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Uremic xerosis among patients on maintenance hemodialysis: Prevalence and correlation with clinical and laboratory markers

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Abstract. *Xerosis, characterized by dry skin, is a frequent manifestation in patients undergoing maintenance hemodialysis. Understanding the prevalence of xerosis in this population and exploring its associations with various clinical and laboratory parameters is crucial for comprehensive patient care. The present study aimed to estimate the prevalence of xerosis in patients undergoing maintenance hemodialysis and to investigate the association between xerosis and various clinical and laboratory parameters, with a specific focus on serum copeptin as a surrogate for antidiuretic hormone.*

Methods. This cross-sectional observational study was conducted at the Hemodialysis Clinic of the Basrah Nephrology and Transplantation Center from March 1, 2022, to September 1, 2022. The prevalence of xerosis and its correlation with clinical characteristics and serum copeptin status were analyzed.

Results. The study findings indicate that among the 48 patients undergoing maintenance hemodialysis, with an average age of 59.8 ± 8.8 years, 60.4% presented with xerosis. Serum copeptin levels, measuring 3.8 ± 2 ng/mL, showed a significant association with diuretic usage and serum parathyroid hormone (PTH) ($p < 0.001$ and $p = 0.031$, respectively). Notably, no correlations were observed with other demographic or laboratory parameters, despite the tendency of serum copeptin levels to be higher in females and patients with low serum albumin and PTH concentrations.

Conclusions. In summary, xerosis was prevalent in 60.4% of patients undergoing maintenance hemodialysis and demonstrated a positive correlation with diuretic use and serum PTH levels.

Key words: *hemodialysis, xerosis, copeptin, prevalence.*

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Уремічний ксероз серед пацієнтів, які лікуються методом гемодіалізу: поширеність та асоціація з клінічними та лабораторними маркерами

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Резюме. *Ксероз, що характеризується сухістю шкіри, є частим проявом у пацієнтів, які лікуються методом гемодіалізу. Розуміння поширеності ксерозу в цій популяції хворих та вивчення його зв'язку з різними клінічними та лабораторними маркерами має вирішальне значення для комплексного лікування пацієнтів. Метою цього дослідження було оцінити поширеність ксерозу у пацієнтів, які лікуються гемодіалізом та дослідити зв'язок між ксерозом та різними клінічними та лабораторними параметрами, приділяючи увагу сироватковому копептину, як сурогату антидіуретичного гормону.*

Методи. Це одномоментне обсерваційне дослідження проведено в клініці гемодіалізу Центру нефрології та трансплантації Басри з 1 березня 2022 р. по 1 вересня 2022 р. Проаналізовано поширеність ксерозу та його асоціацію з клінічними характеристиками та статусом копептину в сироватці крові.

Результати. Результати дослідження продемонстрували, що серед 48 обстежених пацієнтів, із середнім віком 59,8 ± 8,8 років, у 60,4% діагностовано ксероз. Рівень копептину в сироватці крові, який становив 3,8 ± 2 нг/мл, продемонстрував значний зв'язок із застосуванням діуретиків та концентрацією паратиреоїдного гормону (ПТГ) сироватки ($p < 0,001$ і $p = 0,031$, відповідно). Інші долсджувані демографічні і лабораторні маркери не були асоційовані з ксерозом та копептином сироваки, хоча концентрація копептину мала схильність до підвищення у жінок та пацієнтів з низькими концентраціями сироваткового альбуміну та ПТГ.

Висновки. Таким чином, поширеність ксерозу у нашій когорті хворих, які лікувались методом гемодіалізу, склала у 60,4%. Ксероз мав позитивний кореляційний зв язок із застосуванням діуретиків та рівнем ПТГ сироватки крові.

