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Research Article

Comparative Analysis of Salivary and Serum Urea and Creatinine Levels in Pre- and Post-Dialysis Patients with Renal Disease

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Abstract

Introduction: Patients with chronic kidney disease (CKD) on hemodialysis undergo major biochemical shifts. Non-invasive saliva testing could supplement blood investigations but needs validation.

Aim: To compare salivary and serum urea, creatinine, sodium, potassium, and phosphate levels in CKD patients before and after hemodialysis, and assess their correlation.

Materials and Methods: This cross-sectional study included 50 CKD patients on maintenance hemodialysis for over one year. Paired saliva and blood samples were collected pre- and post-dialysis. Biochemical markers were analysed using standard methods. Data were analysed using SPSS v21. Paired t-tests compared values; Pearson's correlation tested associations.

Results: Salivary urea, creatinine, potassium, and phosphate decreased significantly post-dialysis ($P < 0.001$); sodium showed an insignificant rise. All serum parameters declined significantly ($P < 0.001$). The percentage decrease was larger in serum than saliva for urea, creatinine, sodium, and potassium, but phosphate fell more in saliva. Changes were significantly higher in serum than saliva for most markers ($P < 0.001$). No significant correlations were found among salivary parameters. A significant inverse correlation was seen between serum creatinine and sodium ($r = –0.32$, $P < 0.05$) and a direct one between serum creatinine and phosphate ($r = 0.29$, $P < 0.05$). Salivary urea changes correlated inversely with serum phosphate ($r = –0.32$, $P < 0.05$).

Conclusion: Salivary testing shows potential to reflect some serum biochemical changes in hemodialysis patients but needs further validation before routine use.

Keywords: Chronic Kidney Disease; Saliva; Serum Urea; Hemodialysis

Introduction

Chronic Kidney Disease (CKD) is a significant global public health concern, with a rising incidence attributed to lifestyle-related disorders such as diabetes mellitus, hypertension, and cardiovascular diseases. According to the Global Burden of Disease Study 2019, CKD ranks as the 12th leading cause of death worldwide, with over 850 million individuals affected globally and a steady rise in mortality over the past two decades [1,2]. In India alone, the estimated prevalence of CKD is around 17%, with a large proportion of patients presenting at later stages due to a lack of awareness and screening [3]. As CKD progresses, patients often require renal replacement therapy, including hemodialysis, to manage life-threatening disturbances in fluid and electrolyte balance. Accurate monitoring of biochemical markers—particularly urea and creatinine—is essential for assessing the effectiveness of dialysis, residual renal function, and guiding therapeutic interventions [4]. These serum biomarkers are widely established as indicators of glomerular filtration rate (GFR) and nitrogenous waste accumulation. Despite their clinical value, repeated blood sampling poses certain drawbacks. It can be invasive, painful, and anxiety-inducing for patients and may increase the risk of infection or phlebitis, especially in those undergoing long-term hemodialysis [5]. This has led to a growing interest in exploring non-invasive biofluids, such as saliva, as a potential alternative for diagnostic and monitoring purposes in renal disease [6].

Saliva, a complex oral fluid secreted by salivary glands, is gaining increasing attention as a non-invasive and cost-effective alternative for disease diagnosis and monitoring. It contains a rich composition of electrolytes, proteins, enzymes, and metabolic waste products that reflect systemic physiology and pathophysiology. Due to the ease of collection, minimal need for trained personnel, and lower biohazard risk, saliva is emerging as a viable biofluid for large-scale screening and regular monitoring in both community and hospital settings [7].

