ANALYSIS OF ORAL CHRONIC KIDNEY DISEASE WITH HEMODIALYSIS THERAPY IN SOUTH KALIMANTAN - INDONESIA

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Abstract: Chronic kidney disease (CKD) is a world health problem where the incidence continues to increase, has a poor prognosis and high-level financing. Clinical manifestations of the oral cavity can occur in CKD patients with hemodialysis therapy due to a decrease in the immune system. To analyze the descriptively the clinical manifestations of oral cavity in CKD patients with hemodialysis therapy at RSUD Ulin Banjarmasin South Kalimantan, period January-March 2019. This is a descriptive analysis with a cross sectional study design, based on history and clinical examination of the oral cavity. Data was entered and analyzed using chi square test. Sampling by purposive sampling. there is a relationship between uremic odor and duration of hemodialysis (p = 0.017). There was a relationship between xerostomia and gender (p = 0.035) and there was a relationship between xerostomia and the duration of hemodialysis (p = 0.007). There is a relationship between gingival swelling and age (p = 0.010) and there is a relationship between gingival swelling and diabetes mellitus (p = 0,000). Manifestations found in the oral cavity of CKD patients with hemodialysis therapy are uremic odor, mouthache, xerostomia, mucosal lesions, candidiasis, and gingival swelling. There is a relationship between sex with xerostomia, the relationship between age with gingival swelling, the relationship between the duration of hemodialysis with uremic odor and xerostomia, the association between DM with gingival swelling.

Keywords: Chronic Kidney Disease, Clinical Manifestations, Hemodialysis, Oral Cavity

INTRODUCTION

Chronic kidney disease (CKD) is a world health problem whose incidence rate continues to increase, this disease has a poor prognosis and relatively high financing. In the world, the prevalence of CKD is in the range of 11 to 13%.[1] In Indonesia, prevalence of CKD increases with aging. Prevalence increased in the age group 25-44 years (0.3%), then followed by the age of 45-54 years (0.4%), and then age 55-74 years (0.5%), the highest is in the age ≥75 years (0.6%). Based on gender the prevalence of chronic kidney disease in men (0.3%) is higher than women (0.2%).[2] Based on data Riskesdas 2018, the prevalence of CKD in Indonesia over the age of 15 years had been diagnosed with CKD (3.8%). In South Kalimantan in 2018 more than 2.0% of the population with age 15 years suffer CKD based on a doctor's diagnosis.[3]

CKD is characterized by a decline in kidney function that occurs more than 3 months with a glomerular filtration rate equal to or more than 60 ml / minute / 1.73m^2. Globally, diabetes is a factor causing chronic kidney disease, whereas in Indonesia the main cause is glomerulonephritis..[4] The Causes of kidney disease are diabetes mellitus, hypertension, chronic glomerulonephritis, interstitial nephritis,but the main causes of kidney disease is glomerulonephritis.[5] 1,929,000 people with CKD in the world in 2011 supported hemodialysis therapy.[6] In Indonesia, 19.3% of patients diagnosed with CKD undergo hemodialysis therapy and in South Kalimantan the prevalence rate more than 19.3%.[3]

In CKD patients, a decline in kidney function that causes high uremia levels will increase the risk of infection, so the immune system will be abnormal. Continuous haemodialysis therapy in patients with CKD will cause activation of leukocytes and produce cytokines.[7] The repeated contact between the blood and the dialyzer membrane that occurs during haemodialysis causes activation of the alternative use complement system and a membrane attack complex (MAC) which plays a role in lyses target cells, namely leukocytes, erythrocytes and platelets.[8]

CKD and haemodialysis therapy therapy can affect health conditions in the oral cavity, this is related to the presence of interference with the immune system that can lead clinical manifestations of the oral cavity. Clinical manifestations of the oral cavity in CKD patients with haemodialysis therapy is vary including uremic odor, metallic taste in the mouth, xerostomia, mucosal lesions, candidiasis, and gingival swelling.[9,10,11] Until now there is no research on the descriptive study of clinical manifestations of oral cavity in CKD patientswith haemodialysis therapy in South Borneo, especially in Banjarmasin.

