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ORIGINAL ARTICLE
ORİJİNAL ARAŞTIRMA

The Immoderate Decrease in Saliva pH During Hemodialysis is Related to Poor Oral Hygiene in Diabetics

Hemodiyaliz Süresince Tükürük pH'sındaki Aşırı Düşüş, Diyabet Hastalarında Kötü Ağız Hijyeni ile İlişkilidir

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ABSTRACT

Aim: Saliva is a body fluid that significantly balances oral acidity. Notably, saliva pH can also restore oral hygiene that can be labile in hemodialysis patients. Our study thus investigated the saliva pH alterations in a dialysis session and how they affect oral hygiene.

Material and Method: This quasi-experimental study was conducted with patients receiving hemodialysis. An internist took the unstimulated saliva samplings at the beginning and end of one hemodialysis session, and oral evaluations were accomplished by a dentist who was blind to patients' saliva status. Laboratory results were also obtained from monthly orders.

Results: A total of 59 patients participated in this study. The mean saliva pH decrease in all patients was -1.35±0.7. In comparing saliva pH with numerous patient characteristics, the statistical significance of obesity, loss of teeth related to oral hygiene, diabetes, and blood flow rate were notable. The decrease in saliva pH was linked to periodontal inflammation and oral hygiene, impressively higher in patients with diabetes mellitus. The salivary pH tends to decrease during the hemodialysis session. Hence, oral hygiene and related dental health can also be dependent on hemodialysis qualities.

Conclusions: An excessive decrease in saliva pH during dialysis sessions may lead to poor oral hygiene, particularly in patients with Type II diabetes.

Keywords: Diabetic complications, low-flow dialysis, obesity, oral hygiene, saliva pH, tooth loss

ÖZ

Amaç: Tükürük, oral asiditeyi önemli ölçüde dengeleyen bir vücut sıvısıdır. Dikkat çekici şekilde, tükürük pH'sı aynı zamanda hemodiyaliz hastalarında labil olabilen ağız hijyenini de düzenleyebilir. Bu nedenle çalışmamız, diyaliz seansında tükürük pH'sındaki değişiklikleri ve bunların ağız hijyenini nasıl etkilediğini araştırdı.

Gereç ve Yöntem: Bu yarı deneysel çalışma hemodiyaliz tedavisi alan hastalarla yapılmıştır. Hemodiyaliz seansının başındaki ve sonundaki uyarılmamış haldeki tükürük örneklerini bir iç hastalıkları uzmanı aldı, ve oral değerlendirmeler, hastaların tükürük durumu yönünden kör olan bir diş hekimi tarafından yapıldı. Laboratuvar sonuçları ise aylık takiplerden alındı.

Bulgular: Bu çalışmaya toplamda 59 hasta katıldı. Tüm hastalarda ortalama tükürük pH düşüşü -1,35±0,7 idi. Tükürük pH'sı önemli hasta özellikleriyle karşılaştırıldığında, obezite, ağız hijyeni ile ilişkili diş kaybı, diyabet ve kan akış hızının istatistiksel anlamlılıkları dikkat çekiciydi. Tükürük pH'ındaki düşüş, DM'li hastalarda belirgin şekilde daha yüksek olan periodontal inflamasyon ve ağız hijyeni ile bağlantılıydı. Tükürük pH'sı hemodiyaliz seansı süresince düşme eğilimindedir. Bundan dolayı, ağız hijyeni ve ilgili diş sağlığı hemodiyaliz kalitesine de bağlı olabilir.

Sonuç: Diyaliz seansları süresince tükürük pH'sında aşırı bir düşüş, özellikle Tip II diyabetli hastalarda kötü ağız hijyenine yol açabilir.

Anahtar Kelimeler: Diş kaybı, diyabetik komplikasyonlar, obezite, oral hijyen, yavaş-akım diyaliz, tükürük pH'sı

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INTRODUCTION

Saliva is a highly informative body fluid consisting of the interstitial fluid around the salivary gland ducts. Due to the various contents such as water, electrolytes, proteins, and enzymes, saliva acidification (saliva pH) is highly variable. Unstimulated saliva can have a pH as low as 5.6, and its stimulated form can rise to 7.6, though saliva's average pH is 6.4±0.65 (1). Depending on the need, the content and amount of saliva secreted is 0.5 – 2 liters per day (2).

