RESEARCH ARTICLE

The relationship between dermatological findings and serum interleukin 31 and serum uridine diphosphate glucose ceramide glucosyltransferase levels among patients with chronic kidney disease

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Abstract

Background: Cutaneous diseases are observed with increasing duration and severity of renal disease in patients with chronic kidney disease (CKD). This study aimed to elucidate dermatological manifestations at different stages of CKD and determine their relationship with interleukin 31 (IL-31), a T-cell cytokine that induces severe pruritus, and uridine diphosphate (UDP)-glucose ceramide glucosyltransferase (UGCG), an enzyme that metabolizes ceramide, which plays an important role in moisturizing epidermis.

Methods: In this retrospective cohort study 145 patients with a mean age of 46 ± 17 years were categorized into hemodialysis (group 1), peritoneal dialysis (group 2), kidney transplant (group 3), CKD (group 4), and healthy control (group 5) groups. Serum IL-31 and UGCG levels were measured using enzyme-linked immunosorbent assay, and clinical dermatologists evaluated dermatological manifestations.

Results: In the overall cohort, pruritus was significantly and inversely correlated with glomerular filtration rate and serum hemoglobin and albumin levels ($p < 0.005$). Additionally, pruritus was significantly more frequent in group 2 than in group 5; and significantly less frequent in group 3 than in groups 1, 2, and 4 ($p = 0.01$). In group 4, the patients with longitudinal nail ridges had significantly higher serum IL-31 levels than those without longitudinal nail ridges in their nails ($p = 0.02$). Furthermore, in group 2, the patients with pruritus had significantly lower UGCG levels than those without pruritus ($p = 0.045$).

Conclusion: IL-31 might play a role in the development of longitudinal nail ridges, whereas UGCG might provide protection from pruritus and xerosis in patients with CKD. HIPPOKRATIA 2019, 23(2): 75-80.

Keywords: Chronic kidney disease, interleukin 31, nail and skin disorders, pruritus, uridine diphosphate glucose ceramide glucosyltransferase

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Introduction

Chronic kidney disease (CKD), which is defined as the presence of structural and functional kidney damage or decreased kidney function based on an estimated glomerular filtration rate (eGFR) of <60 mL/min/1.73m^2 for three or more months, is a progressive systemic disorder that also affects other organs including skin[1,2]. Cutaneous involvement increases with the severity and duration of CKD, with a prevalence of 50-100 %. The most common dermatological manifestations of CKD are pruritus, xerosis, and pigmentation[3].

Some studies have shown that interleukin 31 (IL-31), a T-cell cytokine predominantly produced by T helper 2 cells, is associated with and a key factor in pruritus[4,5]. Dorsal root ganglia neurons, the primary afferent neurons in skin, express IL-31 receptor α, which is involved in the neuro-immune cross-talk during acute and chronic pruritus[6]. For example, IL-31 was reported to inhibit keratinocyte differentiation and compromise the integrity of the skin barrier, particularly in patients with atopic dermatitis[7]. In addition, peripheral blood eosinophils from patients with bullous pemphigoid were shown to release higher levels of IL-31 than healthy controls[8]. Conversely, ceramides are vital components of the water barrier that arrange lipids in the stratum corneum of the mammalian skin[9]. The skin barrier function is primarily assigned to the outer epidermal layer, stratum corneum, which is composed of corneocytes and lipid-enriched extracellular matrix. Epidermal ceramides are synthesized from glucosylated intermediates, namely glucosylceramides,

by uridine diphosphate (UDP) glucose ceramide glucosyltransferase (UGCG); these ceramides constitute the essential barrier lipids, comprising ultra-long-chain fatty acids[9,10]. UGCG is a metabolizing enzyme in the ceramide pathway. UGCG and IL-31 might be involved in the dermatological manifestations of patients with CKD through different mechanisms.

No study to date has reported the correlation between IL-31 or UGCG and skin and nail disorders in patients with CKD. Therefore the present study aimed to determine changes in UGCG and IL-31 levels and determine their relationship with skin and nail disorders in patients with CKD.