RESEARCH METHOD

This research has gone through ethical feasibility tests published by the Faculty of Dentistry, University of Lambung Mangkurat No.099 / KEPKG-FKGULM / EC / XII / 2018. This type of research is descriptive analysis with cross sectional research design. The sampling technique in this study was taken by purposive sampling. The sample size needed is 30. The tools in this study are data checklist for history, informed consent, stationery, diagnostic tools (mouth glass), nierbekken, flashlight, handscoon, mask, and tissue. The study was conducted by examining the patient's oral cavity in accordance with the inclusion criteria and was willing to sign an informed consent and continued with filling out the clinical examination form. Processing the data obtained includes the editing process, namely re-checking the data collected. Coding is to give a code to the data consisting of several categories, then tabulation is done which is to make data tables and perform calculations from data obtained from tables and made with analytic statistics. Data analysis using non-parametric test with chi square test method with 2x2 table to see the relationship of sex, age, duration of haemodialysis,

hypertension, and diabetes mellitus with clinical manifestations of the oral cavity.

RESULTS AND DISCUSSION

Based on the results of research that has been done in Ulin Banjarmasin Hospital obtained sociodemographic characteristics of respondents which include gender, age, duration of hemodialysis, hypertension and DM in patients with chronic kidney disease with hemodialysis therapy can be seen in table 1.

Table 1.Sociodemographic characteristics of respondents

Variable	N	%
Gender		
Male	17	56.7%
Women	13	43.3%
Age		
≤ 46 years (below average)	13	43.3%
> 46 years (above average)	17	56.7%
Duration of hemodialysis		
≤ 32 months (below average)	16	53.3%
> 32 months (above average)	14	46.7%
Hypertension		
Have	19	63.3%
No	11	36.7%
Diabetes Mellitus		
Have	7	23.3%
No	23	76.7%

Types of clinical manifestations of oral cavity that can be found in patients with chronic kidney disease with hemodialysis therapy in RSUD Ulin Banjarmasin in January-March 2019 is a uremic smell 19 cases (19.28%), metallic taste in the mouth 19 cases (19.28%), *Xerostomia* is 18 cases (18.27%), lesions of the mucosa 2 cases (2.3%), candidiasis 3 cases (3.4%) and swelling of gingiva 7 cases (7.1%). The most clinical manifestations appearing in patients with chronic kidney disease undergoing hemodialiasis therapy in RSUD Ulin Banjarmasin in January-March 2019 is a uremic odor and a metallic taste of the mouth.

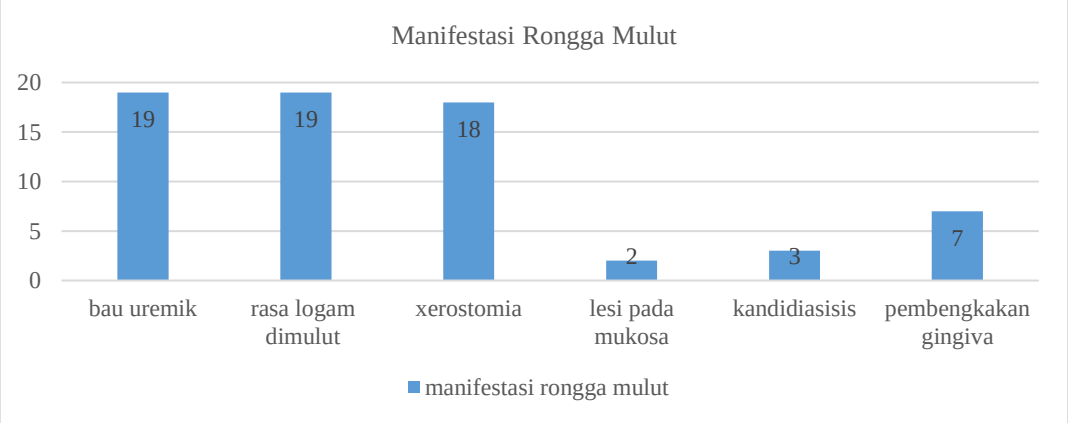

Figure 1. Diagram characteristic of clinical manifestations of oral cavity in patients with chronic kidney disease with hemodialysis therapy in RSUD Ulin Banjarmasin in January-March 2019.

The research results were tested using the Chi-square non-parametric test to determine the relationship between clinical manifestations of the oral cavity with gender, age, prolonged hemodialysis, hypertension and status of diabete melitus in patients chronic kidney disease with hemodialysis therapy in Ulin Hospital Banjarmasin.

Table 2. The distribution of patients with hemodialysis in RSUD Ulin Banjarmasin in January-March 2019 based on uremic smell and related factors.