In patients with renal dysfunction, several metabolic waste products, such as urea and creatinine, accumulate in body fluids, and their levels in saliva have been found to correlate positively with serum levels [8]. In particular, studies suggest that during the pre-dialysis

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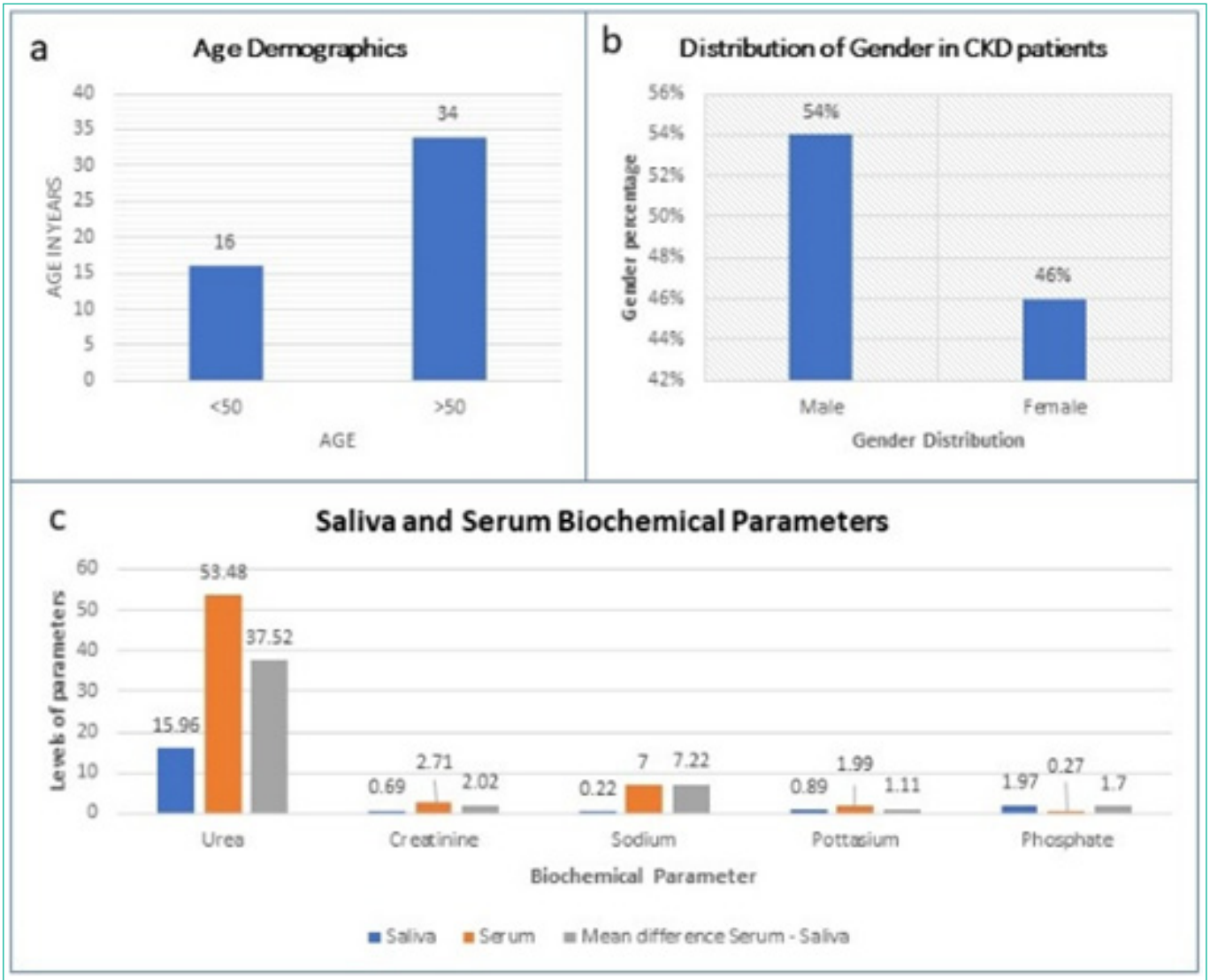