Materials and methods

Study design and patient characteristics

This retrospective cohort study included 145 patients (mean age: 46 ± 17 years) who were treated between 2014-2015 in Karadeniz Technical University, Farabi Hospital. The study subjects were categorized into the following groups based on their diagnoses: hemodialysis group (group 1) comprising 30 patients on chronic hemodialysis for 49 ± 44 months (mean age: 58 ± 16 years, mean Kt/V: 1.43 ± 0.24); peritoneal dialysis (PD) group (group 2) comprising 26 patients on chronic PD for 43 ± 37 months (mean age: 37 ± 14 years, mean Kt/V: 2.40 ± 0.78); kidney transplant group (group 3) comprising 30 patients with functioning kidney allografts (mean age: 40 ± 11 years, mean serum creatinine level: 1.48 ± 0.99 mg/dL, average allograft lifespan: 34 ± 50 months); CKD group (group 4) comprising 29 patients with stage 1-5 CKD (mean age: 57 ± 15 years, mean creatinine level: 4.56 ± 2.56 mg/dL); and control group (group 5) comprising 30 healthy individuals (mean age: 34 ± 12 years, mean serum creatinine level: 0.67 ± 0.25 mg/dL). The exclusion criteria were as follows: active infection, psychosis, primary skin disorders, cholestasis, active malignancy, age <18 years, and no consent. There was no patient fulfilling these criteria in our unit. The study groups were not homogenous with respect to age, sex, and duration of CKD due to the relatively low number of patients followed in the study clinic. Clinical dermatologists evaluated the dermatological manifestations of patients, including pruritus, xerosis, alopecia, excoriations, hyperpigmentation, and skin and nail lesions.

Measurements

Blood samples collected to determine IL-31 and UCGC levels were centrifuged at 3,000 x g for 15 min, and serum samples were stored at -80 °C until analyses. IL-31 and UGCG levels were measured using commercial sandwich enzyme-linked immunosorbent assay (IL-31: lot number: 108993010, catalog number: BMS2041, eBioscience Technology Laboratory, Vienna, Austria; UCGC: lot number: 20150618, catalog number: E0738Hu, Bioassay Technology Laboratory, Korain Biotech Co. Ltd., Shanghai, China). The absorbance of the samples was measured at 450 nm using a VERSAmax (Molecular Devices CA, USA) adjustable microplate reader. Common biochemical parameters, including blood urea nitrogen (BUN), creatinine, and albumin, were measured in all patients and controls according to standard laboratory methods in the clinical laboratory. The study included previous single-pool Kt/V estimates for the hemodialysis group; these values were calculated using the pre- and post-dialysis BUN levels and the pre- and post-dialysis body weight measurements according to the two-BUN method by Daugirdas[11]. Previous records of dialysis adequacy of PD patients were assessed via calculations of urea clearance Kt/V from 24-h urine and dialysate[12]. The creatinine and urea clearance rates of the predialysis and kidney transplant patients were included in the study. In the predialysis and transplant groups, eGFR was estimated by the Modification of Diet in Renal Disease equation (MDRD) and by determining the averages of creatinine and urea clearance rates[13,14].

All patients provided written informed consent after reading the study protocol. The study protocol was approved by the Ethics Committee of the School of Medicine at Karadeniz Technical University (decision No: 2013/144, date: 05/05/2014).

Statistical analysis

SPSS 13.0 (SPSS, Chicago, IL, USA) was used for statistical comparisons. Data are presented as numbers and percentages for categorical variables and as mean ± standard deviation or median (minimum-maximum) for continuous variables. The normality of the data distribution was analyzed with the one-sample Kolmogorov-Smirnov test. Normally and nonnormally distributed data between two independent groups were compared using Student's t-test and the Mann-Whitney U test, respectively. Whereas normally and nonnormally distributed data among three or more independent groups were compared using one-way analysis of variance and the Kruskal-Wallis test, respectively. *Post hoc* comparisons were performed using Bonferroni's test. Correlations were performed using Spearman's test and chi-square test. Results with a p-value of <0.05 were considered to indicate statistical significance.