	Uremic smell		Sig.
	Have 19	No 11	
Gender			
Male	57.9%	54.5%	1,000
Women	42.1%	45.5%	
Age			
≤ 46 years (below average)	36.8%	54.5%	0454
> 46 years (above average)	63.2%	45.5%	
Duration of hemodialysis			
≤ 32 months (below average)	36.8%	81.8%	0.017
> 32 months (above average)	63.2%	182%	
Hypertension			
Have	68.4%	54.5%	0696
No	31.6%	45.5%	
Diabetes Mellitus			
Have	31.6%	9.1%	0215
No	68.4%	90.9%	

Table 2 showed that there is a meaningful relationship between the uremic smell and the old hemodialysis with a value of P < 0.05. There is no meaningful relationship between the uremic smell and gender, age, hypertension, and DM (p > 0.05). Table 3 showed that there is no meaningful relationship between the metallic taste in the mouth with gender, age, prolonged hemodialysis, hypertension, and DM (p > 0.05).

Table 3. The distribution of patients with hemodialysis in RSUD Ulin Banjarmasin in January-March 2019 based on the taste of metals in the mouth and related factors.

	Metallic taste in mouth		Sig.
	Have 19	No 11	
Gender			
Male	57.9%	54.5%	1,000
Women	42.1%	45.5%	
Age			
≤ 46 years (below average)	52.6%	27.3%	0259
> 46 years (above average)	47.4%	72.7%	
Duration of hemodialysis			
≤ 32 months (below average)	57.9%	45.5%	0510
> 32 months (above average)	42.1%	54.5%	
Hypertension			
Have	57.9%	72.7%	0466
No	42.1%	27.3%	
Diabetes Mellitus			
Have	10.5%	45.5%	0.68
No	89.5%	54.5%	

Table 4. The distribution of patients with hemodialysis in RSUD Ulin Banjarmasin in January-March 2019 based on *xerostomia* and related factors.

	Xerostomia		Sig.
	Have 18	No 12	
Gender			
Male	72.2%	33.3%	0035
Women	27.8%	66.7%	*
Age			
≤ 46 years (below average)	55.6%	25.0%	0098
> 46 years (above average)	44.4%	75.0%	
Duration of hemodialysis			
≤ 32 months (below average)	33.3%	83.3%	0.007
> 32 months (above average)	66.7%	16.7%	
Hypertension			
Have	61.1%	66.7%	1,000
No	38.9%	33.3%	
Diabetes Mellitus			
Have	16.7%	33.3%	0392
No	83.3%	66.7%	

Table 4 showed that there is a meaningful relationship between *xerostomia* and the duration of hemodialysis and sex with a value of P < 0.05. There is no meaningful relationship between *xerostomia* and age, hypertension and DM (p>0.05).

Table 5. The distribution of patients with hemodialysis in RSUD Ulin Banjarmasin in January-March 2019 based on mucous lesions and related factors.

	Lesions of the mucosa		Sig.
	Have	No	
	2	28	
Gender			
Male	50.0%	57.1%	1,000
Women	50.0%	42.9%	
Age			
≤ 46 years (below average)	100.0%	39.3%	0179
> 46 years (above average)	0.0%	60.7%	
Duration of hemodialysis			
≤ 32 months (below average)	50.0%	53.6%	1,000
> 32 months (above average)	50.0%	46.4%	
Hypertension			
Have	50.0%	64.3%	1,000
No	50.0%	35.7%	
Diabetes Mellitus			
Have	0.0%	25.0%	1,000
No	100.0%	75.0%	

Table 5 showed that there is no meaningful relationship between lesions of the mucosa with gender, age, prolonged hemodialysis, hypertension, and DM ($p > 0.05$). Table 6 showed that there is no meaningful relationship between candidiasis with gender, age, prolonged hemodialysis, hypertension, and DM due to the value of $P > 0.05$.

Table 6. The distribution of patients with hemodialysis in RSUD Ulin Banjarmasin in January-March 2019 based on Candidiasis and related factors.

	Candidiasis		Sig.
	Have	No	
	3	27	
Gender			
Male	66.7%	55.6%	1,000
Women	33.3%	44.4%	
Age			
≤ 46 years (below average)	100.0%	37.0%	0.70
> 46 years (above average)	0.0%	63.0%	
Duration of hemodialysis			
≤ 32 months (below average)	100.0%	48.1%	0228
> 32 months (above average)	0.0%	51.9%	
Hypertension			
Have	66.7%	63.0%	1,000
No	33.3%	37.0%	
Diabetes Mellitus			
Have	0.0%	25.9%	1,000
No	100.0%	74.1%	