Figure 1: (a) Age distribution of CKD patients showing frequencies of patients below and above 50 years. **(b)** Gender distribution of CKD patients, indicating the percentage of male and female participants. **(c)** Comparison of pre- to post-hemodialysis changes in salivary and serum biochemical parameter levels in renal disease patients. Values are presented as Mean ± SD. Independent Student's t-test was used to compare mean changes between saliva and serum for

state, elevated levels of nitrogenous compounds and electrolytes are detectable in saliva due to diffusion across salivary gland membranes [9]. Furthermore, post-dialysis changes in serum concentrations are often mirrored in salivary levels, highlighting the potential of saliva as a surrogate for serum in monitoring renal function [10]. Salivary sodium, potassium, and phosphate are also of clinical interest in CKD, as these electrolytes often fluctuate in response to dialysis. Several studies have shown that the alteration in electrolyte concentration pre- and post-dialysis is reflected in both serum and salivary samples, although with variable consistency depending on individual physiology and salivary gland function [6]. While serum-based evaluation of renal biomarkers remains the gold standard, the repeated need for venipuncture in dialysis patients presents logistical and patient-centered challenges [7]. The development of a reliable, non-invasive method for monitoring renal function is both a clinical and public health priority. Given this background, the present study aims to bridge this gap by evaluating and comparing the levels of salivary and serum urea, creatinine, sodium, potassium, and phosphate before and after dialysis in patients with chronic kidney disease. The overarching goal is to assess whether saliva can serve as a reliable and non-invasive alternative for routine biochemical monitoring in dialysis patients.

Materials and Methods

Study Design

This cross-sectional observational study was conducted in the Department of Oral Medicine and Radiology at Shree Bankey Bihari Dental College and Research Center, Ghaziabad, Uttar Pradesh, India. Ethical clearance (EC/NEW/INST/2022/2713) was obtained from the Institutional Research Ethics Committee prior to the initiation of the study. All participants were informed about the objectives, benefits, and potential risks associated with the study, and written informed consent was obtained before sample collection.

The study included a total of 50 patients diagnosed with CKD, all above 18 years of age, who were undergoing maintenance hemodialysis

Table 1a: Pre- and post-hemodialysis salivary biochemical parameter levels of renal disease patients. Values are presented as Mean ± SD and compared using the paired Student's t-test.

1a: Salivary Biochemical Parameter	Pre (n=50)	Post (n=50)	Mean change (Post-Pre)	t value	*P* value
Urea (mg/dL)	55.62 ± 9.95	39.66 ± 7.41	-15.96 ± 6.11	18.47	< 0.001
Creatinine (mg/dL)	3.09 ± 0.67	2.40 ± 0.50	-0.69 ± 0.63	7.77	< 0.001
Sodium (mmol/L)	126.42 ± 0.50	126.64 ± 0.85	0.22 ± 1.11	1.39	0.170
Potassium (mmol/L)	4.47 ± 0.09	3.59 ± 0.14	-0.89 ± 0.16	38.17	< 0.001
Phosphate (mg/dL)	21.11 ± 0.11	19.14 ± 0.18	-1.97 ± 0.20	68.14	< 0.001

*Table 1a (Salivary Biochemical Parameters):
Values are expressed as Mean ± SD; *n = 50. Paired t-test applied. Negative mean change indicates a reduction from baseline. P < 0.05 is considered statistically significant.

Table 1b: Pre- and post-hemodialysis serum biochemical parameter levels of renal disease patients. Values are presented as Mean ± SD and compared using the paired Student's t-test.

1b: Serum Biochemical Parameter	Pre (n=50)	Post (n=50)	Mean change (Post-Pre)	t value	*P* value
Urea (mg/dL)	136.33 ± 61.65	82.85 ± 45.71	-53.48 ± 32.43	11.66	< 0.001
Creatinine (mg/dL)	7.60 ± 3.06	4.89 ± 1.93	-2.71 ± 2.28	8.42	< 0.001
Sodium (mmol/L)	133.78 ± 1.39	126.78 ± 0.71	-7.00 ± 1.62	30.63	< 0.001
Potassium (mmol/L)	5.70 ± 0.13	3.71 ± 0.15	-1.99 ± 0.19	75.02	< 0.001
Phosphate (mg/dL)	6.30 ± 0.14	6.03 ± 0.10	-0.27 ± 0.15	13.07	< 0.001