Results

There were 145 patients, including 76 males, and 69 females, with a mean age of 46 ± 17 years, in the present study. The etiologies of kidney diseases, according to the study groups, are summarized in Table 1. The most common causes of kidney disease were hypertension in groups 1 and 3, glomerulonephritis in group 2, and diabetic kidney disease in group 4. The most common underlying cause of CKD in the entire study cohort was hypertension (31.95 %). The demographic characteristics of the study groups are presented in Table 2. The groups were not homogenous with respect to age, sex, eGFR, and duration of CKD ($p<0.001$). Additionally, there were differences in the frequencies of pruritus, xerosis, hyperpigmentation, and alopecia among the study groups (Ta-

Table 1: Etiologies of kidney disease of the 145 patients included in the retrospective cohort study.

Etiology of kidney disease	Group 1	Group 2	Group 3	Group 4
Diabetes mellitus	4 (13.8)	2 (10)	0 (0)	8 (36.4)
Hypertension	12 (41.4)	5 (25)	11 (42.3)	3 (13.6)
Chronic glomerulonephritis	2 (6.9)	9 (45)	4 (15.4)	4 (18.2)
Urologic diseases	2 (6.9)	4 (20)	4 (15.4)	0 (0)
Amyloidosis	1 (3.4)	0 (0)	1 (3.8)	1 (4.5)
Polycystic kidney disease	4 (13.8)	0 (0)	3 (11.5)	0 (0)
Solitary kidney	4 (13.8)	0 (0)	2 (7.7)	5 (22.7)
Analgesic nephropathy	0 (0)	0 (0)	1 (3.8)	1 (4.5)
Total	29 (100)	20 (100)	26 (100)	22 (100)

Values are presented as the number of patients and percentage in brackets. Group 1: hemodialysis, group 2: peritoneal dialysis, group 3: kidney transplant, group 4: chronic kidney disease.

Table 2: Demographic characteristics of the 145 patients included in the retrospective cohort study.

Variable	Group 1	Group 2	Group 3	Group 4	Group 5	pvalue
Age (years)	58 ± 16*	37 ± 14	40 ± 11	57 ± 15**	34 ± 12	**0.0001**
Duration of CKD (months)	113 ± 92	89 ± 52	132 ± 98	39 ± 45¶	-	**0.001**
Duration of RRT (months)	49 ± 44	43 ± 37	34 ± 50			
Kt/V	1.43 ± 0.2	2.4 ± 0.78				
GFR (mL/min/1.73m^2)			58 ± 22[a]	24 ± 29[b]	117 ± 22	**0.0001**
M/F (numbers)	20/10	16/10	15/15	20/9	5/25	**0.0001**

Values are presented as mean ± standard deviation. Group 1: hemodialysis, group 2: peritoneal dialysis, group 3: kidney transplant, group 4: chronic kidney disease, group 5: healthy control. CKD: chronic kidney disease, F: female, GFR: glomerular filtration rate, M: male, RRT: renal replacement therapy, *: group 1 versus groups 2,3, and 5, **: group 4 versus groups 2,3, and 5, [a]: group 3 versus groups 4, and 5, [b]: group 4 versus group 5; ¶: group 4 versus groups 1, and 3.

ble 3). Specifically, the frequency of pruritus was significantly higher in group 2 than in group 5 and significantly lower in group 3 than in groups 1, 2, and 4 (p =0.01) (Table 3). Conversely, there were no differences in the frequencies of prurigo nodularis (one patient in group 2), keratotic papules, bullous lesions (two patients in group 3), herpes labialis (one patient each in groups 3 and 4) and folliculitis among the five study groups. Lichen simplex chronicus and nephrogenic systemic fibrosis were not observed in any of the patients included.

