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Prevalence of oral mucosal and periodontal disease amongst patients receiving dialysis

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ABSTRACT

Introduction

End-stage renal disease (ESRD) requires renal replacement therapy (RRT), namely a renal transplant or renal dialysis or both. Dialysis corrects the electrolyte imbalance and reduces circulating urea and creatinine levels. ESRD patients may present with oral complications and disease due to impaired renal functions, associated comorbidities, or the pharmacological management thereof.

Aims and Objectives

To determine the prevalence of periodontal- and oral mucosal disease in ESRD patients undergoing dialysis. Recommendations will be made regarding dental treatment needs and dental management.

Design

Cross-sectional study.

Methods

Fifty-three ESRD patients were evaluated for mucosal lesions and periodontal disease. Patient's age, race, gender, comorbidities, dialysis duration and medication were recorded. Treatment urgency was determined, and patients referred accordingly for appropriate dental treatment.

Results

Mean age of patients was 42,9 ±10,4 years with a median time on dialysis of 30 months. Majority of patients were hypertensive (94.34%). No oral mucosal lesions was found. PSR score of 3 was mostly found (36.58%). Sixty-two percent of patients had a moderate treatment urgency.

Conclusion

A relationship between chronic kidney disease and periodontitis exists. ESRD patients should thus be enrolled into a periodontal screening and treatment program and all dental treatment should be completed prior to kidney transplantation.

List of Abbreviations

CKD	Chronic kidney disease
GFR	Glomerular filtration rate
RRT	Renal replacement therapy
ESRD	End stage renal disease
HD	Haemodialysis
PSR	Periodontal screening and recording index
WHO	World Health Organization
PD	Peritoneal dialysis
SBAH	Steve Biko Academic Hospital
UPOHC	University of Pretoria Oral Health Center
BOP	Bleeding on probing
PPD	Periodontal probing depth
OHI	Oral hygiene instructions
OLDR	Oral lichenoid drug reactions
CRP	C-reactive protein

INTRODUCTION

Chronic kidney disease (CKD) can be defined as potentially progressive alterations in the kidneys' physiology and histology, which may result in renal impairment.[1] These structural and functional changes in the kidneys should be present for 3 months or more to be classified as chronic. Individuals at risk for renal damage and those with decreased glomerular filtration rate (GFR) are deemed to have CKD.[1] The two main causes of CKD are diabetes mellitus and hypertension, which negatively impact patients' cardiovascular system and renal structure before and after renal transplantation. Other causes of CKD are glomerulonephritis, chronic pyelonephritic urologic disorders and autoimmune diseases.[2]

The incidence of CKD in patients is on the rise worldwide, and patients over the age of 60 with uncontrolled hypertension, diabetes and cardiovascular disease are particularly at risk.[3,4] These patients are burdened with multiple health problems of which oral diseases go undiagnosed.[3] The dental practitioner will inevitably manage patients suffering from renal failure and should be aware of some oral diseases (mucosal lesions, periodontal disease, dental decay) that may be more prevalent in this group of patients.

The kidneys have multiple essential functions: 1) metabolic waste product excretion; 2) regulation of electrolytes; 3) acid-base homeostasis; and 4) endocrine

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function (particularly renin-angiotensin system, vitamin D metabolism and erythropoietin production). These renal functions are involved in various physiologic pathways that maintain health.[3,4]

As kidney disease progresses, the nephrons are gradually destroyed, and the GFR deteriorates. The GFR is used to stage these patients from 0 – V. Their corresponding treatment needs are categorised according to these categories.[2] The final stages of CKD requires renal replacement therapy (RRT), where the patient requires a renal transplant or renal dialysis or both.[2]

Dialysis is a life-saving intervention to prolong a patient's life[2,5] with or without eventual renal transplantation.[6] Management of end-stage renal disease (ESRD) aims to correct the electrolyte imbalance and reduce the level of urea and creatinine in the circulation.[2,5-7] Patients with ESRD require haemodialysis (HD) for three to five hours, two to three days per week. [2,6] HD replaces the lost filtration function of the defective nephrons to reduce retained salt, water and metabolic waste products that are potentially fatal.[8]

While HD may prolong the patient's life expectancy, uraemia to some degree persists, resulting in various systemic complications.[2] Peritoneal dialysis (PD) employs the patient's peritoneum as a filtration device instead of a machine, giving the patient more daily independence.[2,7] Haemodialysis patients require anticoagulant treatment with local or systemic heparin to facilitate filtration. Haemodialysis patients are only heparinised on the day of dialysis, and PD patients are on continuous anticoagulant treatment; this adds to the haemorrhagic risk.[2]

