Original article

ORAL ULCERATIONS IN CHRONIC KIDNEY DISEASE PATIENTS: EXPLORING THE RELATIONSHIP BETWEEN CLINICAL PRESENTATION OF THE ULCERS AND BLOOD UREA CONCENTRATION

Oyetola EO,[1] Ojo MO,[1] Mogaji I K,[1] Aremu AO,[2]

[1]Department of Oral Medicine and Oral Pathology, Obafemi Awolowo University, Ile Ife, Nigeria. [2] Renal Unit, Department of Medicine, Obafemi Awolowo University, Ile Ife, Nigeria.
.

ABSTRACT

BACKGROUND: Oral ulceration is one of the commonly reported oral mucosa lesions in Chronic Kidney Disease (CKD) patients and it is strongly associated with increased systemic inflammatory burden which worsen the underlying kidney diseases.
OBJECTIVE: This study was aimed at determining the relationship between oral ulcerations and blood urea concentration.
METHODS: This study was designed as a cross sectional study. Participants were randomly selected chronic kidney disease patients attending Renal clinic of Obafemi Awolowo University Teaching Hospitals between January 2019 to December, 2019. They were interviewed and examined. Oral mucosa was carefully examined for ulcers and other oral features. Blood samples were taken to determine blood urea concentration. Information was obtained using a structured questionnaire and stored in a passworded computer. Data analysis was done using STATA 14. Analysis of the blood urea concentration in both participants with and without oral ulceration was determined using student t-test and ANOVA as appropriate, p value set at <0.05.
RESULTS: A total of 151 participants, 108(71.5%) male and 43 (28.4%) females participated, their mean age was 38.6years $\pm$14.1. Twenty-nine (19.2%) patients had oral ulcerations. The ulcers were more frequent on the lower lips (17, 58.6%). Of all the patients with oral ulcers, 20 (69.0%) were recurrent, 24 (82.6%) presented in acute stage, 23 (79.3%) were painful and 22 (75.9%) were solitary ulcers. Blood Urea concentrations of patients with oral ulcerations were significantly higher than those without oral lesion p=0.001 likewise the blood urea concentration of patients with painful ulcers were significantly higher, p=0.001.
CONCLUSION: About one out of five CKD patients would develop oral ulcer. Participants with Oral ulcerations had significantly higher blood urea especially when the ulcers present as acute, multiple, painful and recurrent lesion.

Correspondence address:

Dr. E.O. Oyetola
Department of Oral medicine and Oral Pathology, Obafemi Awolowo University.
phemyhoye12@yahoo.com
Tel: +2348035375713

KEYWORDS: Oral ulcers, Chronic Kidney Disease, Blood Urea

INTRODUCTION

Oral mucosa lesion is one of the common oral manifestations in chronic kidney diseases (CKD)[1, 2]. The lesions usually present as a mucosa patch, plaque, erosion or frank oral ulcers covered with pseudomembrane on the mucosa and may be associated with pain and discomfort[1]. Oral ulcers in renal patients may be attributable to the effects of urea on the oral mucosa which occurs when the blood urea is greater than 300mg/dl. The resulting clinical condition generally called uremic stomatitis may present in any of the four variants: erythematosus membranous stomatitis, ulcerative stomatitis, hemorrhagic stomatitis, and the hyper-parakeratotic stomatitis[3].

The ulcerative variant is the most common clinical forms of uremic stomatitis and usually present as frank ulcers in the mouth.[4] Other possible causes or predisposing factors of oral ulcers in CKD patients include the impaired salivary production which reduces oral mucosa immunity. It also enhances mucosa bacterial, viral and fungi infections on the mucosa. The accompanied exaggerated inflammatory response from local trauma due to impaired local and systemic immunity would lead to formation of frank ulcers [5].

