



Tükürük kreatinin ve üre değerleri kullanılarak çocuklarda kronik böbrek hastalığı tanısı konulabilir mi?



Dr. Rahime Renda

# Tükürük Özellikleri

Major ve minor tükürük bezlerinden salınır

- Günlük sekresyon ort. 1000ml (800-1500ml)
- pH : 6.0- 7.0
- %98'si su, %2'si elektrolit, mukopolisakkaridler, glikoproteinler, antimikrobiyal maddeler (IgA, hidrojen peroksit) ve enzimler (amilaz, lizozim, lingual lipaz)
- Kolay ve non-invazif, enfeksiyon gelişme riski düşük, kan ya da idrara göre hastadan temini rahat ve ucuz
- Vücuttaki fizyolojik ve patolojik değişikliklerin tespit edilmesini sağlayan biyoişaretleyiciler (DNA, RNA, proteinler, glikoproteinler, immünglobulinler, metabolitler, hücresel materyal, mikroorganizmalar)
- Otoimmün, kardiyovasküler, hormonal, enfeksiyon, böbrek, onkolojik, psikiyatrik hastalıkların ve ilaç bağımlılığının tespiti
- 2400'den fazla protein- iyi bir biomarker

# Etkileri

- Remineralizasyon
- Tamponlama
- Antimikrobiale
- Glukoz klirensi
- Mukozal bütünlüğünün korunması
- Tat
- Sindirim

A.M.Benn et al. Saliva: an overview, N.Z.Dent.J 110(2014) 92-96.

P.V. De Almeida et al. Saliva composition and functions: a comprehensive review.

J.Contemp.Dent.Pract.9 (2008)72-80.