In this study there was no significant relationship between ages with uremic odor. In the elderly, uremic odor can be exacerbated by the use of dentures.[12] In this study there was no significant relationship between age and a metallic taste in the mouth. The metallic taste experienced by patients with chronic kidney disease with hemodialysis therapy can be caused by an increase in phosphate and protein levels which can change the pH of saliva[10, 13,14] In this study there was no significant relationship between age and xerostomia. In old age, xerostomia is associated with degeneration due to the aging process. This causes a decrease in the function of the salivary gland so that the loss of the parenchymal gland is replaced by fat tissue and connective tissue, in addition, atrophic intermediate ductal lining cells can reduce the production of saliva.[13, 14,15]

In this study there was no significant relationship between age and mucosal lesions. Mucosal lesions are more common in elderly people due to repeated habitual factors such as trauma due to chewing, smoking, and consumption of alcoholic beverages.[16] In this study there was no significant association between age and candidiasis. In CKD patients undergoing hemodialysis therapy can experience a decrease in the immune system. Factors that can increase immunocompromised risk are uremia, malnutrition, and abnormal immune cell function. Immunocompromised conditions can increase the risk of opportunistic bacterial infections, namely Candida sp. In addition, candidiasis can also be caused by xerostomia, decreased salivary rate, use of dentures, poor oral hygiene, age, and DM.[17]

In this study there was a significant relationship between age and gingival suppression. Most elderly respondents found gingival swelling which can be caused by poor oral hygiene conditions.[18] Degeneration caused by aging can affect periodontal tissue. Decreasing and thinning keratin tissue in the gingival epithelium can increase epithelial permeability of bacteria.[19] This can increase the risk of gingival swelling.

In this study there was no significant relationship between gender with uremic odor. This is supported by Alirezaei's research (2018) where there is no significant relationship between uremic odor and gender in patients with chronic kidney disease undergoing hemodialysis therapy.[20] Uremic odors can also be caused by smoking, periodontal disease, and xerostomia.[21] In this study there was no significant relationship between gender and a metal taste in the mouth. The metallic taste experienced by patients with chronic kidney disease with hemodialysis therapy caused by increased phosphate levels and proteins that can change the pH of saliva.[10.14]

In this study there was a significant relationship between gender and xerostomia. In CKD patients men are at risk of having xerostomia which can be caused by smoking habits and alcoholic drinks that can reduce the body's defense system. In female patients at risk of xerostomia associated with aging, where natural processes occur called menopause. When women have entered the menopause process, the production of estrogen will stop, this affects the condition of the oral cavity so that it is susceptible to xerostomia..[22]

In this study there was no significant relationship between sex and mucosal lesions. In Sami's study (2018) there were many male respondents found mucosal lesions (64.5%) compared to female respondents (59.5%).[16] In this study there was no significant relationship between gender with candidiasis. In CKD patients undergoing hemodialysis therapy can experience a decrease in the immune system. Factors that can increase immunocompromised risk are uremia, malnutrition, and abnormal immune cell function. In CKD patients undergoing hemodialysis therapy oral manifestations of candidiasis can be found due to an immunocopromised condition that

suppresses immune cells and causes granulocyte dysfunction due to high uremia levels.[17]

In this study there was no significant relationship between sex with gingival swelling. Gingival swelling found in CKD patients results from the use of drugs namely cyclosporine which is used as an immunosuppresant in CKD patients undergoing kidney transplants, and calcium channel blockers (nifedipine, aminodipine, diltiazem, verapamil) used in pre-dialysis and dialysis patients to control hypertension. This condition can be aggravated by a bad oral cavity.[10,18]

The duration of hemodialysis therapy can cause uremic odor. In this study there was a significant relationship between the duration of hemodialysis and uremic odor. In this study the duration of hemodialysis over 32 months can increase uremic odor complaints in CKD patients with hemodialysis therapy. This is in accordance with a study from Alirezaei (2018) where 72% of respondents with hemodialysis therapy with a duration of less than <72 months complained of uremic odor.[20] The duration of hemodialysis is not the only factor that can affect the emergence of uremic odor complaints. Uremic odor can also be caused by other factors such as smoking, periodontal disease, decreased salivary rate, xerostomia, and mucosal lesions.[23]

In this study there was no significant relationship between the duration of hemodialysis and the mouth taste of metal. Along with hemodialysis therapy, urea levels will be reduced by the process of transferring a metabolic waste product that aims to reduce albumin release in CKD patients and reduce uremia symptoms, so that the clinical picture in patients can improve.[2] This can reduce the risk of PGK patients having a metallic taste on the mouth. In this study there was a significant relationship between the duration of hemodialysis and xerostomia. Previous research said 30 of 43 patients who were undergoing hemodialysis therapy had xerostomia accompanied by a decrease in oral health.[24]

