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The Impact of End-Stage Renal Disease Duration on Xerosis and Pruritus in Patients Undergoing Hemodialysis

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ABSTRACT

Background: Uremic pruritus and xerosis, also called chronic kidney disease (CKD)- associated pruritus and xerosis, are common and debilitating symptoms experienced by patients with end-stage renal disease (ESRD) and cause significant discomfort.
Objectives: Our research aimed to determine the influence of disease duration on the dermatologic status of these patients.
Methods: The Bioethics Commission of Tbilisi State Medical University approved the study protocols and data collection procedures. Written informed consent was obtained from all participants. Based on the presence of uremic pruritus and/or xerosis, study 82 selected subjects divided by two groups: group 1 – the duration of ESRD <5 years (n=42, mean duration 2.1±1.1); and group 2 – the duration of ESRD ≥5 years (n=40, mean duration 12.5±6.3).
Results: Uremic xerosis was observed in 76.2% of cases in group 1 and in 85.0% in group 2. The difference between groups was not significant (Chi2-test=1.00, p=0.317). However, the distribution of patients by degree of xerosis differed. The percentage of patients with mild xerosis in group 1 was significantly higher compared to group 2 (54.8% vs. 32.5%, respectively; Chi2-test=4.07, p=0.044); whereas the patients with a severe degree of xerosis prevailed in group 2 (2.4% vs. 22.5%, respectively; Chi2-test=7.65, p=0.006). Uremic pruritus was observed in 28 cases (66.7%) in group 1 and in 26 cases (65.0%) in group 2. The difference between groups was not significant (p>0.05). The distribution of patients by degree of pruritus was not statistically different either.
Conclusions: Based on the results of the present study, the duration of ESRD and hemodialysis treatment significantly impacts patients' dermatologic status and health-related quality of life. The severity of xerosis and pruritus increased with the increase in years with hemodialysis.
Keywords: Chronic kidney disease; dialysis; end-stage renal disease; pruritus; xerosis.

BACKGROUND

Uremic pruritus and xerosis, also called chronic kidney disease (CKD)–associated pruritus and xerosis, are common and debilitating symptoms experienced by patients with end-stage renal disease (ESRD), causing significant discomfort to patients. The condition is characterized by ESRD-related itching. More than 40% of hemodialysis patients suffer from chronic pruritus, with half experiencing generalized pruritus.[1] The prevalence of uremic xerosis exceeds 50%.[1] The underlying pathogenic mechanisms of uremic pruritus and xerosis remain obscure. Histamine, parathyroid hormone (PTH), magnesium, and calcium have been associated with its pathogenesis. Many studies are evaluating opioid receptor abnormalities and microinflammation as potential causes of uremic pruritus, although more data are required.[2] Pruritus can be extremely difficult to manage due to limited treatment options. Stepwise management is recommended, starting with topical emollients, gabapentin, and phototherapy. More novel options, such as μ-opioid receptor antagonists or κ-opioid receptor agonists, may be chosen in refractory cases. In advanced cases, patients may undergo transplantation, as a successful renal transplant can relieve patients of uremic pruritus and xerosis.[3,4]

The etiopathogenesis of uremic pruritus and xerosis is poorly understood.[5] In the pathogenesis of itching, compounds such as histamine, prostaglandins, cytokines, neuropeptides, and proteases activate neurons that send itch signals to the central nervous system via secondary neurons in the dorsal horn of the spinal cord. Proposed pruritogenic toxins in CKD include aluminum, calcium, phosphate, and parathyroid hormone. However, the Dialysis Outcomes and Practice Patterns Study (DOPPS; 2012–2015) did not show any association between pruritus and serum calcium or phosphorus levels.[6]

Other contributory factors include increased blood urea, β_2-microglobulin, magnesium, and vitamin A.[7,8] Some studies have found that lower serum albumin levels and higher white blood cell counts are significantly associated with moderate-to-extreme pruritus.[8,9] In addition, anemia, low erythropoietin levels, elevated ferritin, and low transferrin have also been explored as potential risk factors for CKD-associated pruritus.[10] Current proposed pathophysiological mechanisms for uremic pruritus include skin alterations, inflammation, nociceptive receptor dysfunction, and opioid receptor dysfunction. Although many patients with CKD experience dry skin (xerosis), not all individuals with severely dry skin experience itching.[11] Skin microinflammation is also proposed to contribute to uremic pruritus, as elevated C-reactive protein levels have been observed in ESRD patients on hemodialysis with this condition. In addition, the opioid pathway is increasingly linked

to the sensation of itch.[12] A prevailing theory postulates that an imbalance between μ-opioid and κ-opioid receptors - specifically μ-overstimulation and κ-antagonism - may cause itching.[8] Moreover, other potential triggering factors include uremic toxins, cutaneous xerosis, systemic inflammation, and common comorbid conditions, including diabetes mellitus, viral hepatitis, and endocrinopathies.[13,14]