*Table 1b (Serum Biochemical Parameters):
Values are expressed as Mean ± SD; *n = 50. Paired t-test applied. Negative mean change indicates a reduction from baseline. P < 0.05 is considered statistically significant.

for more than one year at a private hospital in Ghaziabad. A detailed clinical history was recorded for each participant. Most of the patients were undergoing dialysis due to late-stage presentation of renal disease. Patients were included if they were willing to participate, had been diagnosed with CKD, and were either under conservative management or had been receiving hemodialysis for a minimum of six months, and were between 18 and 70 years of age. Only those who provided signed informed consent were enrolled in the study. Patients were excluded if they were below 18 years of age, were uncooperative or unwilling to participate, had systemic illnesses other than renal failure (excluding diabetes and hypertension as etiological factors), or were undergoing chemotherapy or radiotherapy. Patients receiving hemodialysis due to acute kidney injury or traumatic causes were also excluded, as were patients diagnosed with viral hepatitis.

Sample Collection

For each participant, both saliva and venous blood (serum) samples were collected immediately before and after dialysis to assess and compare changes in key biochemical markers, including urea, creatinine, sodium, potassium, and phosphate. Each patient underwent a brief oral examination using a dental mirror and artificial light to assess oral health status. Any notable findings were documented for reference. Saliva samples were then collected under standardized conditions to minimize biological variability. Patients were instructed to rinse their mouths with distilled water prior to sample collection. Unstimulated whole saliva was collected using the spitting method for five minutes. To maintain consistency, all samples were collected in the morning between 9:00 AM and 11:00 AM, at least one hour after food intake. Approximately 3 mL of saliva was collected per patient and immediately placed in sterile containers. Samples were transported in cooler boxes to prevent bacterial degradation and centrifuged at 3000 rpm for 10 minutes. The supernatant was separated and stored at –20°C until biochemical analysis. Simultaneously, venous blood samples were drawn by trained personnel using sterile technique. Blood was collected into lithium heparin tubes to prevent clotting, again in the same time window (9:00 AM to 11:00 AM) as saliva collection. Participants were advised to fast for at least two hours before sample collection. This timing was standardized to ensure uniformity and reduce potential diurnal variation in biochemical marker levels.

Biochemical Analysis

Biochemical analysis of both saliva and serum was carried out using automated analyzers. Salivary creatinine was measured using the Randox Creatinine Manual Kit on the Biolabo-Kenza Max Biochemistry Analyzer**,** following the colorimetric method described by Bartels et al. (1972). In this method, creatinine reacts with picric acid in an alkaline medium to form a colored complex; the intensity of the color corresponds to the creatinine concentration. Calibration was performed using double-distilled water, and the analyzer was operated in CREA mode for accurate measurements. Salivary urea levels were measured using the Roche Cobas C 111 Analyzer with the Cobas Urea Kit, based on a kinetic test involving the enzymes urease and glutamate dehydrogenase, as described by Talke and Schubert (1965) and Tiffany et al. (1972). The analyzer automatically computed urea concentration using internal calibration standards and pre-programmed algorithms.

Venous blood samples were similarly analyzed for urea, creatinine, sodium, potassium, and phosphate using the same analyzer and methodology, ensuring comparability of results between saliva and serum. Prior to analysis, all frozen samples were thawed at room temperature and re-centrifuged at 3000 rpm for 10 minutes to remove residual debris. The consistency in sampling conditions and analytical techniques was aimed at enhancing the reliability of comparisons between the pre- and post-dialysis states.