The functions of the kidneys are vital for survival and inability of the kidney to function leads to immunosuppression which would encourage oral lesions to occur. Among these functions are: excretion of metabolites, particularly urea, regulation of blood volume and electrolyte concentration (homeostasis), regulation of erythrocyte production and participation in calcium metabolism through hydroxylation of cholecalciferol to Vitamin D3 the active metabolite[1]. Loss of the excretory function as a result of kidney failure leads to accumulation of waste products (urea) in the blood. Excessive salivary urea (up to 300mg/dl) predisposes to developing uremic stomatitis which may manifest as frank oral ulceration. Salivary urea can also be used as a good marker of assessing severity of renal failure[6]. Previous studies had reported that increased blood urea is associated with oral symptoms[7, 8].

Oral ulcers in renal patients affects the quality of life of the patients as the patients find it difficult to chew, swallow, taste and speak well. The resulting oxidative stress on the patients causes systemic inflammation which in turn enhances the progression of kidney diseases[9, 10]. Oral ulceration presents on various locations in the mouth such as tongue, lips buccal mucosa and floor of the mouth. There are limited information relating the varying clinical presentations of oral ulcers to the severity of the underlying kidney disease, but it is established that the relationship between CKD and oral health is bidirectional just like diabetes mellitus and stroke[11].

Oral lesions may predicts the severity of the underlying systemic problems[12]. Therefore, it becomes important to investigate the relationship between various patterns of presentation of the oral lesions and the severity of the renal problems. This study was aimed at determining the relationship between oral ulcerations and blood urea concentration. The findings of this study are therefore, expected to provide baseline data that will enables Oral physicians to give necessary advice to nephrologists, encouraging the multidisciplinary management of chronic renal diseases.

MATERIALS AND METHODS

This study was designed as a cross-sectional study to determine the clinical presentations of oral ulcerations in chronic kidney diseases and to relate the clinical picture to respective blood urea concentration.

Participants for this study were randomly selected CKD patients from the pool of patients who are being managed at the Renal Unit of Obafemi Awolowo University Teaching Hospitals complex, Ile Ife. Participants were selected using simple random sampling method. Each consenting patient in the clinic and renal wards were asked to blindly pick from a box containing papers marked YES or NO. Only those who picked YES were recruited. The details of the study were duly explained to the patients. Unconscious and unstable patients were excluded from the study as well as patients with Behcet diseases or other forms of ulcer related

conditions. Ethical approval to carry out this study was obtained from the Ethics and Research Committee of Obafemi Awolowo University Ile Ife.

Data was collected with the use of questionnaire which was organized into various sections. Section 1 recorded the patients' biodata such as age, sex, and marital status. The section 2 recorded information on oral symptoms associated with their kidney disease. Specific oral symptom/lesion was oral ulcerations. Information recorded were site, number, size and location of the ulcer. Other oral lesions seen were also recorded.

Section 3 recorded findings from examinations. Examination was done with patient comfortably sitting on a chair of a well illuminated room in the clinic. Extra oral examination was carefully done. The mouth was then thoroughly examined to determine the oral hygiene status using Simplified Oral hygiene index (S-OHI) as reported by Green and Vermilion criteria[13]. Oral hygiene was categorized as good, fair and poor when the index score falls, using the range of 0-0.9, 1-1.9 and >2.0 respectively. Mouth opening was assessed by measuring interincisal distance with the aid of Veneer caliper findings, interincisal distance of between 3-6cm was taken as normal. Each tooth was examined also for gingival recession, the migration of apical gingival below mucogingingival junction was taken as gingival recession. Oral mucosa was also examined for presence of macular, papillary and white lesions and the findings were recorded accordingly.

Blood samples of the subjects were also taken with 5ml hypodermic needle into a heparinized bottle and were transported to the laboratory for assessment of blood urea and creatinine.

Data was analyzed using STATA 14 statistical software. Continuous variables such as age, blood urea and blood creatine were analyzed using mean, media and mode. For qualitative variables they were analyzed with frequency and percentages, comparison made using Fischer's exalt. Continuous variables were subjected to parametric test and comparison done using Students t-test for normally distributed variables. Analysis involving comparison of mean in a normally distributed data was done using Analysis of Variance test (ANOVA), p set at $p< 0.05$.