# Tükürük akış hızını etkileyen faktörler

- Fizyolojik

1. Dehidratasyon
2. Egzersiz
3. Çiğneme
4. Tat
5. Gebelik
6. Menapoz
7. Psikolojik

- Patolojik

1. Hastalıklar (Sjogren, Sarkoidoz, DM, malignite, KBH)
2. Enfeksiyon
3. Radyoterapi
4. İlaç
5. GIS uyarımı

# Transfer of biomolecules from blood to saliva

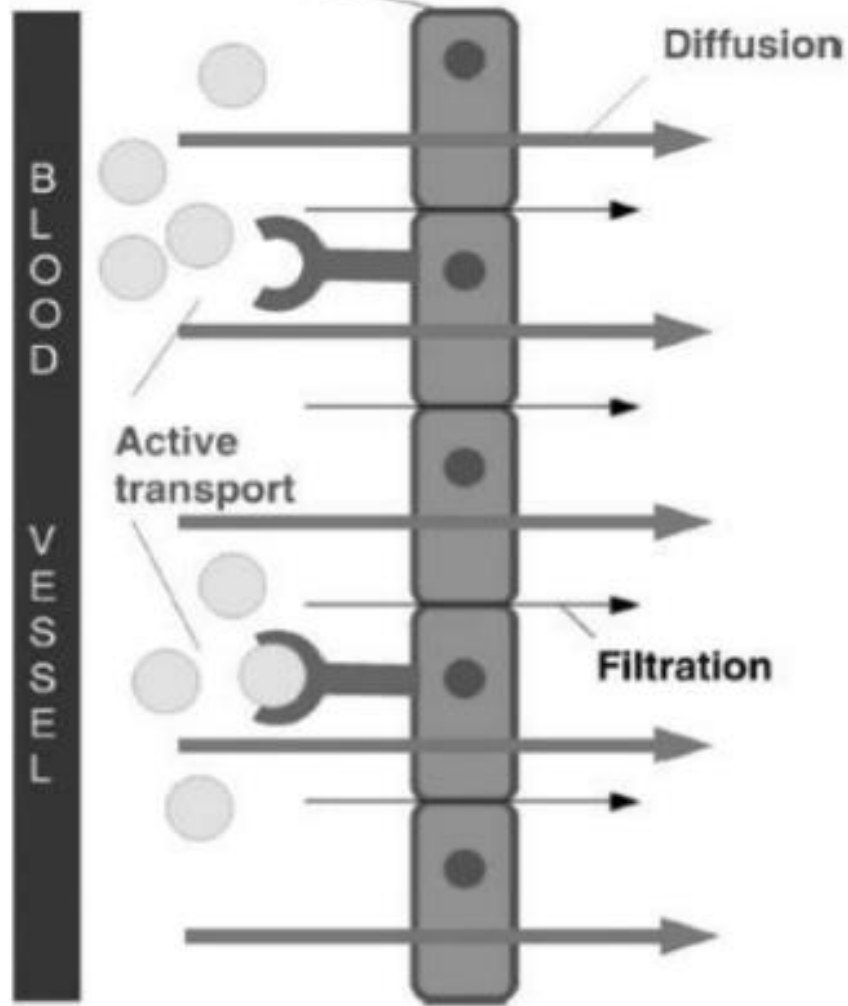
**DIFFUSION**

**ACTIVE  
TRANSPORT**

**ULTRA  
FILTRATION**

**TRANSUDATION**

Cells of salivary glands



**Table 1**  
Clinical studies of salivary markers in renal diseases.

Salivary marker	Groups	Patient number	Result	Interpretation	Year/reference
Urea (mmol/l)	Controls	78	5.36	Salivary urea reliable factor for testing azotemic states in CKD patients	2009/[40]
	GFR < 50 ml/min	154	17.86		
Urea (mmol/l)	Controls (GFR > 90 ml/min)	186	4.42	Salivary urea is stable marker with application in CKD patients	2013/[36]
	GFR < 90 ml/min	96	16.33		
Urea	Controls	56	$r = 0.735$	Significant correlation of urea and salivary urea in CKD patients	1987/[38]
	Diabetes/hypertension/CKD	50	$r = 0.99$		
	Hemodialysis	50	$r = 0.99$		
Urea (mmol/l)	Controls	N/A	39.27	(Children with CKD)	1987/[43]
	Before hemodialysis	10	183.14	Changes in salivary urea concentrations as result of dialysis	
	After hemodialysis	10	86.04		
Urea (mmol/l)	GFR < 10 ml/min/1.73 m <sup>2</sup>	11	Cut-off for salivary urea 14.28 mmol/l and GFR < 80 ml/min/1.73 m <sup>2</sup>	Salivary urea is useful for discrimination of CKD patients from healthy population	2012/[41]
	GFR 11–20 ml/min/1.73 m <sup>2</sup>	10			
	GFR 21–50 ml/min/1.73 m <sup>2</sup>	12			
	GFR 51–80 ml/min/1.73 m <sup>2</sup>	26			
	GFR 81–170 ml/min/1.73 m <sup>2</sup>	42			
Urea (mmol/l)	Controls	64	0.008	Higher salivary concentrations of urea in CKD patients than controls, conditioned by severity of CKD	2008/[42]
	GFR 15–60 ml/min	22	0.017		
	GFR < 15 ml/min	28	0.026		
Urea (mmol/l)	Before hemodialysis	94	2.5	Significant effects of dialysis on salivary urea concentrations	2007/[44]
	After hemodialysis	94	15.3		
Urea (mmol/l)	Controls	10	12.21	Salivary urea is useful non-invasive marker	2014/[9]
	Hemodialysis	20	272.13		
	Kidney transplantation	15	25.54		
Creatinine (μmol/l)	Controls	23	8.5	Salivary creatinine as useful marker to distinguish CKD patients, cut-off value 16.8 μmol/l	1996/[47]
	CKD	25	84		
	Creatinine vs salivary creatinine in CKD	47	$r = 0.784$		
Creatinine (μmol/l)	Controls	37	10.61	Higher concentrations of salivary creatinine in CKD patients, correlation between salivary and plasma creatinine	2014/[48]
	GFR < 30 ml/min/1.73 m <sup>2</sup>	105	58.34		
	Creatinine vs salivary creatinine	105	$r = 0.731$		
Creatinine (μmol/l)	Controls	64	31.19	Higher concentrations of salivary creatinine in CKD patients compared to healthy people	2008/[42]
	GFR 15–60 ml/min	22	30.07		
	GFR < 15 ml/min	28	99.01		
Sodium (mmol/l)	Controls	64	8.03	Higher concentrations of sodium in saliva of CKD patient than in healthy population	2008/[42]
	GFR 15–60 ml/min	22	11.82		
	GFR < 15 ml/min	28	15.48		
Potassium (mmol/l)	Controls	64	22.48	Higher concentrations of potassium in saliva of CKD patient than in healthy population, influenced by the severity of CKD	2008/[42]
	GFR 15–60 ml/min	22	27.03		
	GFR < 15 ml/min	28	34.02		
Chloride (mmol/l)	Controls	64	24.84	Higher concentrations of chloride in saliva of CKD patient than in healthy people	2008/[42]
	GFR 15–60 ml/min	22	31.50		
	GFR < 15 ml/min	28	34.14		
Calcium (mmol/l)	Controls	64	1.78	Lower concentrations of calcium in saliva of CKD patient compared to healthy controls	2008/[42]
	GFR 15–60 ml/min	22	0.9		
	GFR < 15 ml/min	28	0.66		
Phosphate (mmol/l)	Controls	30	Cut-off for control subjects 4.76	Salivary phosphate is useful for monitoring hyperphosphatemia in CKD patients	2008/[55]
	Various stages of CKD	110			
	Chronic hemodialysis	68			
Phosphorus	N/A	N/A	Increased	Increased salivary phosphorus in CKD patients	2009/[56]
Amylase activity (units/l)	Controls	64	129,031	Composition of saliva is influenced by the CKD	2008/[42]
	GFR 15–60 ml/min	22	145,681		
	GFR < 15 ml/min	28	222,750		
N-methyl-2-pyridone-5-carboxamide	Controls	N/A	Increased	Higher salivary N-methyl-2-pyridone-5-carboxamide in CKD patients compared with controls, positive correlation with serum creatinine	2010/[58]
	CKD	N/A	N/A		
Beta(2)-microglobulin (mg/l)	Controls	7	0.38	Salivary beta(2)-microglobulin test is useful for CKD-related amyloidosis prediction	2007/[62]
	Diabetes mellitus	7	0.68		
	CKD	20	0.83		
	Hemodialysis	19	1.62		
Testosterone (nmol/l)	Controls eugonadic	112	0.413	Morning salivary testosterone as reliable marker of androgen deficiency in CKD patients	2011/[80]
	Controls hypogonadic	40	0.134		
	Terminal CKD with androgen deficiency	60	0.338		
Hepatocyte growth factor (ng/ml/protein)	Controls	20	0.68	Salivary HGF as index of periodontitis without CKD and in patients on peritoneal dialysis	2012/[81]
	Chronic hemodialysis	26	1.06		
	Continuous peritoneal dialysis	15	0.85		
	Predialysis CKD	28	0.83		
	Advanced periodontitis	26	1.87		
Epidermal growth factor (ng/mg/protein)	Controls	30	5	No significant difference in EGF concentration, however a salivary bioactivity of EGF significantly depressed in patients on hemodialysis	2001/[82]
	Chronic hemodialysis	47	4.2		
	Controls	EGF activity	1.55		
	Chronic hemodialysis	EGF activity	0.59		