In this study there was no significant relationship between the duration of hemodialysis and lesions on the mucosa. Mucosal lesions can be found due to habits such as smoking, drinking alcoholic and repeated trauma.[16,25] In this study there was no significant relationship between the duration of hemodialysis and candidiasis. In CKD patients with hemodialysis therapy can experience a decrease in the immune system. Factors that can increase immunocompromised risk are uremia, malnutrition, and abnormal immune cell function. Immunocompromised conditions can increase the risk of opportunistic bacterial infections, namely Candida sp. In addition, candidiasis can also be caused by xerostomia, decreased salivary rate, use of dentures, poor oral hygiene, age, and DM. [17.26]

In this study there was no significant relationship between the duration of hemodialysis and swelling of the gingiva. Gingival swelling can occur due to the use of drugs or transplants. Gingival swelling can be seen in the labial part of the interdental papilla. This can affect the patient's psychological condition, reduce the function of the oral cavity, interfere with speech function, and can be an indicator of oral hygiene. Increased oral hygiene can reduce inflammation which causes swelling of the gingiva.[14]

Patient with hypertension has blood pressure above normal or more than 120/80 mmHg can increase the risk of kidney damage, the higher the blood pressure is also the risk of PGK.[27] In this study there was no significant relationship between hypertension and uremic odor. In hypertension, increased activity of the renin-angiotin-aldosterone system increases pressure on the kidneys and decreases GFR which decreases kidney function.[28] Changes in mouth taste can occur due to uremic toxins in taste receptors affecting the central nervous system and peripheral nervous system.[29]

In this study there was no significant relationship between hypertension and mouth taste in metal. Changes in growth factor beta 1 (TGFβ1) are found in hypertensive patients. Stage of embryogenesis TGFβ1 functions to break the branches of the salivary gland and play an important role in regulating the proliferation and differentiation of epithelial cells, this can affect homeostasis in the oral mucosa, and reduce saliva production. [30]

In this study there was no significant relationship between hypertension and mucosal lesions. Mucosal lesions can also be found in a person due to daily habits, such as smoking, drinking alcoholic beverages and repeated trauma[16.25] In this study there was no significant relationship between hypertension and candidiasis. In CKD patients with hemodialysis therapy the immune system will decrease. Factors that can increase immunocompromised risk are uremia, malnutrition, and abnormal immune cell function. Immunocompromised conditions can increase the risk of opportunistic bacterial infections, namely Candida sp.[17.26] This immunocompromised condition can reduce phagocyte function in the complement system so that it cannot destroy bacteria and viruses.[31] In addition candidiasis can also be caused by xerostomia, decreased salivary rate, use of dentures, poor oral hygiene, age, and DM.[17.26]

In this study there was no significant association between hypertension and gingival swelling. Gingival swelling can occur due to the use of drugs or transplants. Gingival swelling can be seen in the labial part of the interdental papilla. This can affect the patient's psychological condition, reduce the function of the oral cavity, interfere with speech function, and can be an indicator of oral hygiene. Increased oral hygiene can reduce inflammation which causes swelling of the gingiva.[14]

Creatinine is an indicator for measuring kidney function, in patients with DM, creatinine levels will increase and increase CKD risk. [32] In this study there was no significant relationship between DM with uremic odor and a metallic taste in the mouth. In patients with DM there will be a change in mouth taste caused by neuropathy.[33] Previous studies have suggested that in DM patients saliva has urea content, increased protein levels, and a decrease in microalbumin.[34]

In this study there was no significant relationship between DM and xerostomia. Changes in growth factor beta 1 (TGFβ1) are found in DM patients. Stage of embryogenesis TGFβ1 serves to break the branches of the salivary gland and has an important role in regulating the proliferation and differentiation of epithelial cells, this can affect homeostasis in the oral mucosa, and reduce salivary production. [30] In this study there was no significant relationship between DM and mucosal lesions. Mucosal lesions can also be found in a person due to daily habits, such as smoking, drinking alcoholic beverages and repeated trauma.[16.25]

In this study there was a significant relationship between DM and gingival swelling. In DM patients, glucose contained in the gum fluid and blood can change the environment of the microflora, including qualitative changes in bacteria that can affect the severity of periodontal disease. [35]

CONCLUSSION

It can be concluded that the manifestations found in the oral cavity of CKD patients with hemodialysis therapy are uremic odor, mouthwash metal taste, xerostomia, mucosal lesions, candidiasis, and gingival swelling. There is a relation between gender and xerostomia, the relation between age and gingival swelling, the relation between the duration of hemodialysis and uremic odor and xerostomia, and also the relation between DM and gingival swelling

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