RESULTS

Sociodemographics of the participants

A total of 151 patients with Chronic Kidney Diseases with mean age of 38.6+14.1 years participated in the study, 108 (71.5%) males and 43 (28.4) females. More than two-third (100, 66.2%) of the patients practiced Christian religion, married and were of Yoruba ethnicity. More than half of all respondents were in their fourth and fifth decade of life. Twenty-nine (19.2%) participants were being managed for hypertension, while 39 (25.8%) were known diabetic patients. Habitual smoking and alcohol intake were not frequent among the participants. (Table 1).

Prevalence of Oral Ulceration among Participating CKD Patients

Out of a total of 151 participants, oral ulcers were found in 29 patients, accounting for 19.2% (Figures 1 and 2).

Fig 1 Oral ulcerations on the lower lip

Clinical presentations of participants with oral ulcerations

Oral ulcerations were significantly more frequent among males. They occurred

predominantly in the third and fourth decades of life. None were found among those below 20 years of age. In most cases, the ulcers presented as recurrent (20, 69%), acute (24, 82.6%), painful (23, 79.3%) solitary (22, 75.9%) ulcers with varying sizes most (20, 69.0%) of which were greater than 1cm in largest diameter. Lower lip (17, 58.6%) was the most frequent intra oral site affected (Table 2). The ulcers present as multiple (Fig 1) and solitary ulcers (Fig 2). The majority (22, 75.9%) were solitary ulcers.

Fig 2: Dark pigmentation, white patch and ulceration on the buccal mucosa

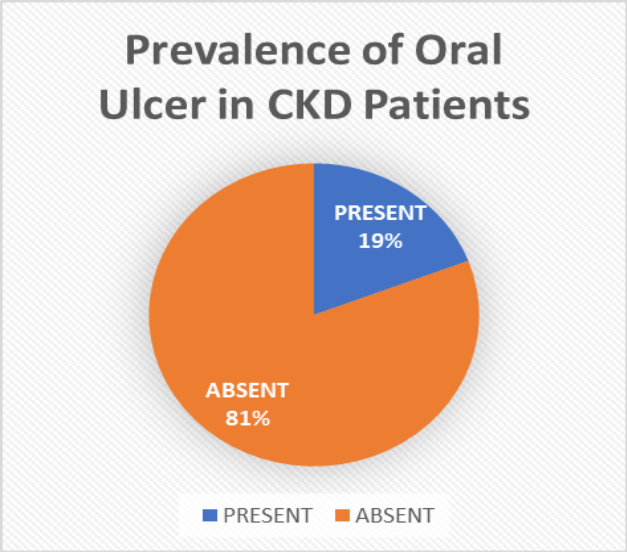


Fig 3. Prevalence of Oral Ulceration among Participating CKD Patients

Table 1: Sociodemographic and relevant history of the participants

Variables	Ulcer Present (%)	Ulcer Absent (%)	Total	P value
Sex				
Male	23	85	108	0.213
Female	6	37	43	
Age group (years)				
<20	0	12	12	0.168
21-30	8	25	35	
31-40	4	26	36	
41-50	4	31	36	
51-60	3	14	16	
>60	10	14	16	
Religion				
Christianity	11	89	100	0.001*
Islam	18	33	51	
Ethnicity				0.109
Yoruba	25	116	141	
Hausa	1	4	5	
Ibos	1	1	2	
Others	2	1	3	
Marital Status				0.267
Single	6	39	45	
Married	23	83	106	
Hypertension				
Present	13	16	29	0.104
Absent	73	49	122	
Diabetes mellitus				
Present	10	19	29	0.171
Absent	29	93	122	
Smoke				
Present	18	11.9		
Absent	133	88.1		
Alcohol				
Present	15	9.9		
Absent	136	90.1		

Fischer's exact test and chi square test *Statistical significance.

Relationship between Oral ulceration and some selected variables

Table 3 shows the relationship between presence of oral ulcerations and mean blood urea, creatinine, age and blood pressure. The mean blood urea, creatine and mean systolic blood pressure were significantly higher among subjects with oral ulceration when compared to

those without oral ulceration, both subjects had p=0.001. Patients with oral ulceration also had a higher diastolic pressure but the difference was not statistically significant, p=0.240. Oral ulcerations were more frequent among older participants but the difference was not statistically significant. (Table 3).