The saliva types are not always the same, either. Unstimulated saliva form represents basal release and is found 14 hours a day in the mouth (3). It covers the mouth tissue and makes a protective border. Stimulation of the salivary glands, such as the initial biting of food and a particular scent, causes an increase in saliva flow rate (SFR) and production. However, stimulated saliva lasts only 2 hours a day in the mouth and is more related to digestive functions (3). In addition, protein, sodium, chloride, and bicarbonate levels also increase in the stimulated state (4). Further, parotid saliva demonstrates seasonal characteristics, notably a decrease in the summer (5). There is also a significant relationship between body posture and saliva secretion, with the greatest occurring when standing. This circumstance is related to blood pressure (6). Moreover, salivary secretion activity is at its lowest level in the geriatric population (7). The practical features such as easier, without preparation and non-invasive sampling have saliva tested in many comorbidity studies (8). Accordingly, the chronic kidney disease (CKD), in which fluid volume is extremely important, is also included in these researches (9).

In hemodialysis (HD), which usually takes 4 hours, there may be instant fluid and electrolyte changes between body-fluid compartments [10]. Therefore, changes in saliva content are also likely. Here, saliva buffering systems, prominently bicarbonate, try to normalize drops in saliva pH (9-11). As the lowest tolerable saliva pH is 5.5, dental demineralization is inevitable below this level (12). In this case, dental caries, periodontal diseases, oral hygiene impairment, and related dental loss should be expected (13). Nevertheless, a high incidence of periodontitis was reported in CKD patients, particularly in those with diabetes mellitus (DM) (14).

Many studies on saliva have researched dental and related oral care in CKD patients. Poor oral hygiene, particularly in HD patients, may be related to the disease progression or the contribution of HD complications. This study thus aimed to investigate how oral and dental health is affected by the change in salivary pH during HD.

MATERIAL AND METHOD

This quasi-experimental study was conducted in a university nephrology clinic between 2019 and 2020. Study approval was obtained from the university ethics committee, and informed consent forms were received from all participating patients prior to the study. Fifty-nine of 68 patients registered in the dialysis center were included in our study. The patients had HD sessions three days a week for 4 hours using one of three HD access modes (arteriovenous fistula, permanent catheter, and graft). Patients hospitalized for other causes started HD within the last three months, had clinical diagnoses about infection, had abnormal vital signs, had a history of taking drugs that interact with the saliva (autonomous effects), or were satiated were excluded from the study. Patients' demographic features, HD session periods, and dialysis efficacy evaluations such as urea reduction ratio, blood biochemistry, HD fluid and dynamics [blood flow rate (BFR), dialysate electrolytes] as ordered for the previous month were recorded. On the sampling day, the patients were provided with the same position and meals during HD sessions. At the initial sampling, all patients were hungry, and there was no saliva-stimulating food or beverage on the menu. The study design was summarized in **Figure 1**.

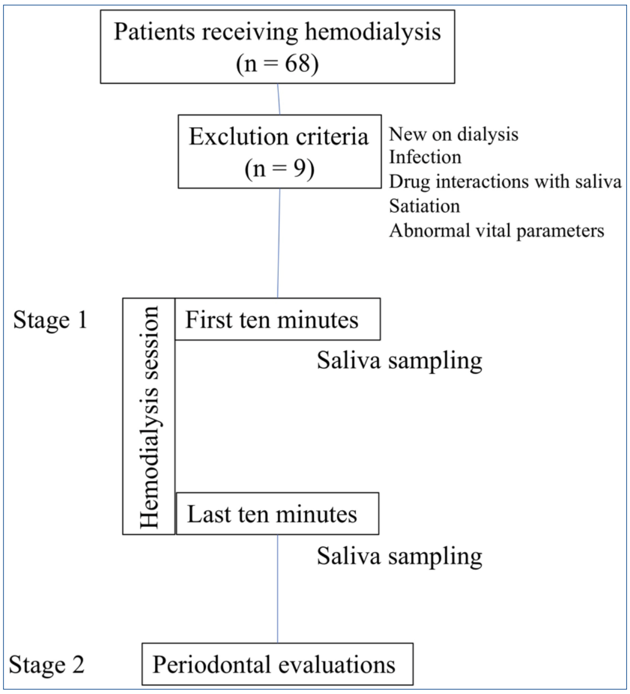

Figure 1. Study design & sampling definitions.