Ключові слова: *гемодіаліз, ксероз, копептин, поширеність.*

Introduction. Xerosis is common in patients on maintenance hemodialysis (MHD) [1, 2]. The estimated prevalence of xerosis in this patient population is between 50% and 85% and 30-40% in dialysis-independent patients [3, 4]. It is characterized by widespread distribution with marked involvement of the legs, back, chest, and hands, which differs from the common cause of xerosis where the distribution is more on the extensor surfaces of lower limbs [5]. Uremic xerosis is caused by skin dehydration due to atrophy and decreased sweat and sebaceous glands [6–9]. Low stratum corneum hydration was evident experimentally in patients on maintenance hemodialysis [10]. Histological skin findings include mast cell infiltration, elastin fragmentation, hyperpigmentation, hyperkeratosis, and epidermal atrophy [11]. Skin dehydration due to fluid shift during hemodialysis sessions and impaired skin perfusion had been implicated as a cause of xerosis [12]. The altered metabolism of vitamin A may also be a contributing factor [13]. Disturbances in the pH of the stratum corneum have also been implicated as a cause of xerosis [14].

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Antidiuretic hormone (ADH) plays a crucial role in regulating body water content. The likely cause of uremic xerosis is skin dehydration, possibly linked to body water content and, consequently, ADH levels. Copeptin serves as a reliable surrogate for ADH measurement, offering advantages such as increased stability and ease of laboratory assessment compared to ADH.

This study aimed to determine the prevalence of xerosis in individuals undergoing maintenance hemodialysis. Additionally, the investigation focused on examining the association between serum ADH levels (measured through serum copeptin due to challenges in direct ADH measurement) and various laboratory parameters in relation to xerosis among these patients.

Patients and Methods. This was a cross-sectional observational study of 48 patients with end-stage kidney disease (ESKD) maintenance hemodialysis who were seen in the hemodialysis clinic at Basrah Nephrology and Transplantation Center from March 1, 2022, to September 1, 2022. The study was approved by the ethical committee of the University of Basrah and the Iraqi Ministry of Health, and the study was carried out following the Helsinki Declaration Principles.

Inclusion criteria were patients with end-stage kidney disease on maintenance hemodialysis whose ages were more than 18 years and were taken randomly (24 patients from the morning shift and 24 patients from the afternoon shift). The total number of patients at our center was 270 so we thought that 48 patients were

representative of them. The selection of the study patients was a random alternate selection between chair and chair and was similar to morning and night shifts.

Patients with dialysis-independent chronic kidney disease and patients on peritoneal dialysis were excluded from the study.

Patients' demographics including age, gender, body mass index (BMI) and comorbidities such as hypertension, diabetes, and viral hepatitis status were documented. A nephrological examination was performed, looking for the type of vascular access, whether central venous catheter or arteriovenous fistula.

An expert specialist dermatologist who has worked as a senior dermatologist at Al-Sader Teaching Hospital since 2009 performed a dermatological exam looking for the presence or absence of xerosis. The signs of xerosis including the presence of scales, erythema, roughness, and/or cracks were noted. As the study didn't test the grading or severity of xerosis and only assessed the presence or absence of xerosis, no scoring system for grading of xerosis was used.

Blood investigations included complete blood count, serum creatinine, serum uric acid, serum albumin, liver transaminases, serum alkaline phosphatase, serum parathyroid hormone, and serum copeptin which was documented. The measurement of copeptin is an effective surrogate for the measurement of ADH. The advantages of testing for copeptin over ADH are that it is more stable and easier to measure in the lab.

The assay procedure includes the preparation of all reagents, samples, and standards, then adding 100 µL (microliter) anti-copeptin to each, incubating for 1.5 hours at room temperature or overnight at 4 degrees Celsius. Adding 100 µL standard or sample to each well, incubating for 2.5 hours at room temperature or overnight at 4 degrees Celsius. Adding 100 µL prepared Streptavidin solution and incubating for 45 minutes at room temperature. Adding 100 µL TMP One-Step Substrate Reagent to each well, incubating for 30 minutes at room temperature. Finally, add 50 µL Stop Solution to each well and read at 450 nm immediately. The machine used for analysis and output of the results is the BioTek 800 TS Absorbance Reader, which is manufactured in the United States.