As mentioned previously, impaired metabolic and endocrine kidney function results in various systemic complications. End-stage renal disease is characterised by decreased endocrine and metabolic kidney functions, leading to retention and accumulation of toxic metabolites that can't be eliminated, resulting in uraemia. Patients may develop anaemia due to decreased erythropoietin, while reduced erythropoietin, combined with uraemia, impairs platelet function, resulting in a haemorrhagic tendency. Immunodeficiency due to uraemia and diabetes mellitus, which is often a comorbidity as it can also be a cause of CKD, increases ESRD patients' susceptibility to infections.[2, 7, 9]

Finally, it is important to note that many drugs are excreted to some extent by the kidneys. Drug distribution, metabolism, bioavailability, and elimination are impaired when renal excretion is reduced, necessitating dose adjustments.[2]

Patients suffering from ESRD may present with oral complications and disease due to impaired renal functions and the associated comorbidities or the medical management thereof.[4,6,7] Mucosal, glandular, gingival, periodontal, bony and dental hard tissues are affected collectively (Table I).[4] This should be kept in mind when examining these patients, and they should be managed accordingly. End-stage renal disease patients should be screened for periodontal disease and treated accordingly.[4,9] The Periodontal Screening and Recording index (PSR) is supported by the World Health Organization (WHO) to reliably indicate the treatment needs of patients suffering from periodontal disease.[10,11]

Table I: Oral and Periodontal manifestations in ESRD [adpated from Constantinides et al. (2018)][2]

Oral and Periodontal manifestations in ESRD	
Mucosal and glandular manifestations	Mucosal pallor (anaemia) Ecchymoses, petechiae and heamorrhage Xerostomia Uremic fetor (halitosis) Burning sensation Uremic stomatitis Angular cheilitis Candidiasis Oral lichenoid drug reactions
Periodontal manifestations	Calculus deposition Gingivitis Periodontitis Gingival enlargement (drug -induced)
Bone manifestations	Renal osteodystrophy Tooth mobility Malocclusion Pulp stones Enamel hypoplasia Bine demineralization Giant cell lesions Spontaneous jaw fracture Abnormal healing after tooth extraction
Dental tissue manifestations	Lower caries rate Dental erosion Enamel hypoplasia and delayed eruption in children Pulp narrowing and calcification

This study aims to determine the prevalence of periodontal- and oral mucosal disease in patients with ESRD undergoing dialysis. Accordingly, recommendations will be made regarding the dental treatment needs and dental management of patients with ESRD.

MATERIAL AND METHODS

This was a cross-sectional study done among ESRD patients receiving dialysis at the Department of Nephrology, Steve Biko Academic Hospital (SBAH). Dental screenings were conducted to prepare patients for receiving a kidney transplant from October 2019 to February 2020. Consent to access data from the patient files were obtained from the CEO of the University of Pretoria Oral Health Center (UPOHC) and SBAH. The project was submitted to and approved by the Health Research and Ethics committee (Ethics reference number 850/2019).

Participants:

The clinic serves 130 ESRD patients, 50 receiving HD and 80 receiving PD. After obtaining consent, haemodialysis patients included in the study were seen at the dialysis clinic, while PD patients were referred to the Periodontics and Oral Medicine department at the UPOHC.

Inclusion and exclusion criteria:

All renal dialysis patients treated at Steve Biko Nephrology clinic, who consented to have dental screenings done,

were included in the study. While patients who did not give consent, were deemed unfit for dental screening due to oxygen requirements or whose full medical records were not accessible were excluded from the study. Patients with medical conditions like cardiac lesions that may predispose them to bacterial endocarditis were also excluded when periodontal probing is done.

Clinical examination and indices:

The dental screening of all dialysis patients was carried out by one dental practitioner.

Examinations in the dialysis clinic were performed while the patients received HD in hospital beds. The primary dental practitioner conducted the visual examination with a dental mirror, UNC-15 periodontal probe, and handheld flashlight held by the second dental practitioner. In contrast, those examinations conducted at the UPOHC were performed under standard dental conditions in a dental chair with an attached light source with a dental mirror and UNC-15 periodontal probe.

All findings were documented in standardised examination forms drawn up specifically for the study.

The following clinical examinations were performed:
Extra-oral examination by visual examination and palpation noting for:

- Swelling.
- Lymph node enlargement and/ or tenderness.
- Temporomandibular joint and facial muscle abnormalities.
- Skin and lip abnormalities.