Table 2: Clinical presentations of Participants with oral ulcerations

Variable	Frequency (%) n=29	P value
Sex Variation		
Male	23 (79.3)	0.001*
Female	6 (20.7)	
Age category (years)		
< 20	0 (0)	0.236
21-30	8 (27.6)	
31-40	4 (13.8)	
41-50	4 (13.8)	
51-60	3 (10.3)	
>60	10 (34.5)	
Duration of the ulcer		
<2 weeks	24 (82.6)	0.001*
>2 weeks	5 (17.2)	
Number of ulcers		
Solitary	22 (75.9)	0.001*
Multiple	7 (24.1)	
Associated with pain		
Present	23 (79.3)	0.001*
Absent	6 (20.7)	
Size		
<1cm	9 (31.0)	0.001*
>1cm	20 (69.0)	
Associated with recurrence	20 (69.0)	0.001*
Yes	9 (31.0)	
No		
Intraoral site involved		
Lower lips	17 (58.6)	0.001*
Tongue	3 (10.3)	
Buccal Mucosa	5 (17.2)	
Upper lips	4 (13.8)	

Fischer's exalt and chi square test, * statistically significant.

Oral Ulceration and Ora Hygiene status

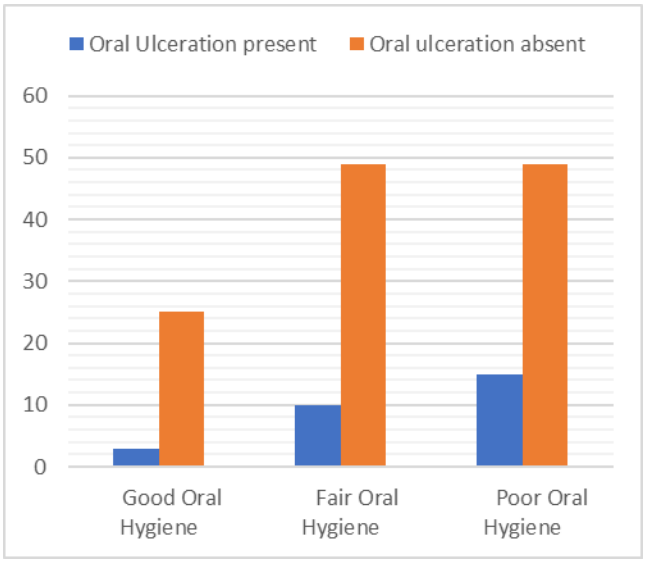
Among participants with oral ulcerations, the frequency of oral ulceration increases as the oral hygiene becomes worse, the difference not statistically significant, p=0.411. Many (99, 65.6%) of Participants without oral ulceration showed fair and poor oral hygiene status. (Figure 4)

Table 3: Relationship between Oral ulceration and some selected variables

Characteristics	Oral Ulceration present (mmol/L)	Oral ulceration absent (mmol/L)	P value
Blood Urea (SD)	22.3 (11.9)	14.5 (6.4)	0.001*
Blood Creatinine (SD)	150.9 (60.3)	130.8 (46.7)	0.026*
Systolic blood pressure (SD)	143.6 (43.7)	121.9 (18.4)	0.001*
Diastolic blood pressure (SD)	78.0 (10.7)	75.4 (9.7)	0.240
Age (SD)	38.4 (13.6)	38.7 (14.2)	0.531

T-test, * statistically significant, SD=standard deviation

Fig 4: Relationship between presence of Oral Ulceration and Oral Hygiene status



Fischer's exalt, p= 0.411

Relationship between Pattern of presentation of oral ulceration and blood urea concentration (mmol/L)

The mean blood urea concentration was significantly higher among participants with oral ulceration, p=0.001. Specifically, blood urea concentration was significantly higher when comparing acute to late presentation of ulcer, solitary to multiple ulcers, larger to smaller ulcers sizes, recurrent to non-recurrent presentation, ulcers associated with pain comparing with those without pain as well as

poor oral hygiene versus good oral hygiene, p=0.001 (Table 4).

