

Physiological Changes of Salivary Parameters in Patients with End Stage Renal Failure

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ABSTRACT

Background: Many oral diseases were recorded in ESRD patients including as gingivitis, tooth mobility, xerostomia, ammonia-like smell, mucosal pallor and lesions, malocclusion and an increased risk of dental erosion. Salivary changes among ESRD patients might be attributed to renal failure, use of multiple medications, vomiting, depressive mood and low oral health hygiene.

Aim of study: to assess the salivary changes of patients with end stage renal disease. To determine whether there is changes in salivary compositions and biochemical parameters (urea, creatinine, salivary PH) of patients with end stage renal failure. To find whether there is change in salivary trace element (zinc, copper). To identify whether there is change in salivary electrolyte (sodium, potassium, calcium, phosphate). Determine whether there is a change in salivary enzymes (amylase).

Subjects, Materials and Methods: A cross sectional study carried out in two dialysis centers in Baghdad (Al-Khadhimya Teaching Hospital and Al-Karamah Teaching Hospital) through a period from 1st of March to end of 30th of July, 2015 on convenient sample of 64 patients with end stage renal diseases and on 64 healthy controls. Salivary samples were collected by the researcher at the end of dialysis. Saliva was collected using the standard way of collection. The samples controlled to avoid drooling or swallowing. Whole saliva was collected under resting conditions in a quiet room. Duration was between 0900 and noon at least 1 h after dialysis. Each patient was asked to chew a piece of Arabic gum (0.5-0.7 gm) for one minute, all saliva was removed expectoration, chewing was continued for five minutes with the same piece of gum and saliva was collected in sterile screw capped bottle. Salivary urea and Amylase were analyzed by specific kits, while salivary PH was tested by a hand-held pH meter. Salivary trace elements of saliva were analyzed at the Poisoning Consultation Center/Specialized Surgeries hospital by flame atomic absorption following standardized procedure.

Results: Mean age of ESRD patients was 50.1±14.9 years, males were more than females. No significant difference was observed between patients and controls regarding age and gender. There was a highly significant difference in salivary Potassium, Sodium, Calcium, Copper, Urea and Amylase levels between ESRD patients and controls ($p < 0.001$). There was a significant difference in salivary Zinc level between ESRD patients and controls ($p = 0.02$). There was a significant association between increased age of ESRD patients and HT ($p = 0.04$). A significant association was observed between HT among ESRD patients and high salivary Zinc level ($p = 0.008$).

Conclusion: Abnormal high Salivary Urea concentration in ESRD patients are associated with or was high and it was a significant predictor of ESRD. This study showed that salivary minerals (Potassium, Sodium, Calcium and Copper) were more likely to be reduced in ESRD patients undergone hemodialysis.

KEYWORDS

Salivary Parameters, Renal Failure.

المستخلص

مقدمة: سجلت العديد من أمراض الفم في مرضى الداء الكلوي بمراحله الأخيرة بما في ذلك التهاب اللثة، وضعف الأسنان، وجفاف الفم، رائحة الامونيا، الأقيان والشحوب المخاطية، سوء الإطباق وزيادة خطر تآكل الأسنان. قد يعزى التغييرات اللعابية لدى مرضى الداء الكلوي بمراحله الأخيرة إلى الفشل الكلوي، واستخدام الأدوية المتعددة، والتقيؤ، والمزاج الاكتئابي وانخفاض النظافة الصحية الفموية.

الهدف من الدراسة: لتقييم التغيرات اللعابية للمرضى الذين يعانون من المرض الكلوي في مراحله الأخيرة.

طرق ووسائل ومنهجية البحث: دراسة مقطعية في مركزين لغسيل الكلى في بغداد (مستشفى الكاظمية التعليمي ومستشفى الكرامة التعليمي) خلال الفترة من 1 مارس إلى نهاية 30 يوليو 2015 على عينة ملائمة من 64 مريضاً مصاباً بالفشل الكلوي بمراحله الأخيرة وعلى 64 من الأصحاء. تم جمع عينات من اللعاب من قبل الباحث في نهاية غسيل الكلى. وقد تم جمع اللعاب باستخدام طريقة قياسية لجمع العينات الخاضعة للرقابة لتجنب سيلان اللعاب أو البلع. تم جمع اللعاب كله في ظل ظروف مريحة في غرفة هادئة. وكانت الفترة الزمنية بين 9 صباحاً إلى الظهر و 1 ساعة على الأقل بعد غسيل الكلى. طلب من كل مريض مضغ قطعة من الصمغ العربي (0.5-0.7 جم) لمدة دقيقة واحدة، وإزالة كافة اللعاب. وقد تم تحليل اليوريا والأميليز اللعابية من قبل تحاليل مختبرية محددة، في حين تم اختبار فحص هيدروجينية اللعاب الحصص الهيدروجيني اليودي. وقد تم تحليل العناصر النزرة اللعابية في مركز التسليم التابع لمستشفى الجراحات التخصصية بواسطة جهاز الامتصاص الذري.