Legend: CKD — chronic kidney disease, GFR — glomerular filtration rate, N/A — not available,  $r$  — correlation coefficient, EGF — epidermal growth factor.

# Çalışmamızda

- 35 tane evre 2-5 KBH hasta
- 7 (20%) hasta evre 2 KBH, 8 (22.8%) hasta evre 3 KBH, 10 (28.6%) hasta evre 4 KBH ve 10 (28.6%) hasta (7'si HD, 3'ü PD) evre 5 KBH.
- 28 tane sağlıklı kontrol grubu
- Sabah 9:00 ile 11:00 arasında aç olarak (dializ hastaları için dializ öncesi) plastik kaplara en az 3ml olacak şekilde (her 60 sn'de, spitting method).



## SALIVA SAMPLE INSTRUCTIONS PLEASE FOLLOW THESE INSTRUCTIONS CAREFULLY

### Contents of Saliva Collection Kit

One container kit has been included for each participant.

Each kit contains:

- One labeled collection cup
- One "STIM" saliva tray
- One large zip-locked storage envelope
- Consent form

**IMPORTANT:** Store your saliva collection cup and packaging to avoid damage.

### Instructions for Saliva Kit

• You **MUST** use some saliva at least 30 minutes prior to giving your saliva sample. This allows salivary glands to produce your saliva with water to get rid of any food particles. They use at least 1 minute before spitting your sample.