Table 4: Relationship between pattern of oral ulceration and blood urea concentration (mmol/L)

Clinical presentation	Blood Urea concentration (mmol/L)	Statistics
Duration of oral ulceration		
Less than 2 weeks	22.0 (12.2)	P=0.001*, df 2 (between groups) F=16.9
More than 2 weeks	23.2 (12.1)	
No ulceration	14.5 (6.3)	
Number of Ulcers		
Solitary	24.3 (11.3)	P= 0.001*, df 3 (between groups) F=11.38
Multiple	28.9 (22.6)	
No ulceration	14.5 (6.3)	
Size		
Less than 1cm	21.3 (12.2)	P= 0.001*, df 2 (between groups) F=11.82
More than1cm	22.9 (12.1)	
No ulceration	14.5 (6.3)	
Nature of Recurrence		
Ulcers were recurrent	18.9 (8.9)	P= 0.001*, df 2 (between groups) F=18.47
Ulcers not recurrent	23.3 (14.8)	
No ulceration	14.5 (6.3)	
Pain		
Ulcers associated with pain	24.3 (12.1)	P= 0.001*, df 2 (between groups) F=16.89
Ulcers not associated with pain	13.2 (4.7)	
No ulceration	14.5 (6.3)	
Oral Hygiene		
Good	15.1 (7.8)	P= 0.801, df 2 (between groups) F=0.13
Fair	15.8 (7.6)	
Poor	16.1 (8.3)	

DISCUSSION

Oral lesions among patients with chronic kidney disease are very common, this potentially reflects the low usage of preventable dental services and may be helpful in determining the health status of the patients[2, 14]. Chronic kidney disease is characterized by a progressive loss of kidney function ultimately resulting in the need for renal replacement therapy. The basic problem is electrolyte disturbance as well as accumulation of waste products (urea) in the blood which predisposes to many complications. There is continued kidney damage that has continued for more than 3 months as characterized by structural or functional abnormalities of the kidney, with or without decreased glomerular filtration rate (GFR)[7].

Due to the asymptomatic nature of the early stage of the disease, it is difficult to determine the exact prevalence and incidence of the disease. Generally, the prevalence of disease in general population is around 10-14%.[15]. With the increasing prevalence of this disease in the general population, so many patients with chronic kidney disease (symptomatic and asymptomatic) will be presenting for routine dental consultation.

We reported male predilection in this study which was similar to the findings of many hospital-based studies[14, 16]. However a community based study by Chukwuonye et al[17] showed female predilection. The distribution of predisposing factors of kidney diseases in the community is important in presentation. Chronic kidney disease affects a wide range of age groups as reported in this study with mean age of affected individuals being 38.6 (14.1) years. This is similar to earlier reported studies[2, 18].

Oral ulceration is one of the common oral lesions associated with chronic kidney diseases. In the present study 19.2% of renal patients had oral ulcers. This was higher than the findings of Oyetola et al 2015[2] who reported prevalence of 1.11%. Unlike the present study, Oyetola et al. in 2015 focused on aphthous ulceration which had not accounted for other forms of ulcers in the mouth. The local (oral) and systemic effect of urea on oral structures tends to reduce oral mucosa immunity, together with reduced saliva production that may be responsible for the oral ulcerations. More so, hemorrhagic diathesis, a clinical condition common in uremia, causes decrease viability of affected tissues and allowing progression of bacterial infection, resulting in ulceration and pseudomembrane formation.[19, 20]

A closer look into clinical presentations of oral ulcers may be a useful guide to clinical assessment of the severity of underlying renal problems probably in a similar scenario where clinical site of oral candidiasis can predict CD4 count in HIV patient[21]. Our study showed variations in the locations of the ulcer with the majority of ulcers located on the lower lips. This

may be due to the gravitation of the saliva and the associated urea, which tend to pull downwards during jaw movement[22]. This study showed that subjects with multiple ulcers had significantly higher blood urea concentration than solitary ulcers. Multiple oral ulcerations, according to Babu etal al, [12] tends to increase the systemic inflammatory burden and release of C-reactive protein which worsen the underlying renal disease.