To measure saliva pH, we used pH indicator strips (Merck KgaA, 64271 Darmstadt, Germany) with a sensitivity of 0.25 degrees, a color scale of 0–14, and four color blocks. We mainly chose indicator strips rather than electronic tools due to the low saliva we intended to gather (15). Saliva samples taken from each patient without stimulation within the first 10 minutes of the current

HD session were collected in 10 ml plastic containers. There was no foam or mucus in the saliva samples. Each sample was then dropped onto a pH indicator strip with a 1 ml disposable Pasteur pipette, after which we waited 5 seconds for the reaction to take place. We compared the results to the color scale on the strips' box and noted the color-matched pH value. Then, the patients were allowed to eat their meals. Approximately 2.5 hours, when basal saliva was again achieved, we repeated the same procedure in the last 10 minutes of the ongoing HD session.

Finally, an expert dentist who was unaware of the patients' status carried out an oral hygiene examination. Community periodontal index (CPI) was used in dental evaluations, and the results were divided into sextants (16). Accordingly; Code "0" indicates healthy periodontium without pathologic changes; Code "1" indicates bleeding on gentle probing; Code "2" indicates calculus deposition; Code "3" indicates probing depth of 4 to 5 mm; Code "4" indicates probing depth 6 mm or more profound, and Code "X" indicates three or more teeth missing.

Statistical analysis: Statistical analyses were performed using SPSS ver. 22 for Windows (SPSS Inc., Chicago, IL, USA). Continuous variables were given as mean±SD, and categorical variables were specified as frequency counts and percentages. The Pearson test was chosen for correlations between standard distribution data, while the Spearman test evaluated heterogenic data. A chi-square test was preferred for categorized data. A repeated-measures analysis of variance test was performed for repeated categorical data. The Mann-Whitney U-test and Kruskal Wallis test were chosen for subgroup evaluations due to the decrease in groups. For all tests, $p < 0.05$ was considered statistically significant.

RESULTS

Our study was initiated with 59 total patients receiving HD. The patients' mean age was 57.74, and 29 were female. Almost all patients had functional dialysis adequacy, and their age distribution, HD time, and laboratory values were homogeneous (Table 1). More than half of the patients still produced acceptable urine (> 200 ml/day). Forty of the patients evaluated for oral hygiene had at least one caries. Fifteen (37.5%) of those had a total dental prosthesis. The average end-dialysis pH of patients with total tooth loss was 6.23±0.62, while the average pH decrease during HD session was -1.4±0.68. In addition, only 9 (15.25%) of the patients had good oral hygiene (no restoration and no teeth loss). Moreover, only two of these (22.2%) had DM. Additional values are summarized in **Table 1**. In dental evaluations, the total number of patients with CPI value >3 was 43 (73%). Other dental evaluations are given in detail in **Table 2**.

Table 1. Demographics and baseline characteristics of patients receiving hemodialysis

