UMSHA Press

AJDR
Avicenna Journal of Dental Research

Avicenna J Dent Res, 2024; 16(3):155-160. doi:10.34172/ajdr.1871

http://ajdr.umsha.ac.ir

Original Article

Comparison of Oral Health Index and Salivary Levels of Calcium, Phosphorus, and Urea between Hemodialysis Patients and Control Group: Results of a Hospital-Based Case-Control Study

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Article history:
Received: May 22, 2024
Revised: July 10, 2024
Accepted: July 14, 2024
ePublished: September 29, 2024

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Abstract

Background: Patients with end-stage renal disease are at risk of dental and periodontal problems. The aim of this study was to compare the oral health index and salivary levels of calcium, phosphorus, and urea between dialysis patients and the control group.

Methods: Hemodialysis patients and a control group of outpatients referring to the hospital clinics were selected for a case-control study. Socio-demographic data and the decayed, missing, and filled teeth (DMFT) index were collected using a questionnaire and dental examination by a dentist, respectively. The calcium, phosphorus, and urea levels were measured in unstimulated saliva samples. Independent *t* test was used to compare the mean DMFT index, calcium, phosphorus, and urea levels between the two groups.

Results: A total of 50 dialysis patients and 50 control individuals were included in the study. Compared to the control group, dialysis patients had higher mean DMFT index (mean difference [MD]: 7.7, standardized mean difference [SMD]: 0.83; $P<0.001$), calcium level (MD: 1.8, SMD: 1.22; $P<0.001$), phosphorus level (MD: 18.9, SMD: 2.3; $P<0.001$), and urea level (42.7, 2.81; $P<0.001$).

Conclusion: Dialysis patients with end-stage renal disease undergoing hemodialysis had worse dental and periodontal status compared to the control group. The oral and dental health status of patients with chronic kidney disease (CKD) should be regularly evaluated and monitored.

Keywords: Chronic kidney disease, Dental status, Periodontal, Hemodialysis

Please cite this article as follows: Samie L, Ahmadi-Motamayel F, Barkhordar S, Doosti-Irani A, Mehrdad Hajiloo M. Comparison of oral health index and salivary levels of calcium, phosphorus, and urea between hemodialysis patients and control group: results of a hospital-based case-control study. Avicenna J Dent Res. 2024; 16(3):155-160. doi:10.34172/ajdr.1871

Background

Chronic kidney diseases (CKDs) have affected over 15% of the adult population, and the mortality caused by these diseases has been increasing among adults worldwide in recent years. In 1990, they ranked 27th among the leading causes of death, but by 2010, they had risen to the 18th position (1).

In dialysis patients, oral infections can lead to septicemia, endocarditis, or dialysis fistula or peritoneal catheter infections. Additionally, these patients are susceptible to oral-dental problems such as periodontal disease, narrowing of the dental pulp chamber, loss of the dental lamina, enamel disorders, premature tooth loss, and dry mouth. Furthermore, patients undergoing kidney transplantation may be prone to infections through the oral route due to the use of immunosuppressive drugs (2,3).

Although uremic halitosis, enamel hypoplasia, enamel defects, increased dental mass, various periodontal diseases, noticeable delay in skeletal and dental maturation, delayed tooth eruption, and significant decline in oral and dental hygiene are important dental signs in these patients, research indicates relatively lower DMFT

(decayed, missing, and filled teeth) index in these patients. The lower DMFT index has been attributed to higher salivary pH. The high pH is a result of increased blood urea and subsequently urea in saliva and the conversion of urea in saliva by urease-positive microorganisms to ammonia (4,5).

Periodontal diseases involve the periodontal tissues, including the gingiva and supportive structures such as cementum, periodontal fibers, and alveolar bone. Chronic periodontitis is the result of the host's response to bacterial accumulation on the tooth surface. Consequently, it leads to irreversible destruction of the connective tissue attachment, formation of periodontal pockets, and ultimately loss of alveolar bone (6).