There is little data on the impact of ESRD duration on the development of skin disorders, including uremic pruritus and xerosis, in patients undergoing hemodialysis[9,10]. Therefore, our research aimed to establish the influence of disease duration on the dermatologic status of these patients.

METHODS

The Bioethics Commission of Tbilisi State Medical University approved the study protocols and data collection procedures. Written informed consent was obtained from all participants.

82 patients were enrolled in the study to assess their dermatologic condition and quality of life. The enrolment period ranged from September 2023 to November 2024, during which these patients were undergoing hemodialysis in the dialysis center of Tbilisi State Medical University Hospital. These patients were selected for the study according to specific inclusion and exclusion criteria.

Adult patients (age: 63.3±12.5 years) of both sexes (males/females: 36/46) undergoing hemodialysis (n=82) for ESRD were studied. Patients with skin complications (prurigo, superinfection, contact dermatitis) were excluded from the study.

Patients were examined by a dermatologist to assess disease severity using the El-Gammal severity score[15] at various body sites. The El Gammal index includes five items: 0=smooth skin; 1=patches of fine, powdery scales; 2=diffuse ashy appearance with many fine scales; 3=moderate; and 4=intense scaling, moderate cracks. To minimize inter-assessor variability, a photo-grader illustrating each grade was provided. A total score was calculated for each patient by summing the scores across sites.

The researchers assessed the global intensity of uremic pruritus using a 4-point analogue scale (0=no pruritus, 1=mild pruritus, 2=moderate pruritus, 3=severe pruritus).

QoL was evaluated by patients using the Dermatology Life Quality Index (DLQI). DLQI is a specific scale assessing the impact of dermatological diseases on patients' quality of life.[16] It is self-explanatory and easily handled by the patients. It comprises six concepts and 10 items: symptoms and feelings (2 items), daily activities (2 items), leisure (2 items), work and school (1 item), personal relationships (2 items), and treatment (1 item). It is calculated by summing the scores for each item (graded 0-3), yielding a minimum of 0 and a maximum of 30. The higher the score, the greater the QoL compromise. It is the most commonly used instrument for QoL evaluation in dermatology, but it may not detect minor impairments.[17] For each individual, DLQI questionnaires were given as separate sheets in an envelope that was sealed after being completed. All the questionnaires were provided in Georgian language (validated language version).

Based on the presence of uremic pruritus and/or xerosis, study subjects were divided into two groups: group 1 – the duration of ESRD <5 years (n=42, mean duration 2.1±1.1); and group 2 – the duration of ESRD ≥5 years (n=40, mean duration 12.5±6.3).

Mean values ± SD were calculated for all scores. The impact of several variables on DLQI was studied, including categorical variables such as gender, underlying ESRD disease, and the presence or absence of xerosis and pruritus. Continuous variables were the patient's age, the duration of MRD, the duration of xerosis and pruritus, and the clinical intensity of uremic xerosis and uremic pruritus. Statistical comparisons of the DLQI results between stratified subgroups defined by categorical variables were performed using an independent Student's t-test. Chi2-test compared categorical variables. Correlation analysis between variables and QoL scores was performed using Pearson's correlation test. A p-value less than 0.05 is considered statistically significant.

RESULTS

Baseline characteristics of the study participants are presented in Table 1.