Personal characteristics	
Age (year)	57.74±15.25
BMI* (%)	24.99±5.47
DM‡, n (%)	14 (23.7%)
Daily brushing, n (%)	12 (20.3%)
Smoking, n (%)	3 (5%)
HD‡ (year)	4.38 ±4.64
Urine presence n (%)	20 (34%)
Weight Difference (kg)	1.79±0.96
Dialysis Access	**(n)**
Catheter	27
AVF§	29
Graft	3
Dialysis Period	
Daylight	24
Afternoon	25
Evening	10
Laborotary results	
Urea (mg/dL)	112.81 35.77
Creatinine (mg/dL)	7.01±2.08
Hb*§ (g/dL)	11.39±1.59
Albumin (g/dL)	3.48±0.36
T.protein(g/dL)	6.71±0.71
Na (mEq/L)	137.66±3.43
K (mmol/L)	4.51±0.69
ALT (U/L)	11.54±5.51
Ca (mg/dL)	8.75±0.77
P (mg/dL)	4.85 1.45
LDL (mg/dL)	111.03±59.04
HDL (mg/dL)	42.03±12.34
Triglyseride(mg/dL)	153.42 ±69.48
Tot. koll (mg/dL)	184.71±67.61
Uric acide (mg/dL)	5.72±1.12
HCO3 (mmol/L)	22.58±4.58
Ferritine (ng/mL)	397.07±233.59
(Ca X P)†*	44.23±12.72
URR††	74±5.75
KT/v†‡	1.58±0.25
Dialyzate specifications	
DFR†§ (ml/m)	322.20 24.42
Dialysate Ca+2 (mg/dL)	1.46±0.24
Dialysate K+ (mmol/L)	2.48±0.67
Dialysate HCO3 (mmol/L)	2.60±1.69
Salivary results	
Saliva pH	
First sampling	7.82±0.86
Second sampling	6.48±0.79
Total pH decrease	-1.35±0.70

Data are the median (INQ), n (%), or n/N (%); Standart deviation; *,Body Mass Index; †,Diabetes Mellitus; ‡,Hemodialysis; §,Arteriovenous fistüle; *§,Hemoglobine; †*,Calcium-phosphorus ratio; ††,Urea reduction ratio; †‡,(Dialyzer clerance of urea) x (Dialysis time / volüme distribution of urea); †§,Dialysate Flow Rate.

Table 2: Dental properties of patients receiving hemodialysis.

	Diabetic (n=18)	Non-diabetic (n=41)	P value
Mean salivary pH	6.58±0.87	6.43±0.76	0.540
Saliva pH gap	-1 (-0.5, -2)	-1.5 (0, -3)	0.034*
Total lost teeth, n (%)	9 (50%)	6 (14.6%)	0.004*
Dental restoration count, n (%)	16 (88.8%)	10 (24.4%)	0.011*
Number of Daily brushing teeth, n (%)	2 (11.1%)	10 (24.4%)	0.243
Number of weekly brushing teeth, n (%)	7 (38.9%)	22 (53.6%)	0.564
Presence of calculus, n (%)	18 (100%)	41 (100%)	NA†
CPI*			
Category 0, n (%)	0 (0%)	0 (0%)	NA†
Category 1, n (%)	0 (0%)	0 (0%)	NA†
Category 2, n (%)	0 (0%)	16 (39%)	0.001*
Category 3, n (%)	2 (11.1%)	13 (31.7%)	0.094
Category 4, n (%)	6 (33.3%)	6 (14.6%)	0.100
Category 5, n (%)	10 (55.5%)	6 (14.6%)	0.001*

*P values are the comparison of diabetic and non-diabetic groups (Chi-Squared test or Mann Whitney U test); Data are the median (INQ), n (%), or n/N (%); P values less than 0.05 were considered statistically significant (two-tailed); *, Community periodontal index; †, Not applicable.

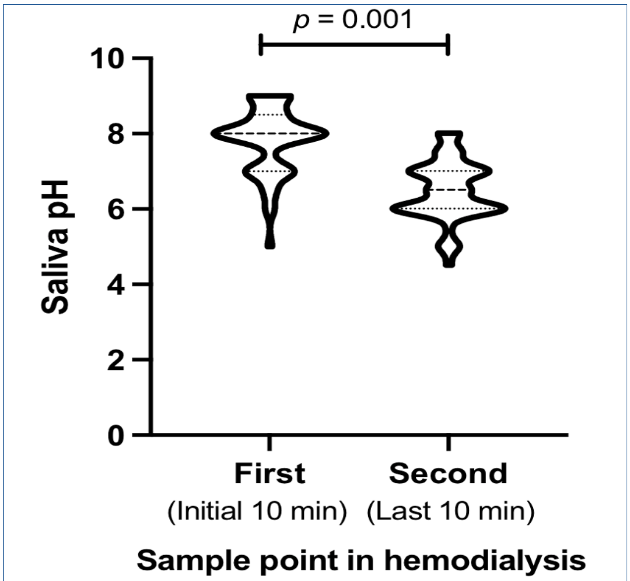

Figure 2: Saliva pH variations among the sampling periods taken in hemodialysis sessions.