Intra-oral examination by visual examination and periodontal probing:

- PSR: This diagnostic index was proposed by the American Academy of Periodontology in 1991 and is simple, fast, and preferred by patients.[12] This evaluates gingival bleeding, calculus accumulation and probing depth. The findings were collected and scored from code 0 to 4 by dividing the oral cavity into six sextants (Figure 1):
  0: Healthy
  1: Bleeding on probing (BOP)
  2: BOP and calculus
  3: Periodontal probing depth (PPD) of more than 3mm, but equal to 5mm
  4: PPD of more than 5mm. Only the highest score per sextant was recorded.
- Noting for caries by visual examination and probing.
- Noting oral mucosal lesions.
- Salivary gland function was measured by milking the salivary glands and the sliding mirror test.

Treatment needs and urgency

The periodontal findings were placed into the following periodontal treatment needs categories according to the PSR index scores:

- Preventative treatment only (PSR 0)
- Oral hygiene instructions (OHI), plaque and debris removal (PSR 1).
- OHI, Subgingival plaque and calculus removal (PSR 2)
- As in 2 with complete periodontal examination and radiographs, possible referral to a periodontist (PSR 3)
- As in 3 + more extensive treatment, possibly surgery, refer to a specialist (PSR 4)

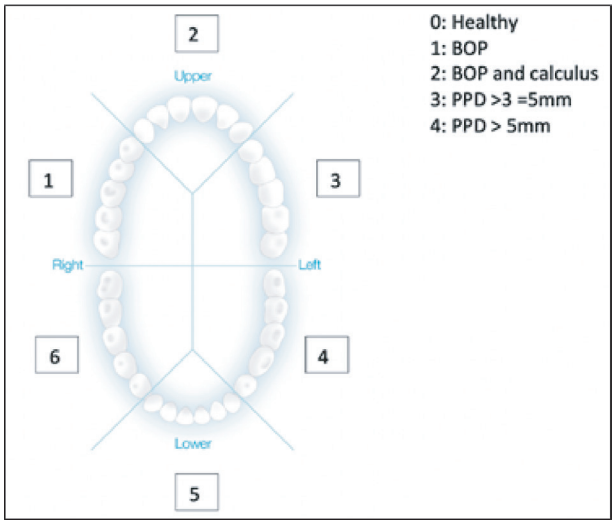

Figure 1: PSR illustration of sextants & description of periodontal probing measurements. (Image courtesy of The Probe: https://the-probe.co.uk/courses/gsk-june-2020-the-bewe-gdc-development-outcome-c/)

Feedback of treatment needs: Feedback regarding the results of the patient's dental screening and treatment was provided to the treating physician in the Nephrology department, as this may influence the treatment and eligibility of the patient for a renal transplant.

A note whether teeth were carious or not was made and whether restorative work, endodontic treatment or extraction is needed. The patients were accordingly referred to the respective clinical departments at the UPOHC.

The treatment urgency of each patient was subjectively determined according to the examiners experience and expertise and characterised into low, medium, and high according to the risk of systemic infection.

Data retrieved from patient records:

Each patient was given a number, and all data assigned to this number was captured on an Excel spreadsheet. The following information was noted: age, race, gender, comorbidities, duration of dialysis and list of drugs.

Statistical analysis:

Initial data analysis included mean, median, standard deviation, and range for continuous variables. Frequencies and proportions and 95% confidence intervals was given for categorical variables.

RESULTS

Epidemiology

A total of 53 patients, 39 men and 14 women, with a mean age of 42,9 ±10,4 (23 – 64) years, were included in the study. Forty three (81.1%) of the patients were Black, 2 (3.8%) Colored, and 8 (15.1%) Caucasian. One patient was excluded due to oxygen requirements and being in isolation.

Medical history & medications

The mean dialysis treatment time was 34.2 ± 16.8 months. Most patients were heparinized (86,8%) on the day of treatment. The majority (n=44, 83.02%) of patients were screened at SBAH, receiving dialysis in hospital, and

the rest (n=9, 16.98%) were screened at the UPOHC, reflecting the sample population of HD and PD patients, respectively. The most common comorbidity was hypertension (94.34%), followed by HIV (13.21%) and diabetes mellitus (5.66%). All patients with diabetes had hypertension as well. Other comorbidities documented were anaemia, hypercholesterolaemia, bone mineral disease, cardiac failure, gastric ulceration, pancreatitis, multiple myeloma, epilepsy and tuberculosis (Figure 2).

Given the prevalence of hypertension, diabetes mellitus and HIV among this population, the most commonly prescribed drugs were antihypertensives, antiretroviral drugs and antidiabetic agents.

