BANTAO Journal 2022; 20(2): 39-44

BJ

BANTAO Journal

Original article

Oral Health Status in Diabetic and Non-Diabetic Patients on Maintenance Hemodialysis Treatment

Emilija Rambabova[1], Gordana Gjorgjievska[2], Vasiliki Krecova[2], Vladimir Pusevski[3], Zaklina Sterjova Markovska[3], Sefedin Biljali[4], Lada Trajceska[3], Oliver Bushljetikj[5], Aleksandar Trifunovski[6], Mile Carcev[7] and Mirjana Popovska[7]

[1]University Goce Delcev-Stip, Stip, [2]Hemodyalisis unit Nefro Plus, Skopje, [3]University Clinic for Nephrology, Medical Faculty North Macedonia, Ss. Cyril and Methodius University, Skopje, [4]University Clinic for Biochemistry, Medical Faculty North Macedonia, Ss. Cyril and Methodius University, Skopje, [5]University Clinic for Cardiology, Medical Faculty North Macedonia, Ss. Cyril and Methodius University, Skopje, [6]University Clinic for Urology, Medical Faculty North Macedonia, Ss. Cyril and Methodius University, Skopje, [7]Department of Oral Pathology and Periodontology, Faculty of Dentistry, Ss. Cyril and Methodius University of Skopje, Skopje, Republic of North Macedonia

Abstract

Introduction. Uremic toxins and inflammation influence the oral health in patients on maintenance hemodialysis treatment. The presence of diabetes additionally aggravates the oral status. The aim of the study was to compare the oral health status in diabetic and non-diabetic patients on chronic hemodialysis program.

Methods. Observational, cross-section, monocentric study was conducted in 72 hemodialysis (HD) patients divided into two groups regarding the presence of Diabetes mellitus (DM). Demographic characteristics as patients age, dialysis vintage, laboratory inflammatory markers as C-reactive protein (CRP), albumin and Interleukin 6 (IL-6) were measured at the start of the study. Also, uremic small and middle molecules as blood urea nitrogen (BUN), creatinine, β2-microglobilin (β2M), myoglobin, albumin, free light chains kappa (FLC-k), and free light chains lambda (FLC-λ) were analyzed. Patients were examined by a dentist specialist scoring the oral hygiene index (OHI) by Greene Vermillion as good, fair and poor. Presence of hyperkeratosis, periodontal disease, erosions, ulceration, erythema, pigmentations, tongue coating and uremic fetor were notified. Gingival hyperplasia (GH) was scored (1-3) with 3 for the worst score. Data was presented as mean and standard deviation for continuous and percentages for nominal values. X squared Fisher exact and Mann-Whitney test were used for statistical analysis. $P<0.05$ was considered as significant.

Results. The patients from group 1-with DM (N=26) didn't differ from the non-diabetic group (N=46) in respect of gender, age but had significantly shorter dialysis vintage (48.68±37.45 vs. 88.13±63.29, p=0.02, respectively). From the inflammatory markers only Il-6 was significantly higher in DM patients (p=0.03). All the analyzed uremic toxins-small and middle molecules also didn't differ between the two groups. Diabetic patients were at 3 fold risk for manifestation of fissure, 4 fold risk for pigmentations and 7 fold risk for erythema (OR 3.58; CI:1.017-12.380, p= 0.003; OR 4.12; CI:0.684-22.870; p=0.02, OR 4.84; CI:1.343-17.498, p=0.000), (OR 7.25; CI:1.123-46.880, p=0.000), respectively. GH was more likely to be present in diabetic patients (35%, 54%, 11% vs 83%, 15, 0%, p=0.000, respectively). The presence of hyperkeratosis, periodontal disease, erosions, didn't differ between the groups. Patients with DM were found with higher percentage of bad oral hygiene index (38% vs 20%), but the overall comparison of OHI showed no significant difference.

Conclusion. Oral health is significantly deteriorated in dialysis patients, especially in those with inflammation. Diabetic patients are at higher risk of developing changes in the oral health status.