Statistical analyses were performed with SPSS version 29. Normally distributed continuous variables were expressed as means and standard deviations (M ± SD), whereas skewed continuous variables were represented by medians and interquartile ranges [Me (Q25-Q75)]. Noncontinuous variables were presented as numbers and percentages. The correlation of xerosis with clinical characteristics and serum copeptin status was analyzed using the Pearson chi-square test. A p-value of < 0.05 was considered statistically significant.

Results. The study comprised 48 patients undergoing maintenance hemodialysis, with an average age of 59.8 ± 8.8 years, and males constituting 58.3% of the participants. The mean BMI was 25.6 ± 5.4, and 68% had hypertension, while 32% had diabetes mellitus. Table 1 provides a summary of the baseline characteristics of the study cohort.

Table 1

Baseline clinical and laboratory characteristics of the study cohort

Characteristics	Overall cohort (n=48)
Age (years)	59.8 8.8
Male sex, n (%)	28 (58.3)
Body mass index (BMI), kg/m^2	25.6 5.4
Hypertension, n (%)	32 (66.7)
Diabetes mellitus, n (%)	16 (33.3)
Arteriovenous fistula (AVF), n (%)	45 (93.8)
Xerosis, n (%)	29 (60.4)
Serum copeptin, ng/mL	3.8 2.0
Hemoglobin, g/dL	10.7 1.7
WBC (White Blood Cell) count per mL3	6584 2381
Platelet count per µL	190.744 80.297
Serum albumin, g/dL	4 0.5
Serum creatinine mg/dL	9.4 (4.24, 16.4)
Serum uric acid, mg/dL	7 1.3
Serum alanine transferase (ALT), U/L	10.3 (1.67, 129.8)
Serum aspartate transferase (AST), U/L	12.8 (1.9, 130)
Serum alkaline phosphatase (ALP), U/L	123 (45.23, 235.5)
Serum parathyroid hormone (PTH), pg/mL	325 (73.4, 1263)
Viral hepatitis status (negative)	32 (66.7)

Values are expressed as mean SD, median (interquartile ranges), and n (%).

As presented in Table 1, 29 (60.4%) of examined patients were presented with xerosis. Table 2 outlines the association between xerosis status and various clinical and laboratory characteristics.