النتائج: كان متوسط عمر مرضى الداء الكلوي بمراحله الأخيرة 50.1 ± 14.9 سنة، وكان الذكور أكثر من الإناث. لم يلاحظ أي فرق كبير بين المرضى والأصحاء فيما يخص العمر والجنس. كان هناك اختلاف كبير جداً في مستوى البوتاسيوم، الصوديوم، الكالسيوم، النحاس، اليوريا ومستويات الأميليز اللعابية بين مرضى الداء الكلوي بمراحله الأخيرة والأصحاء ($P > 0.001$). كان هناك اختلاف كبير بين مرضى الداء الكلوي بمراحله الأخيرة والأصحاء ($P = 0.02$). كان هناك ارتباط كبير بين زيادة عمر مرضى الداء الكلوي بمراحله الأخيرة وارتفاع ضغط الدم ($P = 0.04$). ولوحظ وجود ارتباط كبير بين ارتفاع ضغط الدم بين مرضى الداء الكلوي بمراحله الأخيرة وارتفاع مستوى الزنك اللعابي لهؤلاء المرضى ($P = 0.008$).

الاستنتاج: يرتبط ارتفاع تركيز اليوريا اللعابي مع مرضى الداء الكلوي بمراحله الأخيرة وكان مؤشراً كبيراً على الداء الكلوي بمراحله الأخيرة. وأظهرت هذه الدراسة أن

المعادن اللعابية (البوتاسيوم، الصوديوم، الكالسيوم والنحاس) كانت أكثر عرضة للانخفاض في مرضى الداء الكلوي بمراحله الأخيرة.

INTRODUCTION

Renal failure is a process in which the nephrons lose their functional capacity and failure in filtering waste products caused by many causes. The renal failure is mostly reversible but chronic renal failure (CRF) had a progressive course deteriorated towards end stage renal disease (ESRD), although the cause of

the initial nephropathy disappears⁽¹⁾.

The saliva is a unique biological fluid that described as the "mirror of the body". It is produced by salivary glands and composed mainly of water (98%) and 2% other compounds (minerals, electrolytes, etc.)⁽²⁾. Many oral diseases were recorded among ESRD

patients as gingival inflammation, tooth mobility, dry mouth, bad smell, mucosal changes and high liability for dental abrasion. Salivary changes among ESRD patients might be attributed to renal insufficiency, use of medications, vomiting, depressive mood and low health hygiene (3,4).

There is no wide researches on long term effect of dialysis on oral health and saliva, although, many literatures reported the harmful effect of renal transplant on oral health (5).

The main symptom of renal failure is an electrolyte disturbance and break in albumin-creatinine ratio that affect directly on saliva. Some literatures reported the significance of oxidative stress during dialysis in responsibility of salivary changes (6).

SUBJECT, MATERIALS AND METHODS

The study included sixty four patients with end stage renal diseases diagnosed by specialist physician in Internal Medicine and treated regularly with dialysis. The patients were selected from two dialysis centers in Baghdad (Al-Khadhimya Teaching Hospital and Al-Karamah Teaching Hospital) as a convenient sample.

The study was carried out for period from 1st of March to end of 30th of July, 2015. The inclusion criteria of the study were end stage renal diseases patients with dialysis duration more than one month. The exclusion criteria were mental disorder, hematological disease, diabetes mellitus and use of drugs interfering with salivary metabolism. The data was collected by direct interview and fulfilling a prepared questionnaire. The questionnaire included the following information:

1. Sociodemographic characteristics: Age and gender.
2. Clinical findings: Hemodialysis duration and hypertension.
3. Salivary parameters investigation results: Salivary Potassium, Sodium, Calcium, Copper, Zinc, PH, Urea and Amylase results.

Control subjects were recruited from Baghdad Medical City, private clinics and some friends from systemically healthy people but that required treatment due to dental problems. All controls had no systemic illnesses, including diabetes mellitus and renal or liver disease. Duration of dialysis was 4 hours per session, with 300 – 350 mL/minute blood flow rate or with a dialysate flow of 500 mL/minute. Patients with active infection or that were on medication influencing salivary flow rate, such as antidepressant drugs, were excluded.