Keywords: hemodialysis, oral health, diabetes

Introduction

Chronic kidney disease (CKD) is the global health burden and one of the most frequent causes of morbidity and mortality in the 21st century. The dominant risk factors are still hypertension, obesity and diabetes mellitus. According the published reports more than 850 million individuals worldwide have some degree of CKD, and most of them have been diagnosed in the later stage, even in terminal stage of the disease. About 4 million people require kidney replacement therapy (KRT) [1,2]. According to the Kidney Disease: Im-

Correspondence to: Emilija Rambabova, University Goce Delcev-Stip, Republic of North Macedonia; E-mail: emilija.rambabova@ yahoo.com

proving Global Outcomes (KDIGO) CKD Work Group chronic kidney disease is defined as a persistent abnormality in kidney structure or function (e.g. glomerular filtration rate [GFR] <60 mL/min/1.73 m^2 or albuminuria ≥30 mg per 24 hours) for more than 3 months [3]. There are 5 stages of CKD, where the fifth stage with GFR below 15 ml/min/1,75m2 requires renal replacement therapy (RRT). For patients who do reach terminal stage of CKD, there are several modalities of RRT. The mostly frequent is intermittent hemodyalisis treatment (in centre or home HD). The other modalities are peritoneal dialysis and transplantation [4]. Dialysis treatment are associated with systemic changes in this group of patients, including cardiovascular disease, mineral bone disease, anemia, lower health-related quality of life compared with the general population as well as oral health complications [5,6]. Incidences of diabetes mellitus (DM) have increased rapidly in the past 2 decades as a result of the lifestyle changes, behavioral and human environmental changes. In situation when a patient has been diagnosed with both CKD and DM, the two diseases intensify each other with consequence of difficult-to-treat clinical manifestations. Chronic hyperglycemia, microvascular damage, hypoproteinemia and dyslipidemia make patients with DM prone to many systemic alterations [7].
Oral health in patients on hemodialysis needs more attention and multidisciplinary approach. Published data reports oral manifestations as present in almost 90% of dialysis patients, affecting the soft or hard tissues of the oral cavity [8,9]. It is evidently a great decline of periodontal health among dialysis patients, very low level of awareness regarding the dental care [10]. According to the small number of published studies, there are diversity of oral manifestations in chronic dialysis patients. Oral manifestations include mucosal tissues, the gingival and the periodontal apparatus, and also the dental status [11,12].
The most common mucosal oral finding is xerostomia, which means the subjective sensation of dry mouth. Characteristic halitosis called "uremic fetor" and a metallic taste are frequently described in hemodialysis patients. Other uremic manifestation reported in the literature include covered tongue, mucosal inflammation and petechiae, oral ulceration. A high incidence of periodontitis was also reported in the published literature [13,14].

Material and methods

This observational, cross-section, monocentric study was conducted in 72 hemodialysis (HD) patients from different hemodialysis units in western region of N. Macedonia, divided into two groups regarding the presence of Diabetes mellitus (DM). We have evaluated demographic characteristics as gender, patients age, dialysis vintage, as well as laboratory inflammatory markers as C-reactive protein (CRP), albumin and Interleukin 6 (IL-6) and those were measured at the start of the study. Also, uremic small and middle molecules as blood urea nitrogen (BUN), creatinine, β2-microglobilin (β2M), myoglobin, albumin, free light chains kappa (FLC-k), and free light chains lambda (FLC-λ) were analyzed. Patients were examined by a dentist specialist scoring the oral hygiene index (OHI) being good, insufficient and bad. Hyperkeratosis, periodontal disease, erosions, fissure, erythema, pigmentations, covered tongue and oral fetor were notified. Gingival hyperplasia (GH) was scored (1-3) with 3 as the worst score. Data was presented as mean and standard deviation for continuous and percentages for nominal values. X squared Fisher exact and Mann-Whitney test were used for statistical analysis. P<0.05 was considered as significant.

Results

The patients from group 1-with DM (N=26) didn't differ from the non-diabetic group (N=46) with respect of gender, age but had significantly shorter dialysis vintage (48.68±37.45 vs. 88.13±63.29, p=0.02, respectively).