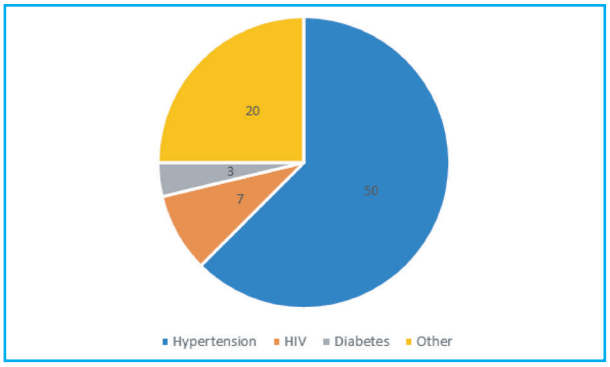

Figure 2: Distribution and prevalence of comorbidities in patients with CKD.

Figure 3 illustrates the percentage of the most common antihypertensive drugs used in this population of CKD patients. The colour index represents the drug class distribution illustrated in Figure 4. Amlodipine (70%) and hydralazine (41%) were the most commonly used vasodilator drugs. Amlodipine was the most common drug used in this study group. Furosemide (Lasix) (51%) was the most popular diuretic and second most common drug prescribed. Doxazosin (Cardura) (39%) and Carvedilol (Carloc) (39%) were the two adrenergic blockers used most often. Figure 4 shows the antihypertensive drug class distribution, with vasodilators (51%) being the most frequently used drug class in this study group.

No abnormal mucosal lesions were detected, and normal variations such as Fordyce granules and leukoedema were not recorded. The prevalence of the different PSR

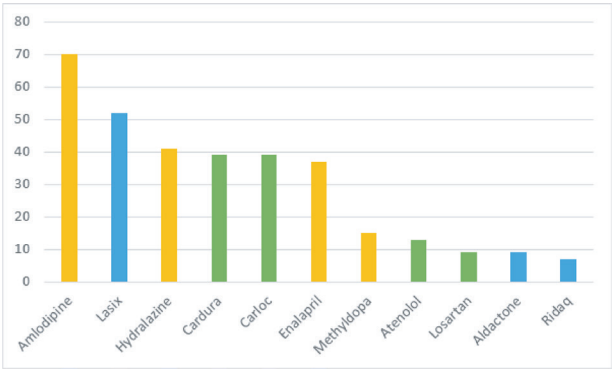

Figure 3: Percentage of most common antihypertensive drugs used in this population of CKD patients.

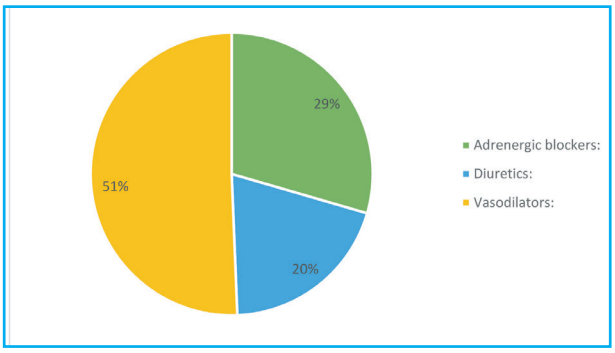

Figure 4: Antihypertensive drug class distribution.
Mucosal and Periodontal involvement

scores were as follows: 0 – 19.46%; 1 – 6.38%; 2 – 23.83%; 3 – 36.58% and 4 – 13,76% (Figure 5).

The PSR score of 3 was encountered most (36.58%), meaning that the patients had PPD of 4-5mm, which according to the Van der Velden periodontal classification,[13] could be classified as mild periodontitis, and according to

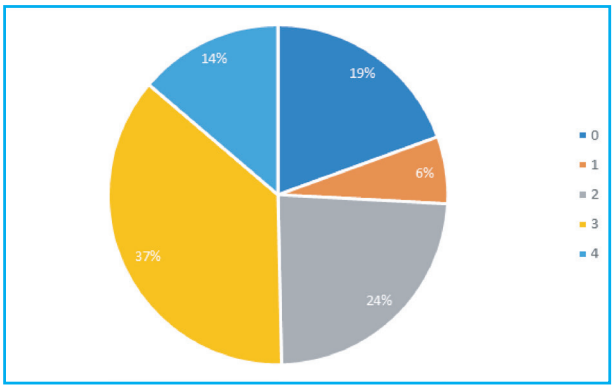

Figure 5: Prevalence of PSR scores

the World Workshop 2017 classification,[14] as Stage I and II periodontitis. The posterior sextants were mostly affected by mild periodontal disease with probing depths of ≤ 5mm. The anterior mandible (sextant 5) harboured most calculus BOP, and the anterior maxilla (sextant 2) was healthy in most cases.