Also, in the present study, it was found that the mean blood urea of participants with painful oral ulcers was significantly greater than those with painless ulcers. The same trend was also found when comparing larger ulcer size to small ulcer size with larger ulcers having higher blood urea concentration. Likewise, recurrent ulcers, and multiple ulcers with acute presentations had higher blood urea values. The increase in blood urea nitrogen in these circumstances is due to increase in systemic inflammation which encourages renal damage[9]. Studies relating the clinical presentation of oral ulcers to blood urea is limited in the literature. Likewise, the presence of pain tends to increase the production of inflammatory mediators which further enhance systemic oxidative inflammation that occurs in renal failure[10, 23]. Management of pain has been reported to encourage recovery from renal problems. Larger surface area of larger ulcers may produce more inflammatory mediators which further impairs renal functions.

In acute cases, there are acute cells infiltration, which secrete their toxins to ensure an inflammatory process, these inflammatory processes may encourage the progression of renal diseases resulting in higher urea concentration. Unfortunately, the results of this study show that most oral ulcers in CKD were multiple, painful, acute, and of larger sizes, a situation that encourages more inflammatory burden and predisposes to further renal impairment in a resource limited environment. Timely treatment of oral diseases has been reported to reduce the progression of underlying systemic disease[11, 12]. Therefore, prompt and appropriate management of oral ulcers and other oral lesions will go a long way in the management of chronic kidney disease[24]. This has reiterated the importance of interdisciplinary approach including Oral physicians in the management of these patients with a view to achieving the desired prognosis.

In conclusion, the prevalence of oral ulcers in chronic kidney disease patients was found to be 19.2%. The clinical presentations of oral ulcers were significantly related to the blood urea concentration. The blood urea concentration of participants with oral ulcers was significantly higher than those without the ulcers. The presence of oral pain, recurrent, multiple ulceration and larger ulcer sizes are associated with significantly higher blood urea concentration

Conflict of interest: None declared

REFERENCES

1. Gupta M, Gupta M, Abhishek. Oral conditions in renal disorders and treatment considerations - A review for pediatric dentist. Saudi Dent J. 2015; 27(3): 113-119.
2. Oyetola EO, Owotade FJ, Agbelusi GA, Fatusi OA, Sanusi AA. Oral findings in chronic kidney disease: implications for management in developing countries. BMC oral health. 2015; 15: 24.
3. Sudarshan R, Annigeri RG, Mamatha GP, Vijayabala GS. Uremic stomatitis. Contemporary clinical dentistry. 2012; 3(1): 113-115.
4. Dioguardi M, Caloro GA, Troiano G, Giannatempo G, Laino L, Petruzzi M, et al. Oral manifestations in chronic uremia patients. Renal Failure. 2016; 38(1): 1-6.
5. Peacock ME, Arce RM, Cutler CW. Periodontal and other oral manifestations of immunodeficiency diseases. Oral diseases. 2017; 23(7): 866-88.
6. Vanholder R, Schepers E, Meert N, Lameire N. What is uremia? Retention versus oxidation. Blood purification. 2006; 24(1): 33-38.
7. Anuradha BR, Katta S, Kode VS, Praveena C, Sathe N, Sandeep N, et al. Oral and salivary changes in patients with chronic kidney disease: A clinical and biochemical study. Journal of Indian Society of Periodontology. 2015; 19(3): 297-301.
8. Oyetola E, Akomolafe R, Owotade F, Egunjobi S. Physio-Chemical Analysis of Unstimulated Saliva of Healthy Nigerian Population. J Oral Biol. 2018; 5(1): 6-12.
9. Mihai S, Codrici E, Popescu ID, Enciu A-M, Albulescu L, Necula LG, et al. Inflammation-