Table 2

Association of xerosis with clinical characteristics and serum copeptin status

Characteristics		Patients with xerosis (n=29)	Patients without xerosis (n=19)	p-value
Age (years)	Young (15-47 yrs)	0	3 (15.8)	0.065
	Middle age (48-63 yrs)	18 (62.1)	8 (42.1)	
	Elderly > 64 yrs	11 (37.9)	8 (42.1)	
Body Mass Index (BMI), n (%)	Normal	26 (89.7)	16 (84.2)	0.577
	Obese	3 (10.2)	3 (15.8)	
Sex, n (%)	Male	15 (51.7)	13 (68.4)	0.251
	Female	14 (48.3)	6 (31.6)	
Hypertension, n (%)		19 (65.5)	13 (68.4)	0.835
Diabetes mellitus, n (%)		10 (34.5)	6 (31.6)	0.835
Diuretics, n (%)	Use	25 (86.2)	3 (15.8)	<0.001
	No use	4 (13.8)	16 (84.2)	
Viral hepatitis status, n (%)	Negative	20 (74.1)	12 (70.6)	0.800
	Positive	7 (25.9)	5 (29.4)	
Hemoglobin status, n (%)	Anemia <11 g/dL	22 (75.9)	10 (52.6)	0.248
	Target 11-12 g/dL	3 (10.3)	4 (21.1)	
	High >12	4 (13.8)	5 (26.3)	
Creatinine status, n (%)	Below 10 g/dL	15 (51.7)	13 (68.4)	0.251
	Above 10 g/dL	14 (48.3)	6 (31.6)	
Albumin status, n (%)	Below <4 g/dL	14 (48.3)	10 (52.6)	0.786
	Above >4 g/dL	15 (51.7)	9 (47.4)	
Uric acid status, n (%)	Below 7 mg/dL	16 (55.2)	11 (57.9)	0.853
	Above 7 mg/dL	13 (44.8)	8 (42.1)	
Alanine transferase (ALT) status, n (%)	Below 40 U/L	28 (96.60	18 (94.7)	0.758
	Above 40 IU/L	1 (3.4)	1 (5.3)	
Alkaline phosphatase (ALP) status, n (%)	Below 150 U/L	18 (62.1)	10 (52.6)	0.517
	Above 150 U/L	11 (37.9)	9 (47.4)	
Parathyroid hormone (PTH) status, n (%)	Below 150 pg/mL	0 (0.00)	4 (21.1)	0.031
	Between 150-300 pg/mL	8 (27.6)	3 (15.8)	
	Above 300 pg/mL	21 (72.4)	12 (63.2)	
Copeptin status, n (%)	Low	0 (0.0)	1 (5.3)	0.433
	Normal	6 (20.7)	3 (15.8)	
	High	23 (79.3)	15 (78.9)	

No statistically significant correlations were observed between age, BMI, gender, viral hepatitis status, and all laboratory tests, including the primary focus of the study, serum copeptin, except for serum PTH and diuretic use.

Figure 1 illustrates that there were no positive correlations between serum copeptin and patients' ages, BMI, serum creatinine, and hemoglobin concentrations.