Study design

A cross sectional study carried out on patients and controls to assess the relationship between salivary parameters and ESRD patients as shown in figure 1.

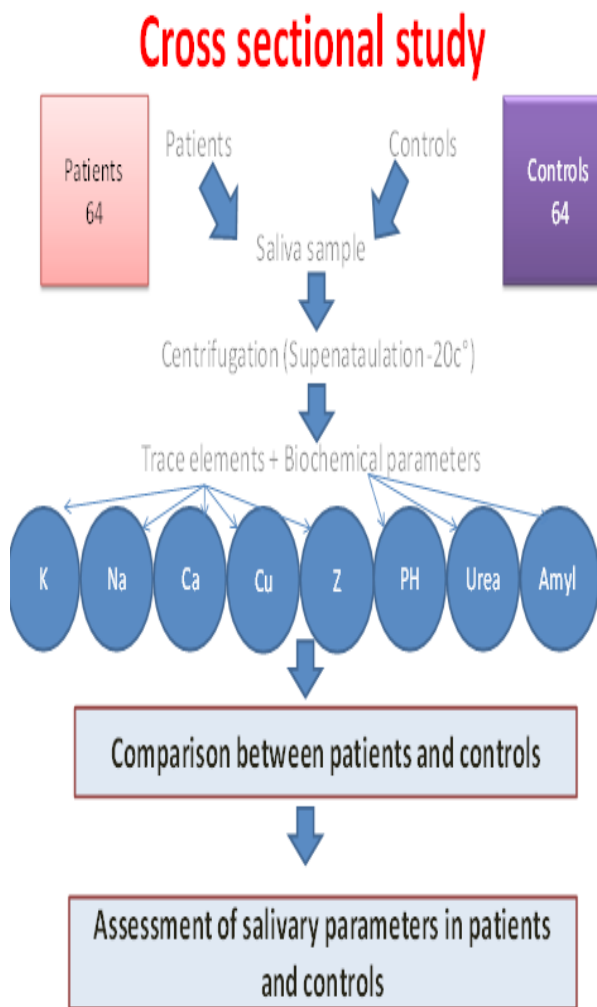


Figure 1: A schematic presentation of study design.

Materials used for salivary parameters estimation

1-Salivary Urea reagent

Table 1: Randox kit.

Materials	Concentration
GAMMA GT (Liquid) (Mono Reagent)	0.05mmol/LL
CARBOXY (RX Daytona™)	0.05mmol/L
Distal water	1mmol/L

2-Salivary Amylase reagent

Table 2: Reagent of α-Amylase.

Materials	Concentration
MES PH 6	100mmol/L
2-chloro-4-nitrophenyl-α-D-maltotrisoside	2.25mmol/L
Sodium chloride	350mmol/L
Calcium acetate	6mmol/L
Potassium thiocyanate	900mmol/L
Sodium azide	0.9gm/L

3-Salivary PH

4-Salivary Potassium, Sodium, Zinc, Calcium and Copper

These parameters were tested through Atomic absorption Spectrophotometer use of special reagents of the device.

RESULTS

Biochemical parameters and trace elements

1. Salivary Potassium

Mean salivary potassium levels significantly ($p < 0.001$) lowered in ESRD patients (0.2 ± 0.03) than control group (0.3 ± 0.02).

2. Salivary Sodium

The mean sodium level in saliva was highly significant lowered in 84.4% of patients with ESRD patients (0.4 ± 0.06) as compared to control group ($0.7 \pm$).

The results of the present study also showed that the mean salivary sodium level was significantly higher ($p < 0.05$) in male (0.52 ± 0.02) than females (0.31 ± 0.01) with ESRD.

3. Salivary Calcium

The results showed that the mean salivary Calcium level is low 67.2% of ESRD patients 1.7 ± 0.2 ml/dl as compared to zero in control group (3.076 ± 0.43) with highly significant differences salivary calcium level between ESRD patients and control group ($p < 0.001$).

The current results revealed that the mean salivary calcium level was significantly higher ($p < 0.05$) in males (1.9 ± 0.82) than females (1.5 ± 0.61) with ESRD.

4. Salivary Copper

The mean salivary Copper level is low in 92% of ESRD patients (1.8 ± 0.4 μ gm/dl), when compared to 4.8% control group. A highly significant difference was observed insalivary Copper level between ESRD patients and controls ($p < 0.01$).

5. Salivary Zinc

The mean salivary Zinc level of ESRD patients was 4.5 ± 1.3 μ gm/dl, 7.8% of them had low salivary Zinc level and mean salivary Zinc level of controls was 3.9 ± 1.5 μ gm/dl, all of controls had normal salivary Zinc level. There was a statistically significant difference in salivary Zinc level between ESRD patients and controls ($p = 0.049$).