Periodontal treatment needs according to the periodontal findings are illustrated in Figure 6. Most patients (81%) required OHI, as all patients with PSR scores from 1-4 had suboptimal oral hygiene. Fifty-one percent of the patients required nonsurgical periodontal treatment and 30% prophylactic treatment only.

The frequency of dental treatment that dialysis patients with CKD required was periodontal debridement (52.3%), followed by restorations (32.1%) and extractions (30.2%), as illustrated by Figure 7.

Sixty-two percent of patients had a moderate urgency for treatment (Figure 8), meaning a moderate risk for systemic infection.

DISCUSSION

Patient population

Fifty-three patients were included in the study, with most patients (83.02%) receiving HD. Unfortunately, many PD

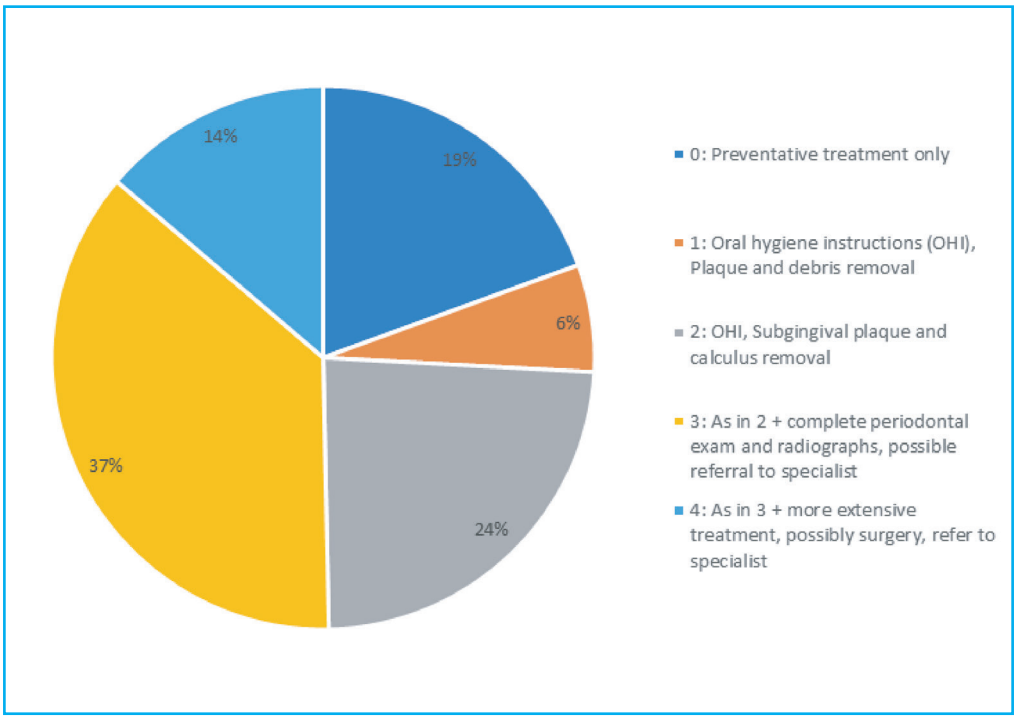

Figure 6: Proportional distribution of periodontal treatment needs according to PSR results

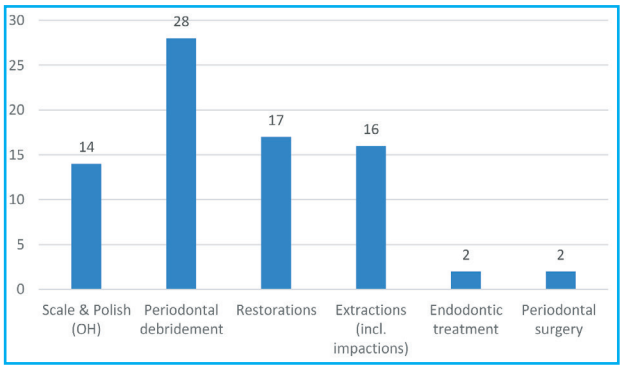

Figure 7: Number of patients needing respective dental treatment.