TABLE 1. Characteristics of the study participants

Characteristic	Measures
Age, years, mean±SD	63.3±12.1
<50, n (%)	12 (14.6%)
50-59, n (%)	19 (23.2%)
60-69, n (%)	24 (29.3%)
70+, n (%)	27 (32.9%)
Gender	
Male, n (%)	36 (43.9%)
Female, n (%)	46 (56.1%)
Duration of ESRD in years, mean±SD	7.2±6.9
<5, n (%)	42 (51.2%)
5+, n (%)	40 (48.8%)
Patients with diabetes mellitus (DM), n (%)	25 (30.5%)
Uremic xerosis, n (%)	28 (34.116%)
Uremic pruritus, n (%)	16 (19.5%)
Uremic xerosis + pruritus, n (%)	38 (46.3%)

Abbreviations: ESRD, end-stage renal disease; n, number; SD, standard deviation.

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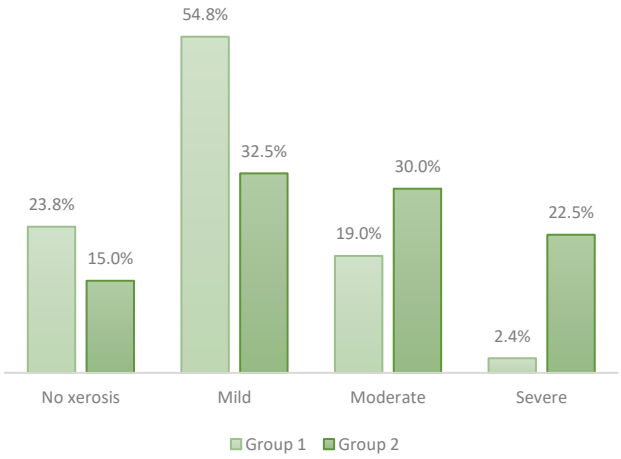
The distribution of patients by gender showed that the male/female proportion in group 1 was 42.9%/57.1%, whereas in the non-diabetic group it was 45.0%/55.0%. The difference between groups was not significant (chi2-test=0.038, p=0.846). The mean age in group 1 (64.9±13.2 years) was almost the same as in group 2 (61.4±12.2 years, t-test=1.25, p=0.217). The distribution of patients by age groups across the study groups showed no difference between groups (Chi2-test=1.26, p=0.739). Therefore, the groups may be considered homogeneous with respect to gender and age distribution.

Uremic xerosis was observed in 32 cases (76.2%) in group 1, and in 34 cases (85.0%) in group 2. The difference between groups was not significant (Chi2-test=1.00, p=0.317). However, the distribution of patients by degree of xerosis differed (Fig.1). The percentage of patients with mild xerosis in group 1 was significantly higher than in group 2 (Chi2-test=4.07, p=0.044). In contrast, patients with severe xerosis were more prevalent in group 2 (Chi2-test=7.65, p=0.006).

FIGURE 1. Distribution of patients by degree of xerosis within the study groups



Uremic pruritus was observed in 28 cases (66.7%) in group 1 and in 26 cases (65.0%) in group 2. The difference between groups was not significant (p>0.05). The distribution of patients by degree of pruritus was not statistically different either (Fig.2).

The mean DLQI scores in the study groups are presented in Figure 3. This chart shows that the DLQI scores between groups did not differ significantly (t-test = 0.82, p = 0.416).

The results of the within-group correlation analysis are presented in Table 2. The DLQI score was significantly negatively correlated with ESRD duration and positively correlated with the degree of pruritus in group 1. The same pattern of association was observed in group 2. The DLQI score was significantly negatively correlated with ESRD duration and positively correlated with the degree of pruritus. Additionally, a positive association was observed between DLQI score and the degree of xerosis in this group.