6. Salivary PH

The mean PH of ESRD patients was 7.9 ± 0.4 , most of ESRD patients had basic salivary PH, 4 ESRD patients had neutral salivary PH and two patients had acidic PH, on other hand, mean salivary PH of controls was 7.8 ± 0.3 , the majority of controls had basic salivary PH and only 4 controls had neutral PH.

No significant difference in salivary PH was observed between ESRD patients and controls ($p = 0.285$).

7. Salivary Urea

The mean salivary Urea of ESRD patients was 0.6 ± 0.2 ; range was 1.1, while mean of salivary Urea for controls was 0.2 ± 0.06 with range as 0.2. There was a highly significant difference in salivary urea between ESRD patients and controls ($p < 0.01$).

8. Salivary Amylase

The mean of salivary Amylase among ESRD patients was 61467.8 ± 29943 . For controls, mean salivary Amylase was 43721.8 ± 14131.6 . There was a highly significant difference in salivary Amylase between ESRD patients and controls ($p = 0.030$).

DISCUSSION

Wide range of oral manifestations have been found among ESRD patients like, gingivitis, xerostomia, ammonia-like smell, mucosal pallor and lesions, tooth mobility, malocclusion and high risk of dental erosion caused by frequent regurgitation. Systemic and salivary imbalance caused by chronic renal failure, multiple medications, vomiting and low self-hygiene may affect oral health in these patients⁽⁸⁾.

The Current results found that half of ESRD patients had dialysis duration more than one year. This finding came in agreement with finding of Al Wakeelet al (2002)⁽⁸⁾ in Saudi Arabia who reported that mean duration of dialysis 5.7 years. The recovery of renal function in patients with prolonged hemodialysis is reported to be a relatively uncommon occurrence. Large observational cohorts of ESRD patients started on long-term hemodialysis from different parts of the world reported renal recovery rates of as low as 1%-2.4%⁽⁹⁾.

In this study, Hypertension was present among 64.1% of ESRD patients. Also this finding is consistent with results of Silva et al (2012)⁽¹⁰⁾ who observed that HT is the main cardiovascular risk factor associated with Brazilian ESRD.

Current study revealed that salivary Potassium level in ESRD patients was significantly lower than salivary Potassium level of control group. In contrast to study of Manley et al (2012)⁽¹¹⁾ who were found significant higher salivary potassium among Australian ESRD patients.

The current study results found highly significant difference ($p < 0.001$) in salivary Calcium levels between ESRD patients and control, while Abdulla et al (2012) didn't find significant difference in the salivary Calcium between ESRD patients and control

groups.

Current results about lower salivary Calcium in ESRD patients are inconsistent with results of Manley *et al* (2012)⁽¹¹⁾ in Australia that didn't find significant difference in salivary Calcium between ESRD patients and healthy controls. The difference may be due to that ESRD patients in Australian study were not on pre-hemodialysis phase and our patients were on post-hemodialysis phase.

Current results revealed that there were highly significant differences in the mean salivary Copper of ESRD patients. Our study was the first study exploring salivary Copper among ESRD patients in Iraq. This findings are close to results of Abdellatif *et al*(2011)⁽¹²⁾in Egyptwho observed deficient salivary Copper in ESRD children.

The results of the present study appeared that the salivary PH of ESRD patients and control were basic (mean=7.9, 7.8) respectively with no significant difference between the two groups regarding PH. This finding is consistent with the findings of results of(Bayraktar *et al*, 2009)⁽¹³⁾ inTurkey who found that highly significant association between ESRD patients and increased salivary PH.Fortunately,the high salivary PH in ESRD patients decreases prevalence of dental caries among them ⁽¹⁴⁾.

According to mean of means salivary Urea there was a highly significant difference between ESRD patients and control group regarding salivary Urea ($p<0.001$). This is similar to findings of previous Iraq study (Abdulla *et al*, 2012)who showed that highly significant difference between patients that includes ESRD, hemodialysis and controls regarding salivary urea. Also Ali *et al*(2013)⁽¹⁵⁾ in Indiareported highly significant increaseof salivary Urea among ESRD patients.

The findings of this study were clarified that salivary Amylase of ESRD patients significantly higher than mean salivary Amylase of control group. This is similar to results of (Tomás *et al*, 2008)⁽¹⁾ in Portugal patients with chronic renal failure (ESRD) compared to healthy controls when measured salivary biochemical parameters of both groups and found highly significant difference in salivary Amylase level between ESRD and control groups.

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