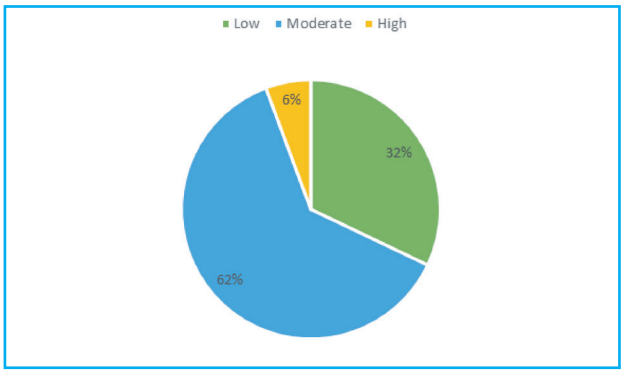

Figure 8: Treatment urgency

patients did not comply with the referral to the UPOHC. We speculate that this may be due to a lack of patient education and understanding of the benefit or purpose of the referral. Time and finances may also play a role as we are dealing with an underprivileged population in this setting. The onset of the Covid-19 pandemic and subsequent restrictions halted further screening at SBAH to reduce any infectious risk to this vulnerable population. One patient was excluded due to oxygen requirements and being in isolation.

Oral complications and disease

Various oral mucosal lesions have been reported in ESRD patients,[15,16] either due to the disease or the treatment thereof. Dialysis has a significant impact on patients' quality of life, which might mean that oral hygiene is not a priority.[17-19] This could increase their risk of periodontal disease and caries.[2,4,17,18] Oral complications and diseases are due to the impairment of various renal functions, associated comorbidities like diabetes mellitus and hypertension and the pharmacological management thereof.[6,7,15] Almost all patients are on antihypertensive medication which is known to be associated with lichenoid lesions, gingival enlargement, and xerostomia.[15,16]

While comorbidities such as diabetes mellitus and the accompanying immune suppression, may also be responsible for some oral lesions. The presence thereof may signify worsening blood glucose control and immunosuppression.[4] A common consequence of immune suppression in ESRD patients and other populations is oral candidiasis,[5,17,20] yet, none of our patients displayed any clinical signs of candida infection. Three percent of the patients screened in this study had diabetes, and all of these had periodontal disease. A bidirectional relationship between diabetes mellitus and periodontitis exists,[21] and ESRD and periodontitis.[22] Both diabetes and periodontitis have been implicated in an increased risk of atherosclerotic disease in ESRD patients.[23,24] A unique phenomenon in ESRD patients, namely uremic stomatitis, was also not seen in this population.[2,4, 25,26]

Uraemic stomatitis

Uremic stomatitis is a rare and infrequently documented disorder associated with longstanding elevated blood urea levels (above 300mg/mL) in patients with CKD.[25] It is characterised by white adherent plaques found mainly on the tongue's dorsal and/or ventral surface, the floor of the mouth, and buccal mucosa with accompanying burning pain and dysgeusia. In addition, an odour of ammonia may be detected in the patient's breath.[25,26] Raised circulating ammonia levels may cause a chemical burn, but bacterial ureases may also alter salivary urea forming ammonia. Reducing the circulating ammonia levels through dialysis and the use of an antimicrobial mouthwash will resolve these lesions.[25] This is likely why we did not find any sign of uraemic stomatitis in this study population.

Pharmacologic agents employed in the management of ESRD and associated comorbidities, and their effects

Pharmacologic treatment of hypertension in ESRD usually consist of combination drug therapy that directly lowers blood pressure and has additional renoprotective and cardioprotective effects.[27]

According to the South African hypertension practice guideline (2014), the initial first-line therapy is a diuretic, angiotensin-converting enzyme (ACE) inhibitor or angiotensin II receptor blocker (ARB) and/or calcium channel blocker (CCB) as mono – or combination therapy. Fixed drug combinations are preferred as patient compliance, and blood pressure control is better.[28] ACE inhibitors and ARB are both renoprotective and cardioprotective, therefore invaluable in patients with CKD. Diuretics reduce volume overload and is used in combination therapy in CKD to offer antihypertensive and cardioprotective effects. CCB is useful in managing CKD and is often used as first-line therapy alone or in combination with ACE inhibitors. Beta-blockers have well established cardioprotective effects and are also renoprotective. Alpha-blockers are frequently used as part of combination therapy.[27]

In this study, most subjects were on combination antihypertensive therapy, with CCB and diuretics being the most commonly used agents and amlodipine the most commonly used CCB. CCB is frequently associated with drug-induced gingival enlargement, largely determined by drug variables, plaque-induced gingival inflammation, and genetics, which influence collagen matrix metabolism by altering the release of matrix metalloproteinases and inhibitors of matrix metalloproteinases.