Table 1. Demographic, clinical and biochemical characteristics comparison regarding the presence of diabetes

N=72	DM N=26	non DM N=46	*P*
Men	14(54%)	33(72%)	0.197
Hemodialysis	19(73%)	23(50%)	0.08
Age (years)	58.34±12.24	53.13±10.39	0.074
Dialysis vintage (months)	48.68±37.45	88.13±63.29	0.02
Albumin (g/L)	37.30±3.67	37.04±3.55	0.774
CRP (mg/L)	0.79±1.07	0.49±0.53	0.195
Glycemia (mmol/L)	8.59±3.01	5.92±1.43	0.0001
Hemoglobin (g/L)	116.92±117.75	115.08±12.43	0.541
Urea (mmo/L)	18.49±4.86	19.33±4.44	0.476
Interleukin 6 (pg/mL)	137.29±497.673	51.21±200.67	0.03

When analyzing the inflammatory markers only Il-6 was significantly higher in diabetic patients (p=0.03). All the analysed uremic toxins-small and middle molecules also didn't differ between the two groups.

Diabetic patients were at 3 fold risk for manifestation of fissure, 4 fold risk for pigmentations or xerostomia or oral pigmentations or covered tongue and 7 fold risk for erythema (OR 3.58; CI:1.017-12.380, p=0.003; OR 4.12;

Table 2. Middle molecules comparison between patients with and without diabetes

N=72	DM (N=26)	non DM (N=46)	*P*
β - 2M (mg/L) Median (IQR)	12.6 (9.5;15.5)	13.10 (8.57;16.40)	0.778
Myoglobin (ng/ml) Median (IQR)	253.84 (199.22; 294.41)	238.52 (151.32; 317.80)	0.650
FLC-k (mg/ml) Median (IQR)	109.00 (91.40; 147.00)	109.00 (70.50; 149.00)	0.650
FLC-λ (mg/ml) Median (IQR)	97.40 (69.30; 133.00)	102.50 (55.70; 136.00)	0.422
IL-6 (pg/mL) Median (IQR)	8.16 (5.66; 10.23)	4.84 (2.49; 8.84)	0.003

CI:0.684-22.870; p=0.02, OR 4.21; CI:1.134-34.77, p= 0.006),OR 4.84; CI:1.343-17.498, p=0.000), (OR 7.25; CI:1.123-46.880, p=0.000), respectively. GH was more likely to be present in diabetic patients (35%, 54%, 11% vs 83%, 15, 0%, p=0.000, respectively). The presence of hyperkeratosis, uremic fetor, periodontal disease and erosions didn't differ between the groups. DM patients were found with higher percentage of bad oral hygiene index (38% vs 20%), but the overall comparison of OHI showed no significant difference.

Table 3. Oral and dental changes in patients with and without Diabetes

N=72	DM N=26	non DM N=46	X^2 *test*	Risk Odds ratio	95% CI lower	95% CI upper
Hyperkeratosis	3(11%)	1(2.2%)	p=0.131			
Periodontal disease	2(8%)	12(27%)	p=0.071			
Uremic fetor	20(77%)	40(86%)	P=0.130			
Erosions	3(12%)	4(8.7%)	p=0691			
Pigmentations	5(20%)	1(2.2%)	p=0.02	4.12	0.684	22.87
Xerostomia	18(69%)	4(9%)	P=0.006	4.21	1.134	34.77
Fissure	8(31%)	2(4.3%)	p=0.003	3.58	1.017	12.38
Covered tongue	11(42%)	2(4.3%)	p=0.000	4.84	1.343	17.498
Mucosal erythema	9(35%)	1(2.2%)	p=0.000	7.25	1.123	46.889
Oral hygiene score						
1 - good	7(26%)	16(35%)				
2 - unsatisfied	9(34%)	20(44%)				
3 - bad	10(38%)	9(20%)	p=0.238			
Gingival hyperplasia						
0	9(35%)	38(83%)				
1	14(54%)	8(17%)				
2	3(11%)	0(0%)	p=0.000			

Discussion

End stage renal disease (ESRD) affect every system in humans including the oral cavity, in a clinical condition defined as uremic syndrome presented with fluid overload, electrolyte disturbance, deterioration in acid-base homeostasis, and uremic toxins retention, normally eliminated through urine output [15].