• Some people may find it hard to spit so much saliva. It is easier to spit more if you place your thumb on your tongue after making your mouth.

- 1** Put your thumb on the bottom of your tongue. This will help you spit more saliva.
- 2** Spit into the amount of saliva that is shown on the side of the cup.
- 3** Do NOT swallow your saliva. Spit it into the cup. Place the cup in the storage bag and seal it.
- 4** Do NOT use the cup for anything else. It is only for saliva.
- 5** Use gently for at least 30 minutes. This will allow the salivary glands to produce saliva.
- 6** Do NOT use the cup for anything else. It is only for saliva.
- 7** Do NOT use the cup for anything else. It is only for saliva.

**axial** Please use the axial saliva collection cup for the axial saliva collection. For more information, please contact us at 1-800-441-4444.

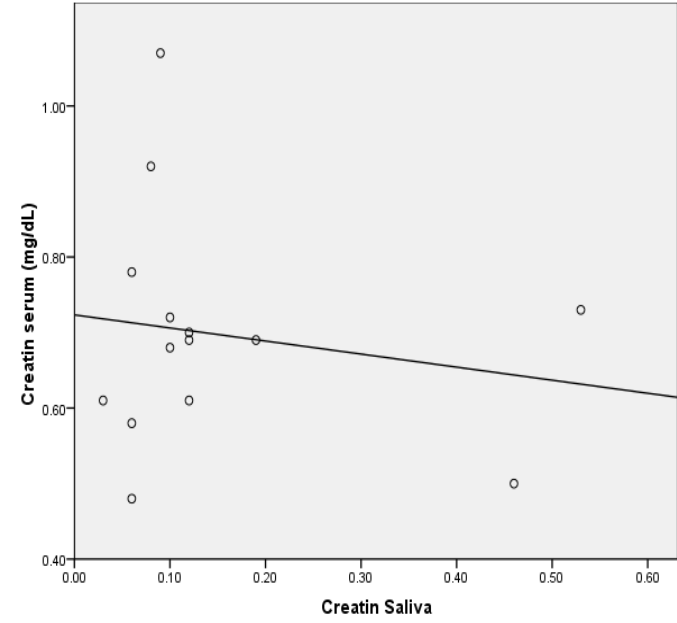
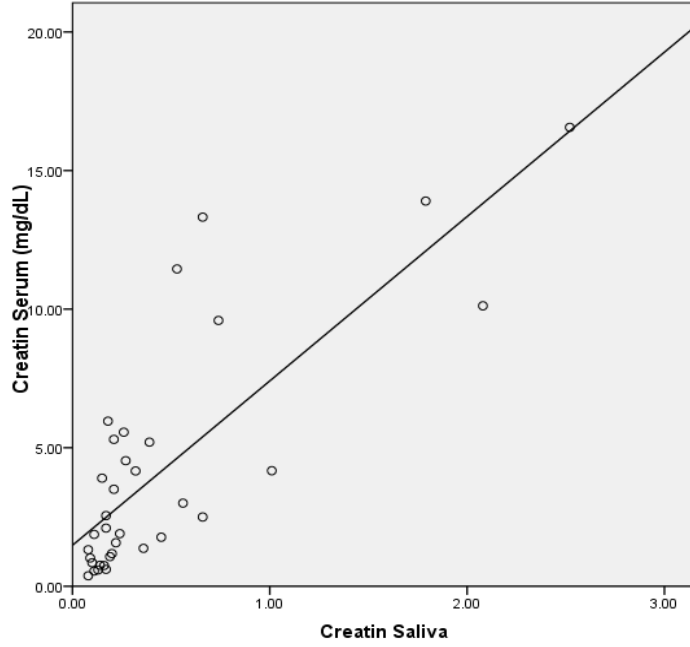


- Eş zamanlı 5 ml serum örneği
- Örnekler  $-20\text{ }^{\circ}\text{C}$ 'de saklandı
- İnceleme oncesi oda ısısında eritildi, 10 dk 3000rpm santrifüj
- Elde edilen serum ve tükürük örnekleri üre ve kreatinin değerleri karşılaştırıldı

	CKD group (n = 35)	Control group (n = 28)
Age (years)	14.49 ± 3.15 (range: 6-18)	14.86 ± 3.11 (range: 7-17)
Male (n)	18	16
Female (n)	17	12

