55(3):459-463.

6. Petti S, Polimeni A, Berloco P, Scully C. Orofacial diseases in solid organ and hematopoietic stem cell transplant recipients. Oral Dis. 2013; 19(1):18-36.

7. Michael Glick; William M. Feagans Burket's Oral Medicine. 12th edition. Shelton, Connecticut: People's Medical Publishing Houset; 2015. 521–543 p.

8. Sahebjamee M, Shahabi MS. Oral Lesions in Kidney Transplant Patients Oral Lesions in Kidney Transplant Patients. Iran J kidney Dis. 2010; 4(7):232-236.

9. Castronovo G, Liani G, Fedon A, Costantinides F, Bevilacqua L, De Iudicibus S, et al. The effect of nonsurgical periodontal treatment on the severity of drug-induced gingival overgrowth in transplant patients. Quintessence Int (Berl). 2014;45(2):115–24.

10. Lopez-Pintor R, Hernandez G, de Arriba L, de Andres A. Oral candidiasis in patients with renal transplants. Med Oral Patol Oral y Cir Bucal. 2013; 18(3):e381-e387.

11. Imko-Walczuk BB, Prędota A, Okuniewska A, Jaśkiewicz J, Zegarska B, Placek W, et al. Superficial Fungal Infections in Renal Transplant Recipients. Transplant Proc. 2014; 46(8):2738-2742.

12. Chapman JR. The KDIGO Clinical Practice Guidelines for the Care of Kidney Transplant Recipients. Transplantation. 2010; 89(6):644-645.

13. da Silva LCF, de Almeida Freitas R, de Andrade MP, Piva MR, Martins-Filho PRS, de Santana Santos T. Oral Lesions in Renal Transplant. J Craniofac Surg. 2012; 23(3):e214-e218.

14. Kojima K. Clinical studies on the coated tongue. Japanies J Oral Maxillofac Sur. 1985; 31:1659-1676.

15. Nenova-Nogalcheva A, Konstantinova D, Nogalchev K. A modified tongue coating index. Scr Sci Med Dent. 2017; 3(1):32-35.

16. Michael G. Newman. Henry H. Takei, Perry R. Klokkevold, Fermin A.Carranza. Carranza ' S Clinical Periodontology 10th edition. St. Louis, Missouri. Saunders Elsevier. 2006. 743 p.

17. Meechan JG. Oral Diagnosis: The Clinician's Guide. Br J Oral Maxillofac Surg. 2002; 38(5):578.

18. Lo´pez-Pintor RM, Herna´ndez G, de Arriba L, de Andre´s A. Comparison of oral lesion prevalence in renal transplant patients under immunosuppressive therapy and healthy controls. Oral Dis. 2010; 16(1):89-95.

19. Aylikci B, Çolak H. Halitosis: From diagnosis to management. J Nat Sci Biol Med. 2013; 4(1):14.

20. Villa A, Connell C, Abati S. Diagnosis and management of xerostomia and hyposalivation. Ther Clin Risk Manag. 2014; 11(1):45.

21. Fox PC, Busch KA, Baum BJ. Subjective reports of xerostomia and objective measures of salivary gland performance. J Am Dent Assoc. 1987; 115(4):581-584.

22. Greene JG, Vermillion JR. The Simplified Oral Hygiene Index. J Am Dent Assoc. 1964; 68(1):7-13.

23. de la Rosa-García E, Mondragón-Padilla A I-CM, MA B-R. Lesiones bucales en un grupo de pacientes con trasplante renal Oral lesions in a group of kidney transplant patients. Med Oral Patol Oral Cir Bucal. 2005; 10(1):196-204.

24. Hardinger KL, Brennan DC. Novel immunosuppressive agents in kidney transplantation. World J Transplant. 2013; 3(4):68.

25. Kasiske BL, Zeier MG, Chapman JR, Craig JC, Ekberg H, Garvey CA, et al. KDIGO clinical practice guideline for the care of kidney transplant recipients: a summary. Kidney Int. 2010; 77(4):299-311.

26. King GN, Healy CM, Glover MT, Kwan JTC, Williams DM, Leigh IM, et al. Prevalence and risk factors associated with leukoplakia, hairy leukoplakia, erythematous candidiasis, and gingival hyperplasia in renal transplant recipients. Oral Surgery, Oral Med Oral Pathol. 1994; 78(6):718-726.

27. Al-Mohaya MA, Darwazeh AM-G, Bin-Salih S, Al-Khudair W. Oral lesions in Saudi renal transplant patients. Saudi J Kidney Dis Transpl. 2009; 20(1):20-29.

28. Spolidorio L, Spolidorio D, Massucato E, Neppelenbroek K, Campanha N, Sanches M. Oral health in renal transplant recipients administered cyclosporin A or tacrolimus. Oral Dis. 2006; 12(3):309-314.

29. Knoll G. Trends in Kidney Transplantation over the Past Decade. Drugs. 2008; 68(Supplement 1):3-10.

30. Vescovi P, Meleti M, Manfredi M, Merigo E, Pedrazzi G. Cyclosporin-Induced Gingival Overgrowth : A Clinical – Epidemiological Evaluation of 121 Italian Renal Transplant Recipients. J Periodontol. 2005; 76(8):1259-1264.

31. Lima RB, Benini V, Sens YAS. Gingival Overgrowth in Renal Transplant Recipients: A Study Concerning Prevalence, Severity, Periodontal, and Predisposing Factors. Transplant Proc. 2008; 40(5):1425-1428.

32. Hyckel P, Schleier P, Meerbach A, Berndt A, Kosmehl H, Wutzler P. The therapy of virus-associated epithelial tumors of the face and the lips in organ transplant recipients. Med Microbiol Immunol. 2003; 192(3):171-176.