New dialysis techniques have been developed for better removal of uremic toxins. Advances in understanding of uremic retention solutes and their role in development of clinical symptoms and outcomes, facilitate personalized and targeted dialysis treatment, and may improve quality of life and decreased morbidity and mortality. In the classic taxonomy, uremic retention molecules are divided into 3 categories: small solutes, middle molecules, and protein-bound toxins [16]. In 2021 a consensus conference was held to develop recommendations for an updated definition and classification scheme on the basis of a holistic approach that incorporates physicochemical characteristics and dialytic removal techniques of uremic retention solutes and their association to clinical symptoms and outcomes [17].

Standard High Flux (HF) membranes are effective in the removal of uremic toxins in a range of small solutes (urea) and middle molecules (β2-microglobulin). But the efficient removal of middle molecules (MM) uremic toxins, in a molecular range of 15-50 KDa, is currently limited. Increased concentration of uremic toxins in ESRD patients, leads to pathophysiological process including anorexia, chronic inflammation, calcification, and cardiovascular morbidity and mortality [18].

We have evaluated 5 middle molecules: β2-microglobilin (β2M), myoglobin, free light chain kappa (FLC-k), and free light chain lambda (FLC-λ) and interleukin-6 (IL6). For all middle molecules we have found increased

values in both groups, but significant difference was found for IL 6. According to the new classification of uremic toxins IL6 with MW >15-25 kDa belongs to the group of Medium-middle molecules and the group of Uremic toxins with the highest toxicity evidence score [17]. Interleukin-6 is a proinflammatory cytokine that play a role in development of insulin resistance and overt type 2 diabetes mellitus (T2DM) through the generation of inflammation, differentiation, proliferation, and cell apoptosis [19]. In our study patients with DM had a shorter dialysis vintage. The published data presents no significant difference between diabetic and nondiabetic patients at 1-year survival (87.1% versus 89.7%, P=.66). but, 3- and 5-year survival were significantly lower in patients with DM (52.2% versus 73.8%, P=.04; zero versus 56.9%, P<.001; respectively) [19]. In another retrospective study of 897 patients the 5-year survival rates after censoring were 20.7 and 38.2% for diabetic and non-diabetic patients, respectively (P <0.001) [20].

In the group of DM patients there was significantly higher blood glucose level. Our study confirmed hyperkeratotic lesion as part of the uremic stomatitis in 11% of DM patients and 2% in non DM patients without statistical difference. Uremic stomatitis is an uncommon complication of uremia in advanced renal failure patients. Since it was first reported by Lancereaux in 1887 and described by Barie in 1889, a few affected patients have been presented in the literature [21]. The etiology is still unclear, but a hypothesis for an increased levels of ammonia complexes produced by the action of bacterial ureases that modify salivary urea has been postulated [22]. Four forms of uremic stomatitis have been described in the literature: Ulcerative form, Hemorrhagic form, Nonulcerative, pseudomembranous form, and Hyperkeratotic form. The last two forms appear as white lesions. The hyperkeratotic form presents as multiple, painful, white hyperkeratotic lesions. This hyperkeratotic lesion can be also due to the effects of chemical substances on the oral mucosa [23]. We have reported 35% DM patients with mucosal erythema and only 2.2% in other group of patients (p=0.000).

We have found oral pigmentation in 20% on patients with DM, and 2% in non DM group (p<0.02). Oral pigmented lesions are one of the most significant changes present in patients with end-stage renal disease. The case control study published by Hasan at al. described the most common oral pigmentation were abnormal lip pigmentation and petechiae. A possible mechanism for this pathological findings was attributed to an increased level of beta melanocyte-stimulating hormone (beta-MSH) as a result of an impaired elimination which resulted in continuous stimulation of melanocytes in oral epithelium [24], abnormal lip hyper pigmentation was the most frequently seen lesion in 90% of the CKD patients [25], whereas our study observed only 7.0% patients with pigmentation.