Statistical Analysis

All statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS), version 21. Descriptive statistics were used to summarize the data, including means and standard deviations for continuous variables and frequencies for categorical variables. Analytical tests applied included the contingency coefficient, Fisher's exact test, the Chi-square test, and Student's t-test for group comparisons. For comparisons involving more than two groups, one-way Analysis of Variance (ANOVA) was used, followed by appropriate post-hoc tests, including the Least Significant Difference (LSD) test and Dunnett's T3, depending on the homogeneity of variances. Pearson's correlation coefficient (r) was employed to assess the strength and direction of associations between salivary and serum biochemical parameters. A p-value of less than 0.05 was considered

Table 2: Inter-correlation (r value) of pre- to post-hemodialysis changes in salivary and serum biochemical parameter levels in renal disease patients (n = 50). Pearson correlation analysis was performed to assess associations between changes in individual parameters.

Variable	Salivary urea	Salivary creatinine	Salivary sodium	Salivary potassium	Salivary phosphate	Serum urea	Serum creatinine	Serum sodium	Serum potassium	Serum phosphate
Salivary urea	1.00									
Salivary creatinine	0.02^{ns}	1.00								
Salivary sodium	0.05^{ns}	-0.07^{ns}	1.00							
Salivary potassium	-0.05^{ns}	-0.06^{ns}	0.05^{ns}	1.00						
Salivary phosphate	0.13^{ns}	-0.18^{ns}	-0.26^{ns}	-0.14^{ns}	1.00					
Serum urea	0.05^{ns}	-0.09^{ns}	0.10^{ns}	-0.01^{ns}	-0.17^{ns}	1.00				
Serum creatinine	-0.13^{ns}	-0.02^{ns}	-0.07^{ns}	-0.12^{ns}	-0.13^{ns}	0.09^{ns}	1.00			
Serum sodium	-0.24^{ns}	-0.20^{ns}	-0.13^{ns}	-0.05^{ns}	0.16^{ns}	0.09^{ns}	-0.32*	1.00		
Serum potassium	-0.02^{ns}	-0.15^{ns}	-0.04^{ns}	0.13^{ns}	0.00^{ns}	0.13^{ns}	-0.05^{ns}	0.22^{ns}	1.00	
Serum phosphate	-0.32*	0.06^{ns}	0.20^{ns}	0.04^{ns}	-0.24^{ns}	0.18^{ns}	0.29*	-0.10^{ns}	0.10^{ns}	1.00

$^{ns}P > 0.05$ or $^{*}P < 0.05$.

statistically significant, while p-values less than 0.01 were considered highly significant. A p-value greater than 0.05 was interpreted as not statistically significant.

Results

Demographic Characteristics

The demographic characteristics of the patients included in the study are illustrated in Figures 1a and b. The age of the participants ranged from 27 to 87 years, with a mean age of 55.50 ± 13.59 years and a median of 59 years. Among the 50 patients enrolled, 16 individuals (32.0%) were aged ≤ 50 years, while 34 individuals (68.0%) were older than 50 years. In terms of sex distribution, the study population comprised 27 males (54.0%) and 23 females (46.0%). Overall, the sample demonstrated a predominance of older adults (>50 years) and a slightly higher proportion of male patients.

Salivary Biochemical Parameters

The pre- and post-hemodialysis salivary biochemical parameters—urea, creatinine, sodium, potassium, and phosphate—of the renal disease patients are summarized in Table 1a. The mean (± SD) pre-dialysis salivary levels of urea, creatinine, sodium, potassium, and phosphate were 55.62 ± 9.95 mg/dL, 3.09 ± 0.67 mg/dL, 126.42 ± 0.50 mmol/L, 4.47 ± 0.09 mmol/L, and 21.11 ± 0.11 mg/dL, respectively. Post-dialysis, these values were observed to be 39.66 ± 7.41 mg/dL for urea, 2.40 ± 0.50 mg/dL for creatinine, 126.64 ± 0.85 mmol/L for sodium, 3.59 ± 0.14 mmol/L for potassium, and 19.14 ± 0.18 mg/dL for phosphate.