The mean unstimulated saliva pH value was 7.82±0.86 at the beginning and 6.48 0.79 at the end of the dialysis session, respectively. The mean pH reduction between the two samplings was −1.35±0.7. This value was statistically significant for all patients (p=0.001). In evaluating the categorized facets that may affect saliva pH (age, gender, weight), we found no influential factor other than BFR and body mass index (BMI) (p < 0.005). However, the mean salivary pH at the beginning and end of HD were lower in geriatric patients (p=0.027, p=0.007). This decrease did not differ in two sequential samplings in diabetic patients; unlike, the pH decrease was higher in geriatric patients with DM (p=0.05).

In addition, in patients with a BMI > 25, the total saliva pH decrease per patient was significant (p=0.033, η2=0.07) (**Figure 3a**). In patients with higher BFS (> 350 ml/min), the pH gap value was again notable (p=0.040) (**Figure 3b**). Interestingly, the pH reduction negatively correlated with the calcium/ phosphorus ratio (p=0.044, r=-0.263). When the ratio was greater than 40, the pH drop was higher. However, an independent-samples T-test could not demonstrate any significance (p=0.071). There were negative correlations between end-dialysis pH decrease and age (p=0.023, r=-0.295), and oral hygiene impairment (p=0.001, r=-0.438). The negative correlation between oral hygiene impairment and the mean saliva pH was also statistically significant (p=0.018) (**Figure 3c**). In evaluating comorbidities, primarily involving patients with DM, a correlation between oral hygiene impairment and saliva pH decrease was more prominent in patients with DM (p=0.047, r=0.26). As shown in **Figure 3d**, this correlation was found significant as well (p=0.003, η2=0.14). There was also a significant statistical increase between the decrease in saliva pH and oral hygiene in diabetic patients (p=0.02, η2=0.08).

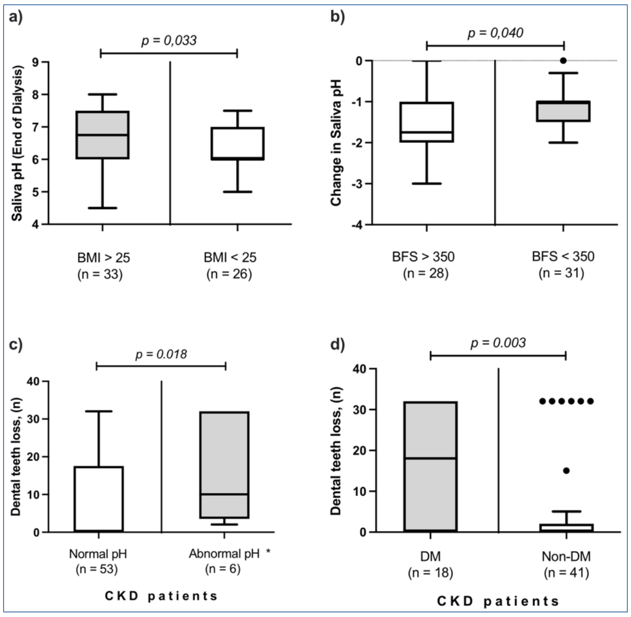

Figure 3: a) Obesity effect on the saliva pH decrease range at the end of the hemodialysis; **b)** Saliva pH variations according to the blood flow rate in hemodialysis; **c)** Saliva pH impact on the teeth loss count in hemodialysis patients; **d)** Teeth loss count in diabetic and non-diabetic CKD groups with marked saliva pH decrease.