The global burden of kidney diseases is increasing, especially in developing countries and emerging economies. However, this trend is either stable or decreasing in developed countries (7-11). These diseases can also cause oral and dental complications, including increased dental mass, various periodontal diseases, noticeable delay in skeletal and dental maturation, and a significant decline in oral and dental hygiene (5,12,13). One of the diseases that affects the periodontal tissues and oral cavity is end-stage renal disease. In this stage, patients with renal disorders need to undergo dialysis treatment. This method acts as a lifesaver and significantly reduces mortality caused by kidney diseases (14).

According to the latest information from the Centers for Disease Control and Prevention in the United States, more than 37 million Americans suffer from CKDs. Among them, 726 000 individuals, which means 2 in every 1000 people, are receiving dialysis treatment or have undergone kidney transplantation (15). Various studies have been conducted on the prevalence of oral complications in dialysis patients, including a study conducted by Malekmakan et al (16). However, a comprehensive study regarding the oral and dental health status of these patients in Hamedan has not been conducted. Therefore, the current study aimed to compare the oral health index, and salivary levels of calcium, phosphorus, and urea between dialysis patients and the control group in Hamadan, Iran.

The information obtained from this study can contribute to the examination of oral and dental health services and necessary dental interventions for the treatment of oral and dental problems (17).

Materials and Methods

Study Design and Population

In this case-control study, patients undergoing hemodialysis who referred to Shahid Beheshti Hospital affiliated with Hamadan University of Medical Sciences, Hamadan, Iran, in 2019 were included. The controls were selected from non-dialysis outpatients referring to the hospital clinics.

The sample size required for each group was calculated considering a type I error of 0.05, a power of 95%, and a mean DMFT index of 17.2 ± 9.9 in the patient group and a mean DMFT index of 11 ± 6.4 in the control group based on previous study (17). Ultimately, a sample size of 50 individuals was estimated for each study group.

Inclusion and Exclusion Criteria for Hemodialysis Patients

Inclusion criteria were being diagnosed with end-stage renal disease undergoing hemodialysis, willingness to participate in the study, and permanent residence in Hamadan province. Pregnant women and those with uncontrolled diabetes, severe periodontal problems, and dry mouth due to medication or certain diseases were excluded from the study.

Inclusion and Exclusion Criteria for the Control Group

Inclusion criteria were not having kidney diseases or diseases related to renal failure, willingness to participate in the study, and permanent residence in Hamadan province, and patients with any type of renal failure-related diseases were excluded from the study.

Measurement and Data Collection

The necessary information was collected using a questionnaire prepared by a dentist and an interviewer through examination, reviewing medical records, and interviews. Unstimulated saliva samples were collected from patients between 8 AM and 11 AM, and all participating volunteers were asked to refrain from eating, drinking, and brushing their teeth for 90 minutes prior to sample collection. Then, individuals, while seated and leaning slightly forward, spat saliva into a graduated tube for 5 minutes. The saliva samples were quickly placed in a cold box at a temperature of 4°C and sent to the laboratory within 20 minutes. In the laboratory, the samples were stored at a temperature of -30 °C. The samples were centrifuged, and 1 mL of the liquid was poured into a cup and placed in a Cobas C311 analyzer (Hitachi, Japan) for the measurement of calcium, phosphorus, and urea in saliva. The measurement of saliva calcium was performed using kits manufactured by Bayer Pars Fars Company in Iran, employing the Arsenazo III method. The measurement of salivary phosphorus was performed using kits manufactured by Bayer Pars Fars Company in Iran, employing the Molybdate (UV) method. The measurement of salivary urea was determined using kits manufactured by Pars Azmoon Company, using the photometric method.

The most common and important epidemiological index for measuring dental caries is the DMFT index. This index is used as a crucial measure to indicate oral and dental health status. To calculate the DMFT index, the total number of decayed, missing, and filled teeth in each individual in the community is counted, and the mean is calculated. The examination of gingival inflammation was conducted in a well-lit room (using a headlamp). All examinations were performed by one person (a final-year dental student), and a disposable dental mirror was used

for each patient, which was discarded after use. The Loe index (1967) was used to assess gingival inflammation.