The inhibition of calcium uptake by gingival fibroblasts is directly proportionate to the inhibition of fibroblast proliferation, meaning that collagen production (gingival tissue bulk) increases, and breakdown is diminished, resulting in enlarged gingival tissues.[29] In this study, we did not find any gingival enlargement that may be drug-associated. This correlates with the studies by Ellis and co-workers, who found that the prevalence of CCB induced gingival enlargement is lower than previously reported. They demonstrated significant differences between CCB, with amlodipine use resulting in gingival overgrowth only 1.7% of the time, compared to 6.3% by nifedipine. [30-32] Both drugs are dihydropyridines, but amlodipine is more polar, requiring active transport mechanisms to enter the fibroblast, while nifedipine is extremely lipophilic and readily enters into the fibroblast cytoplasm.[32] The pharmacokinetic profiles of amlodipine and nifedipine also differ. Amlodipine has a much longer half-life (T1/2 = 34 hours) than nifedipine (T1/2 = 7.5 hours) and high volume of distribution, 21 litres/kg, and 0.78 l/kg, respectively. This means that most of the amlodipine will be inactive (tissue bound) at any given moment instead of circulating freely in the blood.[33]

It has also been hypothesised that drug-induced gingival changes occur above a certain plasma threshold. If this is the case, then amlodipine may rarely reach such a threshold level due to its long half-life and steady plasma state, whereas nifedipine frequently displays marked peak plasma levels.[32] Plaque induced gingival inflammation may exacerbate drug-induced gingival enlargement.[32] In our study, most of the patients suffered from periodontal disease; thus, gingival inflammation is present; however, none of the individuals displayed gingival enlargement.

Antihypertensive medications and the combined use of multiple drugs may cause hyposalivation and xerostomia, making it difficult to establish the exact role of the various antihypertensive drugs in altering salivary flow.[34] Diuretics increase urinary output, thereby reducing circulatory fluid volume and renal and cardiac workload and salivary flow. In 2021, Ramírez and colleagues demonstrated that diuretics are almost exclusively responsible for hyposalivation among antihypertensive drugs. They reported that patients who took ARB's, like losartan (which was also used by many in our current study), suffered less from xerostomia. This drug selectively binds angiotensin II, meaning that systemic collateral effects from the metabolism of other substances do not take effect, subsequently with less hyposalivation and xerostomia.[35] The patients in our study did not suffer from hyposalivation as measured by adequate pooling of saliva, milking saliva from the major salivary glands, and freedom of movement of the dental mirror across the mucosa. This could most likely be due to the combination of drugs, where the agents that act on the renin-angiotensin system counter the unwanted xerostomic effects of the diuretics.

Besides xerostomia, antihypertensive medications have been implicated in many other oral adverse drug events. Oral lichenoid drug reactions (OLDR) may be caused by certain medications and resemble idiopathic lichen planus. The two main drug classes associated with OLDR are nonsteroidal anti-inflammatory drugs and of more significance in this study, antihypertensive medications like beta-blockers, ACE inhibitors and particularly, hydrochlorothiazide diuretics.[36]

The hypothesised pathogenesis for this phenomenon is that susceptible individuals have cytochrome P450 enzyme polymorphisms resulting in insufficient medication metabolism and increased plasma concentration. However, a study in 2010 by Kragelund and co-workers failed to illustrate this possibility due

to the anecdotal nature of OLDR, which is mostly characterised by clinical observation; however, their, as well as our study, was limited by a small population.[37] Despite multiple studies reporting on lichenoid lesions associated with antihypertensive medications, the present study did not report any OLDR.

Periodontal health status

There is conflicting evidence on the periodontal health status in patients with CKD. Multiple studies report that periodontal disease is more prevalent in patients undergoing HD[38-40], while others find no significant increase in periodontal disease in patients with CKD.[17,41,42]

It is argued that an increased uremic state results in immunosuppression; however, patients may still be able to launch an appropriate response against bacterial pathogens.[7,17,41,42] Unfortunately, this population may be overburdened with microbial plaque due to suboptimal oral hygiene [7,17,19,41,42] thereby placing them at increased risk of periodontal destruction.

The current study population reflects the general population, which also displayed suboptimal oral hygiene, with 81% requiring professional dental prophylaxis. However, the mild periodontal destruction measured did not correlate with the increased amount of plaque, calculus, and gingival inflammation. Bayraktar and colleagues in 2007 noted that heavy calculus deposition in the population may be due to an altered saliva phosphorous-calcium balance in CKD patients, which mimics serum changes.[43]

In the present study population with a median age of 42.9 years, 52.3% of patients suffered from periodontitis. This corresponds to the 51.6% prevalence among South African adults of 35-44 years of age that was recently reported.[44]

Therefore, our study population with ESRD does not have a higher prevalence of periodontal disease than the general South African population. However, in 2004 Duran and Edimir noted that periodontal breakdown increases with time on dialysis. This can only be elaborated on if our study is continued in the future, and we use the current measurements as baseline findings.

