

Evaluation of salivary flow rate, pH, and buffer capacities in end-stage renal disease patients versus control – A prospective comparative study

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ABSTRACT

Background: Saliva plays a major role in preserving the integrity of oral tissues. Chronic renal failure patient undergoes many oral and salivary changes for which they require special oral health care. The patient undergoing hemodialysis session has altered salivary composition. Many changes occur during hemodialysis that severely affect the flow rate and the biochemical composition of saliva. **Methods:** A total of 50 patients of end-stage renal disease undergoing hemodialysis for renal insufficiency were selected based on inclusion and exclusion criteria set prior to the study. These patients were compared with the control group who had already undergone hemodialysis. A total of 30 patients were selected as a control group. In this study, unstimulated whole saliva was collected by the spitting method before and after the dialysis session. Salivary flow rate, pH, and buffering capacities were measured. **Results:** Hemodialysis had a significant effect on the salivary flow rate. The mean pH of unstimulated whole saliva showed no significant changes before and after dialysis. The concentrations of urea, creatinine, chloride, and potassium in the whole saliva changed markedly before and after a hemodialysis session, whereas no significant difference was seen in the concentration of sodium and calcium. **Conclusion:** Through this study, we came into a conclusion that hemodialysis had a significant effect on salivary secretion and the biochemical composition of saliva. We conclude that the observed changes in salivary concentrations and the flow rate are mainly due to an increased watery secretion from the salivary glands and also saliva can be used as a tool for monitoring hemodialysis.

Keywords: End-stage renal disease (ESRD), hemodialysis, saliva

Introduction

Among all the systemic disorders, renal system diseases play a major cause of morbidity and mortality worldwide as the kidney

maintains the internal environment of a body, i.e. homeostasis.^[1] As a result, many people suffering from renal diseases require more oral health care often. Chronic renal failure and its treatment have systemic and oral manifestation.^[2,3] Saliva is known as a soldier of oral cavity. Saliva plays a significant diagnostic marker to rule out oral diseases at an early stage. Saliva monitors the health and disease state of an individual that is a highly desirable goal for health promotion and health care research. Over the last decades, the prevalence and incidence of end-stage renal

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Received: 10-02-2020

Revised: 13-03-2020

Accepted: 26-03-2020

Published: 30-06-2020

Access this article online

Quick Response Code:



Website:
www.jfmpc.com

DOI:
10.4103/jfmpc.jfmpc_242_20

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How to cite this article: Kumar T, Kishore J, Kumari M, Rai A, Rai S, Jha A. Evaluation of salivary flow rate, pH, and buffer capacities in end-stage renal disease patients versus control – A prospective comparative study. *J Family Med Prim Care* 2020;9:2985-9.

disease (ESRD) have increased. It has been observed that with age male individuals are more commonly affected than females. The most common causes of ESRD are chronic hypertension, glomerulonephritis, polycystic kidney disease, and endovascular disease and diabetes mellitus.^[4]

The management of chronic kidney disease (CKD) requires a clear understanding of its definition as proposed by the National Kidney Foundation (NKF). For this, the exact interpretation of the estimated glomerular filtration rate (eGFR) is required, because GFR is still considered as the best overall index of kidney function in stable, non-hospitalized patients. Kidney damage is defined by anyone of the following findings:^[5]

- pathologic kidney abnormalities;
- persistent proteinuria;
- other urine abnormalities, e.g. renal hematuria;
- imaging abnormalities; and
- estimated glomerular filtration rate (eGFR).

Classification of CKD stage estimated GFR (mL/min/1.73 m²)^[5]

Stage 1 – ≥ 90 – Normal GFR w/proteinuria
 Stage 2 – 60-89 – Age-related decline in GFR w/proteinuria
 Stage 3-A-3B – 30-59 – Low risk of progression to kidney failure
 Stages 4-15-29 – High risk of progression to kidney failure
 Stage 5-5D – (chronic dialysis) 5T (kidney transplant) – < 15 kidney failure

The above-mentioned literature regarding the ease of collection and performance of various tests on saliva makes it helpful in the primary care of the early detection of ESRD cases. Moreover, salivary changes also indicate the minor to major alterations in any systemic, endocrinal, and exocrine changes.