- Grade 0: No visible signs of inflammation in the gums
- Grade 1: Transient changes in color and surface texture of the gums
- Grade 2: Visible inflammation accompanied by bleeding of the gingival margin immediately after periodontal probing
- Grade 3: Apparent inflammation accompanied by spontaneous bleeding

Statistical Analysis

Continuous and categorical variables were expressed as mean (±standard deviation) and number (percentage), respectively. The *t* test was used to compare the DMFT index and the levels of calcium, phosphorus, and urea in the patient and control groups. Since the units of the salivary levels of calcium, phosphorus, and urea differ, the standardized mean difference (SMD) was calculated to make a proper judgment about the strength of the association. The SMD values of 0.20, 0.50, and 0.80 were interpreted as small, medium, and large effect sizes, respectively. The Chi-square test was used to compare the distribution of demographic variables as well as gingival inflammation in patients and the control group. The significance level of the tests was considered to be P value < 0.05. All statistical analyses were conducted using SPSS version 22.0.

Results

The frequency distribution of demographic variables in case and control groups is shown in Table 1. The gender distribution and the prevalence of oral diseases and periodontal inflammation were the same between the two groups. However, there were statistically significant differences between the two groups in terms of education level, age, and occupation. The individuals in the control group had higher education levels, were younger than 50 years old, and were employed ($P < 0.001$).

The comparison of the DMFT index and salivary levels of calcium, phosphorus, and urea between the case and control groups is shown in Table 2. The mean values of all four selected indices had statistically significant differences between the two groups, and the SMD for all four variables was greater than 0.80, indicating a large effect size. However, the greatest difference was observed in the salivary urea

Table 1. Frequency Distribution of Demographic Variables in Case and Control Groups

Variable	Case Group		Control Group		*P* Value
	Frequency	Percent	Frequency	Percent	
Gender					0.68
Male	33	51.6	31	48.4	
Female	17	47.2	19	52.8	
Education level					<0.001
Academic	8	26.7	22	73.3	
Diploma	13	39.4	20	60.6	
Guidance school	7	70	3	30	
Primary school	10	71.4	4	28.6	
Illiterate	12	92.3	1	7.7	
Age					<0.001
50 and below	19	34.5	36	65.5	
Above 50	31	68.9	14	31.1	
Occupation					
Employee	1	2.4	41	97.6	
Worker	5	83.3	1	16.7	
Self-employed	11	84.6	2	15.4	
Unemployed	4	100	0	0	
Retired	13	100	0	0	
Housewife	16	72.7	6	27.3	
Oral diseases					0.49
Yes	2	100	0	0	
None	48	49	50	51	
Gingivitis					0.58
None	21	47.7	23	52.3	
Mild inflammation	26	50	26	50	
Severe inflammation	3	75	1	25	

Table 2. Comparison of Mean DMFT Index and Salivary Markers between Patients and Controls

Variable	Case Group		Control Group		Standardized Mean Difference	*P* Value
	Mean	SD	Mean	SD		
DMFT	21.3	9.7	13.6	8.8	0.83	<0.001
Salivary calcium level	4.9	2	3.1	0.6	1.22	<0.001
Salivary phosphorus level	29.3	10	10.4	8.5	2.03	<0.001
Salivary urea level	56.1	21.1	13.4	4	28.1	<0.001

level (SMD = 2.81, $P < 0.001$), and the smallest difference was seen in the DMFT index (SMD = 0.83, $P < 0.001$).

Discussion

The results of the present study showed that in hemodialysis patients, the mean values of oral health indices including DMFT, calcium, phosphorus, and urea were higher compared to the control group. The highest and lowest differences were observed in salivary urea levels and DMFT index.

The present study showed that renal patients had higher levels of salivary calcium, phosphorus, and urea compared to the control group, and their differences were statistically significant. Numerous studies have demonstrated the association of salivary markers such as calcium, phosphorus, sodium, potassium, uric acid, and other factors with dialysis. In this study, the level of salivary phosphorus in hemodialysis patients indicated an increase, which is consistent with other studies in this field (18,19,20); however, the significant correlation between salivary and blood levels has been reported in very few studies (21). Savica et al addressed in their study that dialysis patients are capable of excreting a small amount of phosphorus in their saliva daily (22).