A comparative analysis using the paired t-test revealed a statistically significant reduction in salivary levels of urea (mean change = –15.96 ± 6.11, t = 18.47, P < 0.001), creatinine (mean change = –0.69 ± 0.63, t = 7.77, P < 0.001), potassium (mean change = –0.89 ± 0.16, t = 38.17, P < 0.001), and phosphate (mean change = –1.97 ± 0.20, t = 68.14, P < 0.001) following hemodialysis. In contrast, salivary sodium exhibited a slight but statistically non-significant increase post-dialysis (mean change = 0.22 ± 1.11, t = 1.39, P = 0.170) (Figure 1c). At the final evaluation, the percentage mean reduction in salivary levels from pre- to post-dialysis was 28.7% for urea, 22.3% for creatinine, 19.8% for potassium, and 9.3% for phosphate. Salivary sodium, however, showed a marginal increase of 0.2%.

Serum Biochemical Parameters

The pre- and post-hemodialysis serum biochemical parameters—urea, creatinine, sodium, potassium, and phosphate—are summarized in Table 1b. The mean (± SD) pre-dialysis serum levels of urea, creatinine, sodium, potassium, and phosphate were 136.33 ± 61.65 mg/dL, 7.60 ± 3.06 mg/dL, 133.78 ± 1.39 mmol/L, 5.70 ± 0.13 mmol/L, and 6.30 ± 0.14 mg/dL, respectively. Following hemodialysis, these values declined to 82.85 ± 45.71 mg/dL for urea, 4.89 ± 1.93 mg/dL for creatinine, 126.78 ± 0.71 mmol/L for sodium, 3.71 ± 0.15 mmol/L for potassium, and 6.03 ± 0.10 mg/dL for phosphate.

A comparative analysis using a paired t-test revealed a statistically significant reduction in all serum biochemical parameters after hemodialysis. Urea decreased significantly (mean change = –53.48 ± 32.43, t = 11.66, P < 0.001), as did creatinine (mean change = –2.71 ± 2.28, t = 8.42, P < 0.001), sodium (mean change = –7.00 ± 1.62, t = 30.63, P < 0.001), potassium (mean change = –1.99 ± 0.19, t = 75.02, P < 0.001), and phosphate (mean change = –0.27 ± 0.15, t = 13.07, P < 0.001), as detailed in (Figure 1c). In terms of percentage reduction from pre- to post-dialysis values, serum urea showed a mean decrease of 39.2%, creatinine 35.7%, potassium 35.0%, sodium 5.2%, and phosphate 4.3%.

Comparison of Salivary and Serum Biochemical Changes Pre- and Post-Dialysis

Overall, the reduction in mean values was greater in serum compared to saliva for urea, creatinine, sodium, and potassium. In contrast, phosphate levels showed a greater reduction in saliva than in serum. Statistical comparison using Student's t-test demonstrated significantly greater changes in serum than salivary levels for urea (–53.48 ± 32.43 vs. –15.96 ± 6.11; mean difference = –37.52 ± 46.66; t = 8.04, P < 0.001), creatinine (–2.71 ± 2.28 vs. –0.69 ± 0.63; mean difference = –2.02 ± 3.34; t = 6.05, P < 0.001), sodium (–7.00 ± 1.62 vs. +0.22 ± 1.11; mean difference = –7.22 ± 2.77; t = 26.06, P < 0.001), and potassium (–1.99 ± 0.19 vs. –0.89 ± 0.16; mean difference = –1.11 ± 0.35; t = 31.37, P < 0.001). Interestingly, phosphate showed a significantly greater decrease in saliva compared to serum (–1.97 ± 0.20 vs. –0.27 ± 0.15; mean difference = 1.70 ± 0.36; t = 47.89, P < 0.001) (Figure 1c).