Related Mechanisms in Chronic Kidney Disease Prediction, Progression, and Outcome. Journal of Immunology Research. 2018; 2018: 2180373.
10. Gyurászová M, Gurecká R, Bábíčková J, Tóthová Ľ. Oxidative Stress in the Pathophysiology of Kidney Disease: Implications for Noninvasive Monitoring and Identification of Biomarkers. Oxidative Medicine and Cellular Longevity. 2020; 2020: 5478708.
11. Alpert P Oral health: the oral-systemic health connection. Home Health Care Manag Pract. 2017; 29(1): 56-59.
12. Babu NC, Gomes AJ. Systemic manifestations of oral diseases. Journal of oral and maxillofacial pathology: JOMFP. 2011; 15(2): 144-147.
13. Greene JC, Vermillion JR. The simplified oral hygiene index. Journal of the American Dental Association (1939). 1964; 68: 7-13.
14. Ruospo M, Palmer SC, Craig JC, Gentile G, Johnson DW, Ford PJ, et al. Prevalence and severity of oral disease in adults with chronic kidney disease: a systematic review of observational studies. Nephrology, dialysis, transplantation: official publication of the European Dialysis and Transplant Association - European Renal Association. 2014; 29(2): 364-375.
15. Coresh J, Astor BC, Greene T, Eknoyan G, Levey AS. Prevalence of chronic kidney disease and decreased kidney function in the adult US population: Third National Health and Nutrition Examination Survey. American journal of kidney diseases: the official journal of the National Kidney Foundation. 2003; 41(1): 1-12.
16. Chang PY, Chien LN, Lin YF, Wu MS, Chiu WT, Chiou HY. Risk factors of gender for renal progression in patients with early chronic kidney disease. Medicine. 2016; 95(30): e4203.
17. Chukwuonye II, Ohagwu KA, Adelowo OO, Chuku A, Obi EC, Onwuchekwa U, et al. Prevalence and Predictors of Chronic Kidney Disease in a Semiurban Community in Lagos. International Journal of Nephrology. 2019; 2019: 1625837.
18. Chukwuonye, II, Ogah OS, Anyabolu EN, Ohagwu KA, Nwabuko OC, Onwuchekwa U, et al. Prevalence of chronic kidney disease in Nigeria: systematic review of population-based studies. International journal of nephrology and renovascular disease. 2018; 11: 165-172.
19. McCreary CE, Flint SR, McCartan BE, Shields JA, Mabruk M, Toner ME Uremic stomatitis mimicking oral hairy leukoplakia: report of a case. Oral surgery, oral medicine, oral pathology, oral radiology, and endodontics. 1997; 83(3): 350-353.
20. Leão JC, Gueiros LA, Segundo AV, Carvalho AA, Barrett W, Porter SR. Uremic stomatitis in chronic renal failure. Clinics (Sao Paulo, Brazil). 2005; 60(3): 259-62. doi:10.1590/s1807-59322005000300013.
21. Patil S, Majumdar B, Sarode SC, Sarode GS, Awan KH Oropharyngeal Candidosis in HIV-Infected Patients-An Update. Frontiers in microbiology. 2018; 9: 980.
22. Shiller DM, Ostry DJ, Gribble PL Effects of gravitational load on jaw movements in speech. The Journal of neuroscience: the official journal of the Society for Neuroscience. 1999; 19(20): 9073-9080.
23. Matoba K, Takeda Y, Nagai Y, Kawanami D, Utsunomiya K, Nishimura R. Unraveling the Role of Inflammation in the Pathogenesis of Diabetic Kidney Disease. Int J Mol Sci [Internet]. 2019 2019/07//; 20(14). Available from:http://europepmc.org/abstract/MED/31295940, https://doi.org/10.3390/ijms20143393, https://europepmc.org/articles/PMC6678414, https://europepmc.org/articles/PMC6678414?pdf=render.
24. Krane V, Wanner C. Should we aim for oral health to improve outcomes in chronic kidney disease? Nephrology, dialysis, transplantation: official publication of the European Dialysis and Transplant Association - European Renal Association. 2016; 31(10): 1551-4.