Therefore, the present study was performed to assess oral and salivary change, i.e. salivary flow rate, pH, and buffering capacities in ESRD undergoing hemodialysis in comparison with healthy controls.

Materials and Methods

After obtaining Institutional Ethical Committee Clearance, the study was conducted in the Department of Oral Pathology and Microbiology, Patna Dental College and Hospital, Patna (Bihar) in the time period of 18 months from March 2018 to September 2019. The date of approval is 25 November 2018.

A total of 50 patients of either sex having ESRD undergoing hemodialysis for renal insufficiency who visited the college outpatient department were selected [Table 1]. The patients' age ranges from 15 to 60 years with the mean age of 34 years. Among this, 32 patients were male and 18 were female. Before the sample collection complete history was taken from patients regarding dry mouth, tongue and/or mucosal pain, and taste change, complete oral examination

was done such as uremic odor, tongue coating, candidiasis, petechiae, ecchymosis, oral ulcer, enamel hypoplasia, and gingival bleeding.

Inclusion criteria

Patients of either sex in the age group of 15-60 years, with ESRD having a glomerular filtration rate of < 15 ml/min, undergoing hemodialysis were included in the study.

Exclusion criteria

Patients with any of the following features were excluded from the study:

- Diseases affecting water and electrolyte balance like diabetes insipidus, thyroid disorders, etc.
- Patients under medication (other than insulin and antihypertensive drugs) who could affect saliva production.
- Patients with salivary gland disorders.
- Patients who already underwent a hemodialysis procedure (at least not for 3 days).

Thirty patients were randomly selected as a control group who recently underwent hemodialysis (at least within 24 h) with no history of serious illness rather than kidney disease and who were not under any medication that can alter pH and the buffer of saliva. The control group age ranges from 18 to 59 years with the mean age of 34.7 years. Among these patients, 14 patients were female and 16 were male. The mean time of treatment on hemodialysis was 22 months with a range being 1 month to 8 years.

The patients were explained about the procedure, and the written informed consent was obtained. Unstimulated whole saliva was collected by the spitting method. Samples from the patients (a day after dialysis visit) and the control group were collected between 8:00 AM and 11:00 AM. Samples were collected before meals or at least 2 h after meals. During the time of collection, smoking and eating were prohibited. Unstimulated whole saliva was collected for 10 min by the spitting method, and the subjects were instructed to spit out into the sterile calibrated container every 30 s. Each saliva collection period was 5 min, and after the sample collection, the flow rate (ml/min) was calculated.

After this, pH was measured using the pH indicator strip (Merck). One drop of the collected saliva sample was placed on the test strip, and its color change indicated the pH of saliva.

The remaining samples were stored in an icebox at -20°C and sent to a laboratory within the 30 min of sample collection. The

Table 1: Demographic data of patients included in the study group

	Number of patient	Mean age (years)	Mean duration of HD
MALE	32	31.9 \pm 9.6	11.5 month (1 MO- 8 Years)
Female	18	34.6 \pm 11.5	12 months (1 mo- 8 years)
Total	50	33.5 \pm 10.3	11.6 month (1 mo- 8 year)

saliva samples were then centrifuged at 4000 rpm for 10 min, to eliminate cellular debris. Then, the concentrations of salivary urea, creatinine, sodium, chloride, potassium, and calcium were determined using an autoanalyzer.

Statistics

Statistical analysis was done using Descriptive statistics, Chi-square test, and Paired sample 't' test. The statistical analysis was done using the SPSS version 16 statistical software package. Data were collected, tabulated, and then subjected to the statistical analysis. The qualitative data were presented as numbers and percentages, and the Chi-square test was used to examine the significance of the differences in mean and distribution of categorical variables between groups. The data were presented as mean \pm standard deviation, and the paired sample *t*-test was used for comparison of values before and after hemodialysis.

Results

This study was conducted on prediagnosed nephritis patients who regularly undergo hemodialysis and compared with normal healthy controls.

Salivary flow rate

To compare the salivary flow rate before and after hemodialysis paired samples, statistics was applied. The mean flow rate before was 0.42 ± 0.27 mL/min, and the mean flow rate after hemodialysis was 0.81 ± 0.34 mL/min. There was a statistically significant difference between the salivary flow rate before and after hemodialysis, as a *P* value of 0.000 was obtained.