Correlation Between Changes in Salivary and Serum Biochemical Parameters

The correlations between pre- to post-hemodialysis changes in salivary and serum biochemical parameters (urea, creatinine, sodium, potassium, and phosphate) are summarized in Table 2. Pearson correlation analysis revealed no significant associations (P > 0.05)

among the changes in salivary biochemical markers, suggesting that fluctuations in one parameter were not consistently associated with changes in others within saliva. In contrast, serum parameters showed significant correlations. A statistically significant inverse correlation was observed between the changes in serum creatinine and sodium ($r = -0.32$, $P < 0.05$), indicating that a greater decrease in one was associated with a lesser or opposite change in the other (Tables 1,2). Additionally, a significant positive correlation was found between changes in serum creatinine and phosphate ($r = 0.29$, $P < 0.05$), suggesting that both parameters tended to decrease concurrently. Interestingly, a significant inverse correlation was also observed between changes in salivary urea and serum phosphate ($r = -0.32$, $P < 0.05$), implying that a reduction in salivary urea may be associated with a lesser decrease or relative increase in serum phosphate, and vice versa (Table 1,2).

Discussion

The present study was conducted to compare salivary and serum levels of urea, creatinine, sodium, potassium, and phosphate in patients with chronic kidney disease (CKD) before and after hemodialysis, and to assess possible correlations between these parameters. Hemodialysis is known to remove accumulated waste products and maintain electrolyte balance in CKD patients [11,12]. In this study, mean serum urea levels decreased significantly from 136.33 ± 61.65 mg/dL pre-dialysis to 82.85 ± 45.71 mg/dL post-dialysis. Similarly, serum creatinine reduced from 7.60 ± 3.06 mg/dL to 4.89 ± 1.93 mg/dL, sodium from 133.78 ± 1.39 to 126.78 ± 0.71 mmol/L, potassium from 5.70 ± 0.13 to 3.71 ± 0.15 mmol/L, and phosphate from 6.30 ± 0.14 to 6.03 ± 0.10 mg/dL, all with statistically significant differences ($P < 0.001$). These reductions confirm the effectiveness of hemodialysis in clearing nitrogenous waste and excess electrolytes, consistent with previous reports [4]. Correspondingly, salivary levels of urea and creatinine also showed significant decreases post-dialysis, with mean urea dropping from 55.62 ± 9.95 mg/dL to 39.66 ± 7.41 mg/dL and creatinine from 3.09 ± 0.67 mg/dL to 2.40 ± 0.50 mg/dL. Potassium and phosphate in saliva similarly declined from 4.47 ± 0.09 to 3.59 ± 0.14 mmol/L and 21.11 ± 0.11 to 19.14 ± 0.18 mg/dL, respectively. Salivary sodium, however, showed a slight, non-significant increase from 126.42 ± 0.50 to 126.64 ± 0.85 mmol/L. These findings highlight that salivary biochemical markers partly mirror serum changes during dialysis, supporting saliva's potential as a supplementary non-invasive diagnostic fluid [13,14]. Recent literature emphasizes saliva's promise as an accessible, patient-friendly medium for monitoring systemic conditions, including renal diseases [15]. Several studies have demonstrated moderate to strong correlations between salivary and serum urea and creatinine in CKD patients [16]. Our results reinforce this, indicating that while saliva cannot fully replace blood tests, it may serve as a practical adjunct for patient monitoring and follow-up, especially where frequent venipuncture is impractical.