Chronic uremia state and many co-morbid conditions in end stage kidney patients can cause changes in the periodontium leading to an exacerbation of the inflammatory process in the gingival tissue. Poor oral hygiene and development of dental calculus are risk factors for periodontal disease. Prevalence of periodontitis is significantly higher among middle-aged patients with diabetes than among the similarly aged individuals without diabetes [26,27]. In our study periodontal disease was present in 8% and 27% of patients with DM and non DM patients, but without statistical signifycance. The most important is certainly, the patient's education and prevention, as well as frequent clinical check-ups to rule out oral lesions. High prevalence of dental calculus in CKD patients is a common finding. A possible relationship between the amount of biofilm, gingivitis and the amount of dental calculus may be as an additional risk factor for severe destruction of the periodontium. Additionally, hemodialysis patients have faster dental calculus formation as a result of secondary hyperparathyroidism and therapy with calcium-based phosphate binders [28].

Covered tongue (CT) and fissured-dry lips are other frequent oral lesions in hemodialysis patients. Yellowish-white plaque on tongue dorsum, can be seen on the dental examination. Covered tongue is caused by retention of desquamated epithelial cells and leucocytes, and bacterial accumulation on slightly elongated filiform papillae. Reported prevalence are 12.2% to 47.1% in CKD patients, respectively [15,29]. We have found covered tongue in 43% in DM group, and 4% in non DM patients (p<0,000).

In chronic hemodialysis patients, gingival hyperplasia has multiple etiologies among which drug-induced enlargement is a common reason that is related to long term effect of calcium channel blockers, mostly Nifedipine [30]. Overproduction of gum tissue by fibroblasts is the main mechanism of gingival hyperplasia. Poor plaque control, dysregulation of vitamin D metabolism and calcium level acts as a predisposing factor for nifedipine induced gingival enlargement. Neither the dosage, nor the duration of treatment is related to the prevalence of gingival enlargement [30]. In patients with kidney transplants, it is mostly due to the immunosuppressive therapy with cyclosporine [32]. Severe gingival hyperplasia has negative impact to esthetics and function as well as to the overall oral health-related quality of life. Treatment of these conditions requires comprehensive periodontal management by a dentist. In our study, the group of patient with DM have had significantly greater gingival enlargement than non DM group.

There are several risk factors for the prevalence of xerostomia (dry mouth) in chronic hemodialysis patients. The decreased salivary flow may be caused by a direct uremic toxins effect on salivary glands, chemical inflammation, decreased water consumption and chronic de-

hydration and mouth breathing. The study of Swapna *et al*. reported xerostomia presence was seen both in diabetic and nondiabetic patients, with no significant statistical difference. It was opposite of the previous literature reports which showed dry mouth was more severe in the diabetic group compared to the nondiabetics [33-35]. In our study DM patients have signifycantly higher xerostomia compared to the other group of patients.

In association with xerostomia, one third of hemodyalisis patients present a characteristic halitosis called "uremic fetor" and a metallic taste due to the high urea content in saliva and its breakdown in ammonia [36]. In our study majority of patients have bad oral hygiene. According to the literature, less than 45% of hemodialysis patients visited a dentist. Dental care utilization among these patients is very low and this trend can be partly explained by the reason that a greater importance is given to the treatment of systemic diseases rather than dental problems. An another reason can be lack of awareness, physical barriers, because part of these patients come from areas where dental services are rarely available [37]. In a study conducted by Klassen and Krasko in 2002, dental care in dialysis patients was found to be almost completely neglected [38].

Conclusion

Knowledge of oral health among chronic hemodyalisis patients in general is poor and there is an obvious need for an appropriate oral health education. Patients with DM are at increased risk for more severe oral manifestations and complications when compared with non diabetic HD patients due to the chronic inflammatory state.

Supportive dental programs must be established for these patients in order to rise awareness of an urgent need for prevention of dental disease. These patients should be well educated about the significance of oral health on systemic health and should be motivated to have regular dental checkup while undergoing the treatment for kidney disease. Multidisciplinary approach of dental specialist and nephrologist can be crucial in improvement of oral health in chronic hemodialysis patients.