Salivary pH

The mean pH before hemodialysis was 6.49 ± 1.1 , and the mean pH after hemodialysis was 6.65 ± 0.60 . There was no statistically significant difference between the salivary pH before and after hemodialysis, as the *P* value was 0.231.

Saliva composition

Biochemical parameters measured in saliva are shown in Table 2.

The salivary composition of CKD patients differed before and after a dialysis session. The concentrations of urea, creatinine, potassium, and chloride were found to be significantly lower in patients after hemodialysis than it was before hemodialysis. There were no statistically significant changes seen in the concentrations of sodium and calcium, before and after hemodialysis.

The mean concentration of urea before hemodialysis was 162.80 ± 90.21 mg/dl, and the mean urea concentration after hemodialysis was 100.1 ± 62.87 mg/dl, with a *P* value of 0.000, which is statistically significant. The mean concentration of creatinine before hemodialysis was 1.68 ± 0.6 mg/dl, and the mean creatinine concentration after hemodialysis was 1.13 ± 0.56 mg/dl, which was also statistically significant.

The mean sodium concentration before hemodialysis was 12.96 ± 8.07 mmol/L, and the mean sodium concentration after hemodialysis was 13.89 ± 6.95 mmol/L. The mean calcium concentration before hemodialysis was 8.77 ± 0.53 mg/dl, and the mean calcium concentration after hemodialysis was 8.79 ± 0.52 mg/dl, which was not significant statistically with a *P* value of 0.112 and 0.791, respectively [Table 3].

The mean concentration of chloride before hemodialysis was 38.01 ± 13.63 mmol/L, and the mean chloride concentration after hemodialysis was 26.44 ± 11.85 mmol/L. The mean potassium concentration before hemodialysis was 28.56 ± 9.51 mmol/L, and the mean potassium concentration after hemodialysis was 21.90 ± 7.58 mmol/L, which was statistically significant with a *P* value of 0.000 and 0.002, respectively [Table 3].

Discussion

Some of the most frequent and important many pathological conditions of the teeth and the oral cavity are strongly dependent on pH changes. Till now, limited literature is available about the salivary composition and oral manifestation of patients with ESRD. About 60,000 persons annually lose their lives due to kidney-related diseases. Glomerulonephritis constitutes 54.7% of the kidney diseases, pyelonephritis accounts for 12.3% of renal failures and others about 33%. Therefore, patients with end-stage kidney disease, especially those on hemodialysis

Table 2: Mean concentration of the salivary flow rate in ml/min, pH, and biochemical constituents urea in mg/dl, creatinine in mg/dl, sodium in mmol/L, chloride in mmol/L, potassium in mmol/L, calcium in mg/dl, before and after hemodialysis

Parameters	Before hemodialysis (ESRD)	After hemodialysis (control)
Mean Flow Rate	0.42	0.81
Mean pH	6.49	6.65
Mean Urea	162.800	100.1
Mean Creatinine	1.68	1.13
Mean Sodium	12.96	13.89
Mean Chloride	38.01	26.44
Mean Potassium	28.56	21.90
Mean Calcium	8.77	8.79

Table 3: Paired samples' t-test of difference in salivary constituents before and after hemodialysis

Paired differences	t	df	Sig.	
Flow Before-After	-0.363	-10.67	29	0.000
pH Before-After	-0.124	-1.348	29	0.231
Urea Before-After	63.342	9.891	29	0.000
Creatinine Before-After	0.421	6.712	29	0.000
Sodium Before-After	-1.243	-1.659	29	0.112
Chloride Before-After	10.615	7.208	29	0.000
Potassium Before-After	4.83	3.41	29	0.001
Calcium Before-After	0.014	0.154	29	0.791

(df-Degree of freedom, Sig.-Significance).

show a wide range of clinical symptoms and signs including biochemical changes such as hyperkalemia, hyperphosphatemia, hypocalcemia, and hormonal disturbances like secondary hyperparathyroidism, low activity of 1,25(OH)₂ Vitamin D.^[6]

CKD is a life-threatening disorder for which a patient will require either a kidney transplant or hemodialysis. CKD patients exhibit oral manifestations, recognition of which is important since they may be the indicators of the presence or extent of the disease.^[6]