FIGURE 2. Distribution of patients by pruritus severity in the study groups

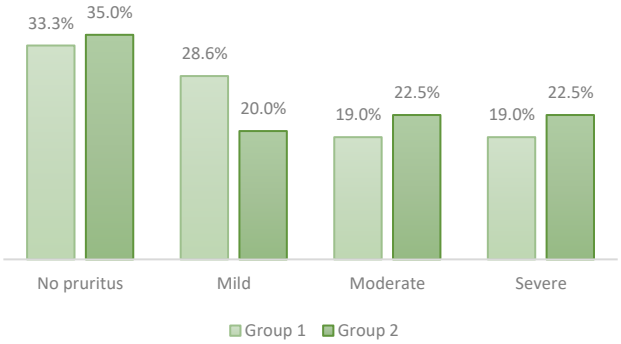


FIGURE 3. The mean values of DLQI scores in the study groups

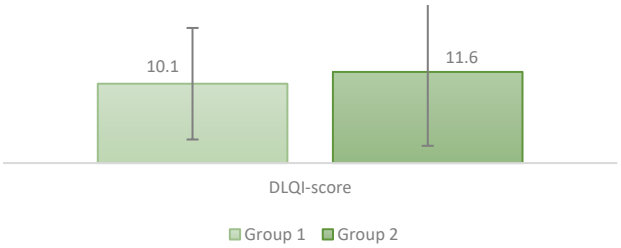


TABLE 2. The results of the correlation analysis in the study groups

	Group 1		Group 2	
	R	P-value	R	P-value
Age, years	-0.228	0.147	-0.009	0.956
ESRD duration, years	-0.349	0.024	-0.335	0.030
Degree of xerosis	0.099	0.531	0.606	<0.001
Degree of pruritus	0.982	<0.001	0.900	<0.001

DISCUSSION

Our study revealed a prevalence of 65.8% for CKD-associated pruritus. In patients with CKD, its occurrence alongside two or more additional symptoms is common. Its prevalence ranges from 20% to 85% across various studies.[18] The results of another study indicated that pruritus was found in 85% of a small group of patients undergoing maintenance hemodialysis.[19] A recent prospective observational study reported that pruritus was reported by 42% of 3685 participants in the Chronic Kidney Disease Cohort (CRIC) study, which included CKD patients not on hemodialysis. The severity of pruritus intensified with the progression of renal failure.[20] A decrease in estimated glomerular filtration rate (eGFR) of 5 mL/min per 1.73 m² correlated with a decline in symptom severity score by two points or fewer.

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RENINE/PROMs registry data showed that half of dialysis patients experienced itching, and in two-thirds of them, the itching was persistent.[21] The authors concluded that the persistence of itching, its impact on health-related quality of life over time, and the additional effects of behavioral and psychological symptoms emphasize the need for recognition and effective treatment of itching to reduce symptom burden and improve quality of life.[21]

We also found that the prevalence of CKD-associated xerosis was 80.5%. Xerosis is observed in approximately 85% of patients with CKD-associated pruritus and is believed to contribute to the intensity of itch.[22] Characterized by rough and scaly skin, xerosis is a common complication in patients with ESRD, with a prevalence of 50%–85%, occurring more frequently in patients undergoing peritoneal dialysis than in patients on hemodialysis.[23]

The development of xerosis is attributed to three primary mechanisms: cutaneous dehydration, altered barrier function, and heightened irritability to external agents.[23] In CKD, dysfunctional sebaceous and apocrine sweat glands lead to reduced skin lipid levels,[11] thereby compromising skin hydration. Additionally, skin barrier dysfunction impairs water content in the stratum corneum.[23] These dermal changes are closely tied to uremia,[24] possibly explaining the higher frequency of xerosis in patients undergoing hemodialysis for <18 months; those with longer hemodialysis durations may have better hemodialysis adequacy, as suggested by Rezaiee et al.[25] Other results of this study showed a significant direct relationship between duration of hemodialysis (months) and hemodialysis adequacy. Patients who had longer hemodialysis sessions had more satisfactory hemodialysis adequacy. However, another study did not find a significant relationship and showed that, over time, hemodialysis quality is reduced.[26]

The results of these studies were inconsistent with those of the present study. In the present study, the duration of treatment ranged from 3 months to 14 years, whereas in the abovementioned study, this range was more limited, which could explain this discrepancy. A longer hemodialysis treatment duration leads to better patient adaptation to the hemodialysis process and higher hemodialysis adequacy.

The presence of pruritus and xerosis significantly impacts quality of life. Our study showed that inadequate hemodialysis worsens patients' dermatologic status and, consequently, their health-related quality of life. The DLQI score in patients with insufficient hemodialysis was significantly higher compared with patients with adequate hemodialysis (p=0.029). This result is in accordance with the findings of Lengton and colleagues.[27] They observed that each one-unit increase in total weekly Kt/V at 12 months was associated with a decrease in pruritus burden score in hemodialysis patients. Over 10 years of follow-up, this relationship persisted.

CONCLUSIONS

Based on the results of the present study, the duration of ESRD and hemodialysis treatment significantly impacts patients' dermatologic status and health-related quality of life. The severity of xerosis and pruritus increased with the increase in years with hemodialysis.

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