Some studies have stated that the amount of salivary phosphorus can be used as a factor in determining whether an individual requires dialysis or not. This is because the increase in phosphorus levels in these patients is directly associated with vascular calcification. Therefore, routine evaluation of salivary phosphorus level, which is a safer and more convenient method compared to blood phosphorus level, can serve as a suitable marker in investigating hyperphosphatemia in these patients (23,24).

The current study also demonstrated a significantly higher salivary calcium level in dialysis patients compared to the control group. Martins et al showed that the level of salivary calcium is higher in dialysis patients than in healthy individuals (25). However, it should be noted that this higher level may be due to the dryness of the mouth in these patients (26). Some studies have also indicated that dialysis patients have a higher prevalence of dental and periodontal inflammation due to poor oral hygiene, and thus the levels of calcium and phosphorus in these patients may be associated with an increased risk of dental inflammation resulting from underlying diseases or accumulated pathogenic bacteria in these patients (27,28).

This study also demonstrated a higher salivary urea level in dialysis patients than in the control group. The increase in urea levels in dialysis patients has been found in almost all studies conducted in this field, including both adults and children (2,12,29,30). The role of urea in pH changes in plaque is approximately 20 times greater than the pH of saliva itself. In this regard, urea is metabolized by bacterial urease into carbon dioxide and ammonium ions, resulting in alkalinization (3,31).

On the other hand, urea exhibits an altered response to plaque in carbohydrate metabolism against acid catabolites, and it has been simultaneously estimated that the production of hydrogen ions decreases up to 10 times in patients with renal insufficiency. Therefore, urea plays a primary role in salivary alkalization and dental plaque changes in patients with renal insufficiency. The mean concentration of salivary urea decreases after dialysis and reaches 60% of its concentration after dialysis. This indicates that the concentration of salivary urea can be effective and useful in monitoring the effects of dialysis (32).

The results showed a statistically significant difference in the DMFT index between patients and the control group. However, the observed DMFT index for patients of this study differs from that of some other studies, including a community-based study in 5 hospitals in Tehran, we mean, the study by Kheirollahi et al and the study by Al-Wahadni and Al-Omari et al in Jordan (33, 34). The study by Ghasemi et al did not show a significant difference in the DMFT index between dialysis patients and the control group, but the mean DMFT index in this study was higher compared to the study by Ghasemi et al (35).

The study had some limitations. First, the difference between the two study groups may be due to differences in age, education, and occupation; however, the impact of these factors on the results is minimal as the distribution of periodontal diseases and oral diseases is the same in the two groups. Additionally, the comparisons between the two groups may be influenced by some variables related to hemodialysis, such as the duration of the dialysis, that have not been measured in the current study. Furthermore, the uneven distribution of these variables makes the comparison of urea and phosphorus levels inconclusive since the standardized difference between the two groups for these two variables exceeds the value of 2.

Conclusion

The mean DMFT index and salivary calcium, phosphorus, and urea levels are higher in hemodialysis patients than in the control group. Regular monitoring of oral and dental health status and implementation of preventive measures

are necessary for these patients.

Acknowledgments

The authors of this article would like to express their gratitude to the Vice Chancellor for Research and Technology of Hamadan University of Medical Sciences and the staff of Shahid Beheshti Hospital for their invaluable support.

Authors' Contribution

Conceptualization: Shaghayegh Barkhordar, Lida Samie, Fatemeh Ahmadi-Motamayel.
Data curation: Shaghayegh Barkhordar, Fatemeh Ahmadi-Motamayel.
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Writing–review & editing: Shaghayegh Barkhordar, Amin Doosti-Irani, Mehrdad Hajiloo, Lida Samie.

Competing Interests

The authors declare that they have no conflict of interests.

Ethical Approval

The present study was approved by the Ethics Committee of Hamadan University of Medical Sciences (IR.UMSHA.REC.1397.787). After explaining the study objectives and obtaining informed consent prior to participation, the study participants were recruited using convenience sampling.

Funding

This Study funded by the Vice Chancellor for Research and Technology of the Hamadan University of Medical Sciences.

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