Conflict of interest statement. None declared.

References

1. Kovesdy CP. Epidemiology of chronic kidney disease: an update 2022. *Kidney Int Suppl* (2011). 2022; 12(1): 7-11.
2. Jager KJ, Kovesdy C, Langham R, *et al*. A single number for advocacy and communication-worldwide more than 850 million individuals have kidney diseases. *Nephrol Dial Transplant* 2019; 34: 1803-1805.
3. Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. *Kidney Int Suppl*. 2013; 3(1): 1-150.
4. Ferguson TW, Tangri N, Rigatto C, Komenda P. Cost-effective treatment modalities for reducing morbidity associated with chronic kidney disease. *Expert Rev Pharmacoecon Outcomes Res* 2015; 15(2): 243-252.
5. MacRae C, Mercer SW, Guthrie B, Henderson D. Comorbidity in chronic kidney disease: a large cross-sectional study of prevalence in Scottish primary care. *Br J Gen Pract* 2021; 71(704): 243-249.
6. Honarmand M, Farhad-Mollashahi L, Nakhaee A, Sargolzaie F. Oral manifestation and salivary changes in renal patients undergoing hemodialysis. *J Clin Exp Dent* 2017; 9(2): 207-210.
7. Zhang JJ, Yang L, Huang JW, *et al*. Characteristics and comparison between diabetes mellitus and non-diabetes mellitus among chronic kidney disease patients: A cross-sectional study of the Chinese Cohort Study of Chronic Kidney Disease (C-STRIDE). *Oncotarget* 2017; 8(63): 106324-106332.
8. De Rossi SS, Glick M. Dental considerations for the patient with renal disease receiving hemodialysis. *J Am Dent Assoc* 1996; (2): 211-219.
9. Popovska M, Spasovski G, Orovcanec N, *et al*. Oral findings in end-stage renal disease. *Pril (Makedon Akad Nauk Umet Odd Med Nauki)* 2013; 34(3): 85-91.
10. Gautam NR, Gautam NS, Rao TH, *et al*. Effect of end-stage renal disease on oral health in patients undergoing renal dialysis: A cross-sectional study. *J Int Soc Prev Community Dent* 2014; 4(3): 164-169.
11. Dioguardi M, Caloro GA, Troiano G, *et al*. Oral manifestations in chronic uremia patients. *Renal Failure* 2015; 38(1): 1-6.
12. Costantinides F, Castronovo G, Vettori E, *et al*. Dental Care for Patients with End-Stage Renal Disease and Undergoing Hemodialysis. *Int J Dent* 2018; 2018: 9610892.
13. Dencheva M, Krasteva A, Gueorgieva Tz, Kisselova A. ORAL FINDINGS IN PATIENTS WITH REPLACED RENAL FUNCTION - a pilot study. *J of IMAB* 2010; 16(4): 54-57.
14. Proctor R, Kumar N, Stein A, *et al*. Oral and dental aspects of chronic renal failure. *J Dent Res* 2005; 84: 199-208.
15. de la Rosa Garcia E, Mondragon Padilla A, Aranda Romo S, Bustamante Ramirez MA. Oral mucosa symptoms, signs and lesions, in end stage renal disease and non-end stage renal disease diabetic patients. *Med Oral Patol Oral Cir Bucal* 2006; 11(6): E467-E473.
16. Vanholder R, Argilis A, Baurmeister U, *et al*. Uremic toxicity: present state of the art. *Int J Artif Organs* 2001; 24(10): 695-725.
17. Rosner MH, Reis T, Husain-Syed F, *et al*. Classification of Uremic Toxins and Their Role in Kidney Failure. *Clin J Am Soc Nephrol* 2021; 16(12): 1918-1928.
18. Ciceri P, Cozzolino M. Expanded Haemodialysis as a Current Strategy to Remove Uremic Toxins. *Toxins (Basel)* 2021; 13(6): 380.
19. Beladi Mousavi SS, Hayati F, Alemzadeh Ansari MJ, *et al*. Survival at 1, 3, and 5 years in diabetic and nondiabetic patients on hemodialysis. *Iran J Kidney Dis* 2010; 4(1): 74-77.
20. Vijayan M, Radhakrishnan S, Abraham G, *et al*. Diabetic kidney disease patients on hemodialysis: a retrospective survival analysis across different socioeconomic groups. *Clin Kidney J* 2016; 9(6): 833-838.
21. Sudarshan R, Annigeri RG, Mamatha GP, Vijayabala GS. Uremic stomatitis. *Contemp Clin Dent* 2012; 3(1): 113-115.
22. Leao JC, Gueiros LA, Segundo AV, *et al*. Uremic stomatitis in chronic renal failure. *Clinics* 2005; 60: 259-262.
23. Antoniades DZ, Markopoulos AK, Andreadis D, *et al*. Ulcerative uremic stomatitis associated with untreated