The significant reduction in serum urea and creatinine after hemodialysis observed in this study aligns with their role as key markers of renal excretory function. Urea, a primary end product of protein metabolism, and creatinine, a byproduct of muscle metabolism, both accumulate in the blood due to decreased glomerular filtration rate in CKD [4]. The observed mean decrease in serum urea by 39.2% and creatinine by 35.7% confirms effective removal by dialysis, which is consistent with similar clearance rates reported by Kim et al. (2021) [17]. Our findings further showed that salivary urea and creatinine also declined significantly—by 28.7% and 22.3% respectively—indicating that these waste metabolites are partially secreted through salivary glands. This supports earlier work by Panchbhai (2012) and more recent findings by Shetty and Patil (2020), who reported moderate correlations between salivary and serum levels [16,18]. However, the mean changes in serum were significantly higher than in saliva, reflecting the more direct and efficient clearance via hemodialysis than extrarenal routes. For electrolytes, serum sodium showed a notable mean decrease of 5.2% post-dialysis (133.78 ± 1.39 to 126.78 ± 0.71 mmol/L), while salivary sodium showed an insignificant slight increase (126.42 ± 0.50 to 126.64 ± 0.85 mmol/L). This pattern is expected because sodium balance during hemodialysis depends on dialysate composition and ultrafiltration rates. Minor salivary variations could be due to local glandular regulation or residual oral fluid shifts [19]. Serum potassium levels decreased significantly by 35.0%, from 5.70 ± 0.13 to 3.71 ± 0.15 mmol/L, matching the target of removing excess potassium to prevent hyperkalemia—a common complication in CKD patients [20]. The parallel reduction in salivary potassium (19.8% decrease) reflects systemic shifts but also indicates that potassium in saliva may not equilibrate exactly with serum levels due to rapid homeostatic adjustments [21]. Interestingly, serum phosphate decreased modestly by 4.3%, while salivary phosphate showed a greater mean reduction of 9.3%. Phosphate is tightly regulated by parathyroid hormone and is less efficiently removed during a single dialysis session due to its intracellular distribution [22]. The slightly higher reduction in salivary phosphate may reflect both serum clearance and local salivary gland excretion, which requires further investigation. Comparative analysis showed significantly greater mean changes in serum than saliva for all parameters except phosphate, which had a higher decline in saliva. This reinforces that while saliva partly mirrors systemic biochemical changes, its utility as a direct substitute for blood monitoring is still limited and parameter-dependent [23]. Overall, these results strengthen the case for using saliva as an adjunctive fluid for non-invasive monitoring, especially for parameters like urea and creatinine, which showed consistent trends.

While this study demonstrates promising trends in the use of saliva as an adjunctive fluid for monitoring biochemical changes in chronic kidney disease patients undergoing hemodialysis, certain limitations must be acknowledged. First, the sample size was limited to 50 patients from a single center, which may restrict the generalizability of the findings. Larger, multicenter studies are needed to validate these trends across diverse patient populations and dialysis protocols. Second, this study evaluated only a single pre- and post-dialysis session per participant. Serial sampling over multiple dialysis cycles would help assess intra-individual variability and strengthen the evidence for saliva as a reliable monitoring tool. Additionally, factors such as hydration status, oral hygiene, residual salivary gland function, and circadian rhythms can influence salivary composition but were not controlled in detail here [15]. Another limitation is that only basic biochemical markers were analyzed. Future research should expand to include other emerging salivary biomarkers such as cystatin C, β2-microglobulin, or inflammatory markers, which may

offer greater diagnostic sensitivity for renal dysfunction. Advanced analytical techniques, such as proteomics or metabolomics, could also help uncover novel salivary indicators relevant to renal clearance and dialysis adequacy [24]. Despite these limitations, the study highlights that salivary urea and creatinine levels significantly reflect changes seen in serum, with phosphate also showing interesting trends. These findings indicate that saliva has potential as a non-invasive, easily obtainable fluid for supplementary monitoring, especially for patients who undergo frequent blood draws or have poor venous access. Future studies should aim to standardize saliva collection protocols, explore confounding factors more thoroughly, and develop robust reference ranges for salivary analytes in CKD populations. With further validation, salivary diagnostics could reduce patient discomfort, lower healthcare costs, and contribute to more accessible renal care in resource-limited settings [21].

Conclusion

The salivary analysis should not yet replace conventional blood tests for monitoring hemodialysis outcomes, but it shows promise as a practical adjunct for selected biochemical parameters. Continued research in this area could help integrate saliva-based tests into routine nephrology practice, advancing patient-centered, minimally invasive monitoring. With further validation, this approach could reduce patient discomfort, lower healthcare costs, and improve access to regular biochemical assessment, especially in resource-limited settings. Exploring additional salivary markers and refining collection protocols will be key steps forward. Ultimately, the future of nephrology may benefit from combining traditional blood diagnostics with simple, non-invasive salivary screening to enhance patient care and quality of life.

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