Saliva is a unique fluid and its significance as a diagnostic medium has advanced exponentially in the past decade. In the present study, the whole saliva collected which is noninvasive, cost effective, and with no training of patient required. No special equipment is needed for the collection of the fluid. Diagnosis of the disease via the analysis of saliva is a potentially valuable tool for children and older adults because the collection of the fluid is associated with fewer compliance problems compared with the collection of blood.^[6]

Therefore, this study was designed to rule out changes in the composition of saliva in CKD patients. The saliva samples were analyzed for sodium, potassium, calcium, phosphorous, bicarbonate, and urea.

More than 30 oral signs and symptoms of patients with ESRD have been reported.^[7] Several cases each of gingival hemorrhage, uremic stomatitis, change of taste acuity, enamel hypoplasia, pallor of oral mucosa, xerostomia, uremic odor have been presented.^[8-12]

With respect to pH and Ericsson's buffer capacity of stimulated parotid saliva, there was no significant difference between the patients with ESRD and the healthy controls. This is because urea is converted to ammonia by oral bacteria.^[4,13] The stimulation itself increases pH and buffer capacity as well as the flow rate. This effect might mask the changes that are due to the disease condition.^[3]

Oral manifestations generally observed in patients with CRF include enamel hypoplasia, pallor of the oral mucosa, xerostomia, uremic odor, low caries prevalence in both primary and permanent dentitions, as well as a large amount of calculus.^[4,13]

Dialysis leads to systemic alterations, oral complications, and variations in the flow and composition of saliva. Salivary functions including lubrication, buffering action, maintenance of tooth integrity, antibacterial activity, and taste and digestion may be disturbed by altered salivary flow and composition.^[14] It is considered that the determination of some biomarkers in saliva can be an effective alternative method for monitoring the efficacy of the treatment with dialysis in CKD patients.

Salivary flow rate and pH: in our study, the salivary flow rate before and after a dialysis session (Before dialysis: -0.4 ± 0.2 ml/min

and after dialysis: -0.8 ± 0.3 ml/min) was found to be statistically significant ($P < 0.005$). Salivary pH before and after dialysis was almost similar, no significant difference in pH was found. A similar result was found in the study of Martins *et al.*,^[15] who also found a statistically significant difference between the salivary flow rate before and after a hemodialysis session, and also between patients on hemodialysis and healthy controls. Similar results were obtained by Kaushik *et al.*,^[16] who found a statistically significant lower stimulated and unstimulated salivary flow rate in patients on dialysis when compared to healthy controls. Khanum *et al.* also found similar results.^[14]

Bayraktar *et al.*^[17] reported the stimulated salivary flow rate to be significantly lower in patients on hemodialysis when compared to patients on peritoneal dialysis and healthy controls. They also found a statistically significant higher salivary pH and buffer capacity in patients on peritoneal and hemodialysis when compared to controls.

Dada OT *et al.* in 2019 mentioned about the salivary creatinine, a reliable diagnostic tool for estimating GFR and previous signaling of renal disease.^[18]

Sirma A. *et al.* in 2020, in his study, also revealed that Salivary IL-6, MMP-8 and GSS mRNA levels in combination with urine test analysis could be a useful diagnostic tool for the evaluation of juvenile pyelonephritis.^[19]

Conclusion

The prevalence of chronic renal failure (CRF) is increasing worldwide. ESRD patient requires special oral health care. Many oral and systemic complications occur due to chronic renal failure or due to its treatment. It has been observed that ESRD patient undergoing hemodialysis shows significant oral changes. The increased level of salivary calcium (Ca), phosphorus (P), urea, potassium (K), and sodium (Na) levels in dialysis patient correlated with renal disease severity. The present study was a small effort to prove salivary composition and functional capacities in evaluating the advanced-stage renal disorders. This qualitative analysis gives a promising preventive approach to avoid further damage in a nephritic emergency.

Key message: Salivary flow rate, dental caries prevalence, and calculus deposition may be due to the presence of urea in saliva. Hence, performing some simple tests at primary care settings on the biochemical analysis of saliva can easily detect advanced-stage renal disorders.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient (s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand who their names and initials will not be published and

due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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