chronic renal failure: report of a case and review of the literature. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2006; 101: 608-613.
24. Ras A, Khalil E, Hussein R, *et al*. "Orofacial pigmentation in hemodialysis patients. A Case Control Study" *Dentistry* 2022; 154.
25. Mainali A, Chettri PK. Oral Manifestations in Hemodialysis Patients and Their Knowledge and Attitude Towards Oral Health. *Nepal Med Coll J* 2020; 22(4): 217-222.
26. Dembowska E, Jaron A, Gabrysz-Trybek E, *et al*. Oral Mucosa Status in Patients with End-Stage Chronic Kidney Disease Undergoing Hemodialysis. *Int J Environ Res Public Health* 2023; 20: 835.
27. Duran I, Erdemir EO. Periodontal treatment needs of patients with renal disease receiving haemodialysis. *Int Dent J* 2004; 54: 274-278.
28. Nascimento MAG, Soares MSM, Chimenos-Küstner EC, *et al*. Oral symptoms and oral health in patients with chronic kidney disease. *RGO, Rev Gaúch Odontol* 2018; 66(2):160-165.
29. Chuang SF, Sung JM, Kuo SC, *et al*. Oral and dental manifestations in diabetic and nondiabetic uremic patients receiving hemodialysis. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2005; 99: 689-695.
30. Barclay S, Thomason JM, Idle JR, Seymour RA. The incidence and severity of nifedipine-induced gingival overgrowth. *J Clin Periodontol* 1992; 19: 311-314.
31. Reali L, Zuliani E, Gabutti L, *et al*. Poor oral hygiene enhances gingival overgrowth caused by calcineurin inhibitors. *Journal of Clinical Pharmacy and Therapeutics* 2009; 34: 255-260.
32. Kendall P, Pugashetti JV & Aronowitz P. Drug-induced gingival overgrowth after renal transplantation. *J Gen Intern Med* 2017; 32: 1406.
33. Swapna LA, Koppolu P, Prince J. Oral Health in Diabetic and Nondiabetic Patients with Chronic Kidney Disease. *Saudi Journal of Kidney Diseases and Transplantation* 2017; 28(5): 1099-1105.
34. Swapna LA, Reddy RS, Ramesh T, *et al*. Oral health status in haemodialysis patients. *J Clin Diagn Res* 2013; 7: 2047-2050.
35. Ravindran R, Deepa Mg, Sruthi AK, *et al*. Evaluation of Oral Health in Type II Diabetes Mellitus Patients. *Oral Maxillofac Pathol J* 2015; 6(1): 525-531.
36. Marti Alamo S, Gavalda Esteve C, and Sarrion Perez M. G. Dental considerations for the patient with renal disease. Journal of Clinical and Experimental Dentistry 2011;3(2): e112-119.
37. Gautam NR, Gautam NS, Rao TH, *et al*. Effect of end-stage renal disease on oral health in patients undergoing renal dialysis: A crosssectional study. *J Int Soc Prevent Communit Dent* 2014;4:164-9.
38. Klassen JT, Krasko BM. The dental health status of dialysis patients. *J Can Dent Assoc* 2002; 68(1): 34-38.