Periodontitis and ESRD

It is encouraging to see the low prevalence of periodontal disease in this population because a known relationship between periodontal disease and cardiovascular disease exists.[24] Periodontal disease is known to cause an increase in serum inflammatory markers like C-reactive protein (CRP) and other acute-phase proteins. Periodontitis is also associated with a decrease in high-density lipoprotein and an increase in low-density lipoprotein and blood glucose.[45] It is evident that periodontal disease increases atherosclerosis.[24,46] The release of pro-inflammatory cytokines associated with periodontal disease results in a local and systemic inflammatory response that may result in vascular endothelial damage and promote atherosclerosis formation.[47] Periodontal pathogens have been found in atherosclerotic plaques which may increase the risk of atheroma's forming in patients with CKD.[48,49]

A strong association between atherosclerotic complications and increased systemic inflammatory burden exists. The major cause of death in patients with ESRD on HD is atherosclerotic complications like acute myocardial infarction, cardiac arrest, cardiac arrhythmia, and cerebral vascular disease, followed by infectious complications.[39] CRP, an acute-phase protein and marker of inflammation, is a major predictor of cardiac and other mortality in the broader, specifically the ESRD population.[50] CRP is implicated in the pathogenesis of atherosclerotic complications by binding to receptors on the cell membranes of macrophages, monocytes and neutrophils, consequently activating the complement cascade. Thus, CRP amplifies inflammatory reactions resulting in atherosclerotic complications.[39] Significantly, the mortality of HD patients can be correlated with the severity of periodontitis[51,] but fortunately, successful periodontal treatment can reduce serum CRP levels in periodontitis patients[52,53], thereby mitigating systemic risks. It is thus evident that there is a bi-directional correlation between periodontitis and CKD.[54]

Management

General routine dental care can safely be done in patients with ESRD, though one should be mindful of drug sensitivities and immunosuppression.[2] The coagulation status should be assessed before any invasive dental treatment that may result in bleeding due to the altered uraemic state and heparin treatment in dialysis patients. A dose reduction of renally excreted drugs may be necessary due to diminished renal metabolism and secretion.[38] Alteration to any drug dose according to renal function can be found in the Drug Prescribing in Renal Failure, Dosing Guidelines for Adults.[55] Orofacial infections like dental abscesses, periodontal infection and maxillary sinus infection should be aggressively treated, keeping the antibiotic dose adjustment in mind, to prevent future graft rejection and bacteraemia. The vitals of ESRD patients with significant hypertension should be monitored throughout treatment to identify changes in blood pressure due to stress or the administration of local anaesthetics containing adrenaline. The blood pressure cuff should not be placed on the arm where the shunt is located [2,38]

Periodontal disease is an important cause of chronic inflammation in CKD patients and even more so in patients with diabetes as a comorbidity.[56] Chronic systemic inflammation is a major risk factor for atherosclerotic disease in this particular population.[57] It is therefore critical that CKD patients are educated about their oral health and treated accordingly. A study done in 2018 by Tasdemir and co-workers demonstrated that nonsurgical periodontal debridement effectively reduces the inflammatory markers of patients receiving dialysis treatment.[56] Patients should be enrolled in an active preventive treatment plan and all invasive dental procedures completed before transplant surgery.[17,58] All parties involved should be knowledgeable about treatment priorities, operative concerns and precautions

that need to be taken in ESRD patients with or without dialysis.[17]

CONCLUSION

The results of our study emphasise the importance of periodontal disease assessment given the significant impact that this disease may have on the mortality of patients with ESRD. Both patients awaiting renal transplants and nephrology clinics should be made aware of the importance of dental screening and treatment to ensure that patients are infection-free while awaiting renal transplantation. Nephrology clinics should implement a dental care protocol to manage all CKD and ESRD patients. We recommend that dental practitioners treating CKD patients should perform a PSR and subsequently a comprehensive periodontal examination and nonsurgical periodontal debridement where indicated. Maintenance of the patient's periodontal condition is essential to minimise additional cardiovascular disease risk and ensure the success of the transplanted kidney.

Finally, it is important to note the sample size of this study was small, and a larger population could have yielded different results. Periodontitis is a progressive disease that worsens over time if not managed. It would be beneficial to continue follow up of the patients in this study to monitor the effects of treatment and non-treatment. Furthermore, the PSR is only a very crude measurement of a patient's periodontal condition, yet it would be interesting to correlate the CRP levels with the PSR score, and among patients who require periodontal treatment, measure the effect of treatment on the CRP levels. Candida can be present subclinically, it would have been more informative to do a cytological smear to detect this.

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