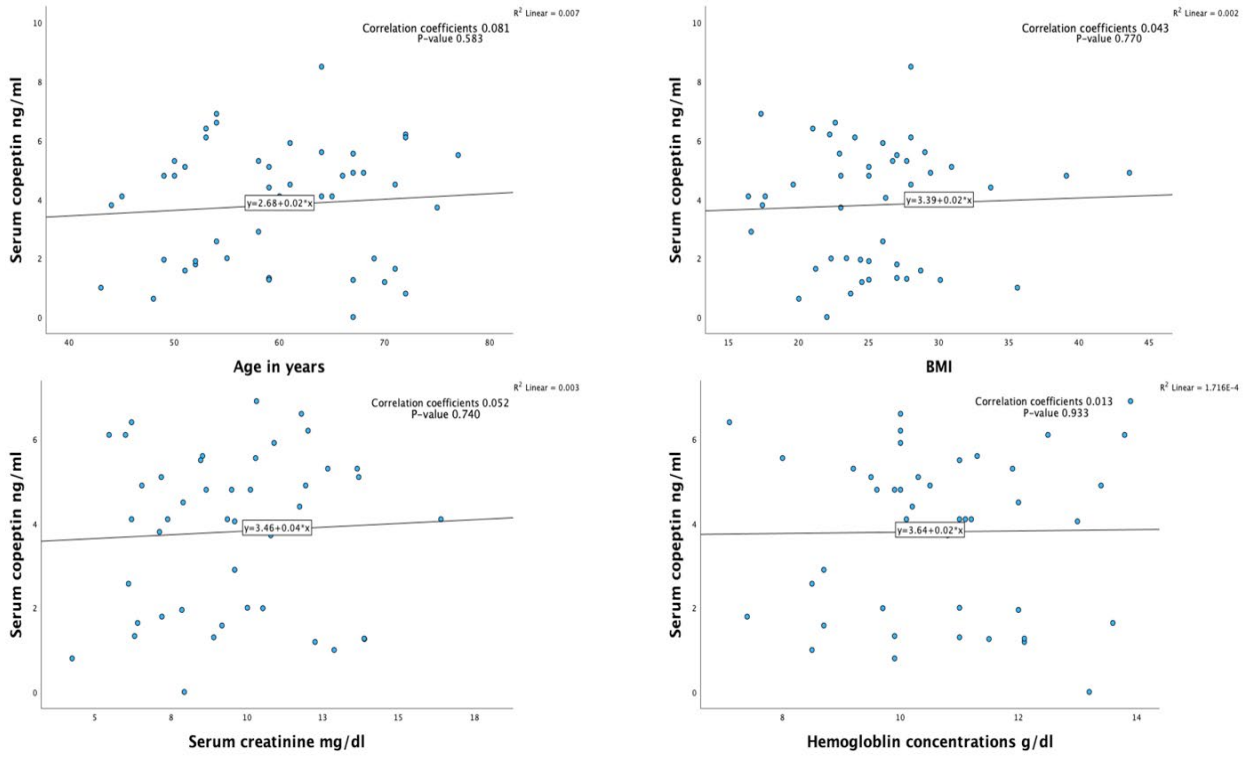

Fig. 1. Correlation between serum copeptin and age, BMI, hemoglobin, and serum creatinine concentrations.

While there was a tendency for serum copeptin concentrations to be elevated in females, as well as in patients with low serum albumin and PTH levels, and high uric acid levels, these differences did not reach statistical significance (Fig. 2).

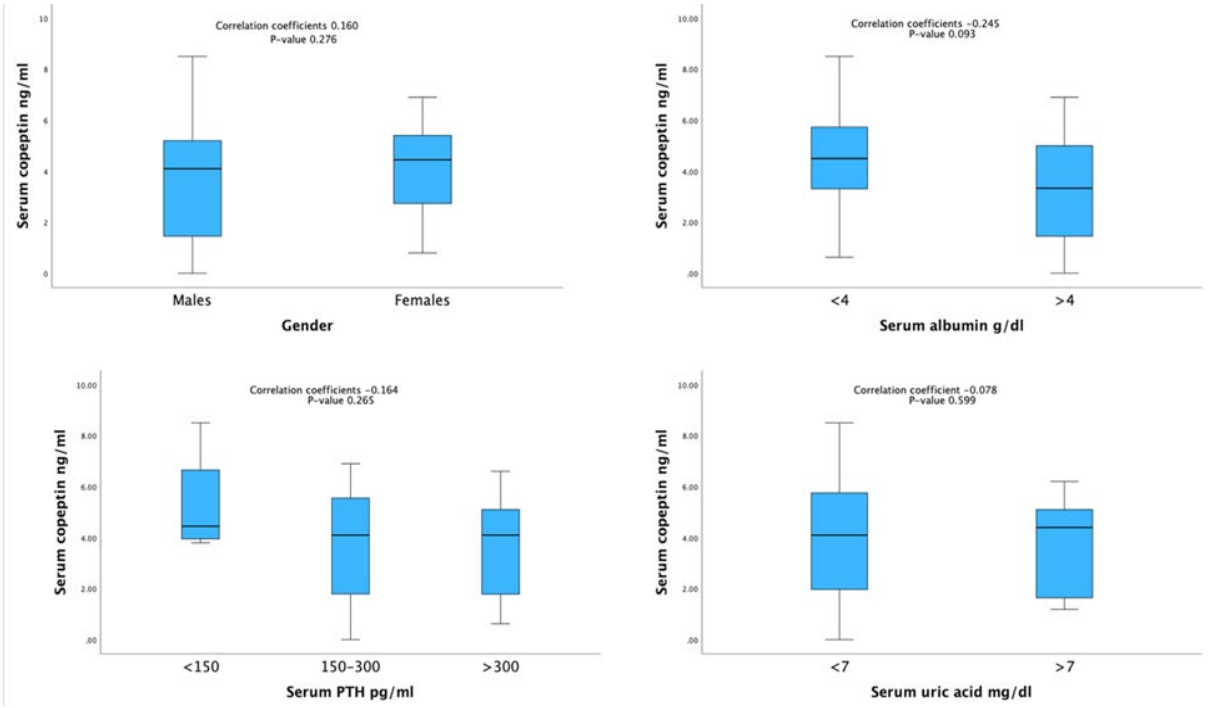

Fig. 2. Serum copeptin concentrations stratified by albumin, uric acid, and PTH levels.