	Group	n	Mean	SD	t	P
Serum urea (mg/ dL)	CKD	35	40.6286	25.01421	4.652	0.000*
	Control	28	9.2857	2.23361		
Serum creatinine (mg/ dL)	CKD	35	4.1409	4.28249	2.989	0.004*
	Control	28	0.6971	0.15504		
Salivary urea (mg/ dL)	CKD	35	28.8286	15.75452	1.516	<b>0.136</b>
	Control	28	21.7857	11.44336		
Salivary creatinine (mg/ dL)	CKD	35	0.4489	0.57186	2.208	<b>0.042*</b>
	Control	28	0.1114	0.13114		

Salivary urea (mg/ dL)	Stage 4-5 CKD	20	31.3500	16.29102	2.191	<b>0.024*</b>
	Control	16	17.7857	11.44336		



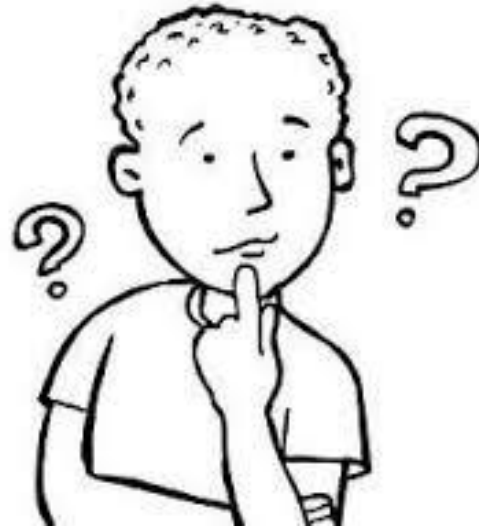
Figür 1. (a) Hasta grubunda tükürük ve serum kreatinin düzeyinde lineer korelasyon (b) Kontrol grubunda tükürük ve serum kreatinin düzeyinde lineer korelasyon

Salivary creatinine (mg/ dL)	Sensitivity (%)	Specificity (%)
0.045	100.0	7.10
0.105	88.6	57.1
<b>0.125</b>	<b>82.9</b>	<b>78.6</b>
0.205	54.3	85.7
0.295	37.1	85.7
0.495	25.7	92.9
0.545	22.9	100.0

# Sonuçlar

- Ortalama serum ve tükürük kreatinin düzeyleri KBH grubunda kontrol grubuna göre anlamlı derecede yüksek ( $P < 0.05$ )
- Ortalama serum üre düzeyi KBH grubunda anlamlı derecede yüksek ( $p < 0.05$ ); ortalama tükürük üre düzeyi anlamlı derecede yüksek saptanmadı
- İleri evre (4-5) KBH hastalarında ortalama tükürük üre ve kreatinin düzeyi anlamlı derecede yüksek
- Tükürük serum ve kreatinin düzeyleri arasında lineer ilişki
- Cut-off değer 0.125 mg/ dL; duyarlılık %82.9 ve özgüllük %78.6

Tükürük kreatinin değeri KBH tanısında  
yeni biomarker???



### **Oral health in children with chronic renal failure.**

[Pediatr Nephrol.](#) 2003 Jan;18(1):39-45.

*The mean salivary urea level* (mmol/l) *was significantly greater* in the CRF children, 11.6 (5.9) compared with 3.6 (1.4) for the controls.

### **The oral health status of children undergoing hemodialysis treatment**

[Turk J Pediatr.](#) 2003 Apr-Jun;45(2):108-13.

In conclusion, probably due to increased concentrations of antibacterial chemicals such as *urea in the saliva of children with ESRD* decreased levels of cariogenic microorganisms were detected.

### **The correlation between dental calculus and disturbed mineral metabolism in paediatric patients with chronic kidney disease.**

[Nephrol Dial Transplant.](#) 2009 Aug;24(8):2439-45

In all patient groups, *salivary U was higher than in the C group with a 2.5-fold increase in the D group.* Salivary Cr resembled the U salivary concentrations.

### **Role of saliva in the caries experience and calculus formation of young patients undergoing hemodialysis.**

[Clin Oral Investig.](#) 2015 Nov;19(8):1973-80

Salivary analysis, HD patients showed significantly higher values of pH, buffer capacity, *and salivary urea concentration* when compared to the controls (p = 0.001).