*Abnormal pH was accepted as pH<5.75 or pH>7.01; BMI: body mass index, BFS: blood flow speed, CKD: chronic kidney disease, DM: diabetes mellitus

DISCUSSION

This prospective study evaluated saliva pH variation during an HD session. We found a significant pH reduction at the end of HD compared to the beginning. In addition, saliva pH results were more decreased in diabetic patients. Moreover, diabetic patients with high saliva pH reduction tended to have poor oral hygiene.

A study set out to determine the dental conditions and saliva characteristics of 60 patients receiving HD and found an increase in saliva pH at the end of HD (9). The researchers reported that SFR and buffering capacity decrease at the end of HD, whereas saliva pH increases. They linked the decrease in the buffering capacity to high urea in saliva samples. However, their samples also included stimulated saliva and were taken at the end of HD. SFR measurements may show higher pH values since the stimulated saliva activates the buffer system. Therefore, the pH values taken in the current study were likely to be buffered by induced bicarbonate.

A supportive study on urea's impact on the saliva pH revealed that the urea's high predilection for pH buffering leads to an increase in saliva pH (17). We thus planned the sampling periods based on basal saliva secretion, which is more critical for oral hygiene. Since our sampling timings included unstimulated saliva, bicarbonate, and even the subsequent urea buffer system would not be activated (3), we were able to get more objective results. There is a double-edged sword here. First, urea drops at the end of HD and cannot sufficiently buffer the saliva pH. Secondly, saliva pH may not increase enough as urea will not be adequate in saliva pH buffering. The absence of a decrease in salivary pH may be a shred of evidence that urea is still at a high level in the blood. That is, the evaluation of the effectiveness of urea dialysis may be considered.

In the study where the samplings were taken as pre and post-dialysis, a mean pH decrease of 0.15 after HD was noticed; however, this reduction was noted not statistically significant (18). In the current study, we were inspired by the evaluation of DM and the selection of two comparable sampling times. Moreover, we had the opportunity to evaluate the circadian saliva secretion, which was their limitation. Our study noticed that the circadian rhythm had no impact on the pH variation.

Dental tribulations and associated oral hygiene will deteriorate when the decreased saliva pH exceeds the demineralization threshold. This situation will predispose patients with DM, as noticed in HD patients. In the study conducted by Chuang et al., the status of saliva pH in diabetic and non-diabetic patients was evaluated, and an objective dental evaluation was performed (14). Accordingly, saliva pH was decreased in the diabetic CKD group. However, they declared that oral evaluations did not differ per HbA1c level. We found a similar pH decrease in our study; however, our saliva pH result was the difference between saliva samples taken twice (at the beginning and end of HD); that is, it reflected the decrease by individual rather than a group. In addition, the decrease in saliva pH was higher in those with poor personal oral hygiene (p=0.018). After our dental evaluations were made objectively, as in a similar study, we found that oral hygiene was not acceptable for diabetic patients. Moreover, in the samples taken at the beginning and the end of HD, the exposure rates were higher in diabetic patients, as oral hygiene will mainly be affected during the pH drop period.

The main weakness of our study was the absence of arterial blood gas samples taken simultaneously with saliva samples. In addition, blood pressure was measured only at the first sampling time. Therefore, we could not comprehensively reveal how the salivary pH is affected by the blood pressure variations during HD. Another liability was that we could not perform an HbA1c levels-based subgroup evaluation in patients with DM as some patients did not have recent HbA1c values. Similarly, the lack of synchronous biochemistry results limits our interpretations about the pH decrease.

CONCLUSION

Overall, this study aimed to evaluate the saliva pH alterations during HD session. We detected a marked reduction in saliva pH between the starting and end of HD. Obesity, DM, and BFR contributed the most to this reduction. Moreover, the relationship between decreased pH and oral hygiene due to periodontal inflammation was also interesting. In addition, the loss of oral hygiene was pronounced more in diabetic HD patients than in those with non-DM. Further studies must be conducted before fully considering saliva pH variation as a factor of oral hygiene in patients receiving HD.

ETHICAL DECLARATIONS

Ethics Committee Approval: Selcuk University Ethics Committee approved the study protocol (2019/381).

Informed Consent: All patients signed the free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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