Discussion. In the current study, the observed prevalence of xerosis at 60.4% is consistent with the findings of studies conducted by Szepietowski et al, Balaskas et al, and Young et al [15–18]. However, it is lower than the prevalence reported in other investigations [19–27] and higher than that reported in additional studies [28–35]. The lower prevalence of xerosis in our study, compared to many others, could be attributed to the reduced likelihood of xerosis during the summer, which corresponds to the period of our data

collection [36]. The statistically significant high prevalence of xerosis among high-dose diuretic users may be explained by causing skin dryness and decreased water content; this finding is consistent with studies by Tsukahara K et al [37]. Forty-three and a half of patients with xerosis have diabetes which is lower than a study by Morton et al. with 64.3% [36]. This may be attributed to the lower prevalence of diabetes mellitus in our study.

To our knowledge, there is no study on the correlation of xerosis with laboratory parameters such as hemoglobin, serum creatinine, serum albumin, serum uric acid, serum ALT, ALP, PTH, and serum copeptin. All of these parameters, except PTH, showed no correlation with xerosis. High serum copeptin has the highest percentage among patients with and without xerosis. This finding agrees with a study by Jae Seok et al. which showed that serum copeptin is higher before hemodialysis and has a positive correlation with pre-dialysis body fluid volume and decreases during hemodialysis in relation to plasma volume and osmolality changes [38]. Also, high serum copeptin in patients on maintenance hemodialysis may be attributed to a high prevalence of LV dysfunction in those populations [38]. In our study, no correlation between serum copeptin and age, gender, BMI, and laboratory parameters such as serum creatinine, serum uric acid, serum albumin, hemoglobin, and serum PTH was found. This is in contrast to a study by Tenderenda-Banasiuk et al., which showed a positive correlation between serum copeptin and these parameters [39]. Inconsistencies between this study's results and findings from previous research, particularly regarding correlations with serum copeptin, highlight the need for further investigation and potential factors contributing to these discrepancies.

Our study is subject to several limitations that warrant acknowledgment. Firstly, it adopted a cross-sectional observational design conducted at a single center, featuring a relatively small sample size. The inherent nature of cross-sectional studies restricts the establishment of causal relationships, despite the identification of associations between xerosis and certain factors. Generalizing our findings to a broader population necessitates careful consideration of potential center-specific influences on xerosis prevalence and its correlations. Furthermore, the study primarily focused on common laboratory parameters, omitting exploration of additional factors that might impact xerosis, including specific skincare practices, environmental exposures, or socioeconomic factors. Notably, confounding factors influencing serum copeptin levels, such as left ventricular function status, volume, and osmolality statuses, were not systematically assessed. The omission of measurements related to plasma volume, even through surrogate parameters like plasma renin and aldosterone, as well as osmolality status, represents another limitation. Future studies addressing these aspects can contribute to a more comprehensive understanding of xerosis in patients undergoing maintenance hemodialysis, thereby enhancing the robustness and applicability of research findings.

Conclusions. Xerosis is a common manifestation among patients on maintenance hemodialysis. There were no correlations of xerosis with serum copeptin as a surrogate marker of water status. Nevertheless, a positive correlation was identified with the use of diuretics and serum PTH, underscoring the necessity for additional exploration and management of these associated factors.

Conflict of interest. The authors declare no conflict of interest.

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Data availability. The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Authors' contribution. Both authors contributed equally to the research and preparation of this manuscript.

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