The correlation analysis of the entire cohort revealed that pruritus was significantly and inversely correlated with eGFR, serum hemoglobin, and serum albumin levels (p =0.024, p =0.002, and p =0.001, respectively; Table 4). Additionally, the patients with xerosis had significantly higher serum ferritin, BUN, creatinine, potassium, and phosphorus levels than those without xerosis (Table 5). The laboratory results of all the study groups are presented in Table 6. There were no significant differences in serum IL-31 and UGCG levels among the study groups (Table 6).

Subungual hyperkeratosis was the most common nail pathology in group 4 (66.1 %), followed by longitudinal ridges (41.7 %). The nail changes were more frequent in patients with lower eGFR than in those with normal eGFR (p =0.043 and p =0.039, respectively). The fre-

Table 3: Dermatological findings in the study (hemodialysis, peritoneal dialysis, kidney transplant, chronic kidney disease, and healthy control) groups.

Dermatological findings	Group 1	Group 2	Group 3	Group 4	Group 5	p-value
Pruritus	10 (33.3)	10 (38.5)[a]	2 (6.7)[b]	8 (26.7)	3 (10)	**0.01**
Xerosis	25 (83.3)[c]	12 (46.2)	9 (30)	13 (44.8)	1 (3.3)[d]	**0.0001**
Hyperpigmentation	13 (43.3)	13 (50)	13 (43.3)	11 (37.9)	1 (3.3)[e]	**0.001**
Alopecia	16 (53.3)[f]	11 (42.3)[g]	7 (23.3)	5 (17.2)	4 (13.3)	**0.003**

Values are presented as the number of patients and percentage in brackets. Group 1: hemodialysis, group 2: peritoneal dialysis, group 3: kidney transplant, group 4: chronic kidney disease, group 5: healthy control. [a]: group 2 versus group 5, [b]: group 3 versus groups 1,2, and 4, [c]: group 1 versus groups 2,3, and 4, [d]: group 5 versus groups 1,2,3, and 4, [e]: group 5 versus groups 1,2,3, and 4, [f]: group 1 versus groups 3,4, and 5, [g]: group 2 versus group 5.

Table 4: Correlation of the laboratory parameters with pruritus.

Pruritus	GFR (mL/min/m^2)	Hemoglobin (g/dL)	Hematocrit (%)	BUN (mg/dL)	Albumin (g/dL)
Present	11 (7-76)	10.9 (8-13)	32.1 (24-41)	59 (20-122)	3.55 (2-5)
Absent	43.5 (6-139)	11.7 (7-16.5)	34.7 (21-49)	50 (6-102)	4.1 (2-5)
p-value	**0.024**	**0.002**	**0.002**	**0.007**	**0.001**

Values are presented median and minimum-maximum in brackets. GFR: glomerular filtration rate, BUN: blood urea nitrogen.

Table 5: Correlation of laboratory values with xerosis.

Pruritus	MCV (fL)	TS (%)	K (mEq/L)	Ferritin (ng/mL)	Phosphorus (mg/dL)	BUN (mg/dL)	Cre (mg/dL)
Present	92.7 (72.2-101)	35 (8-75)	4.8 (2.8-6.4)	413 (42-1245)	4.6 (2.8-6.4)	56 (15-122)	7.6 (0.71-16)
Absent	90 (73-100)	27 (8-52)	4.5 (3.1-6.1)	156 (2-1232)	3.75 (1-8)	38 (6-102)	2.7 (0.48-15.5)
p-value	**0.005**	**0.013**	**0.014**	**0.004**	**0.036**	**0.007**	**0.001**

Values are presented median and minimum-maximum in brackets. BUN: blood urea nitrogen, Cre: creatinine, K: potassium, MCV: mean corpuscular volume, TS: transferrin saturation.

Table 6: Laboratory values in the study (hemodialysis, peritoneal dialysis, kidney transplant, chronic kidney disease, and healthy control) groups.

Variable	Group 1	Group 2	Group 3	Group 4	Group 5	p-value
Hb (g/dL)	11.3 ± 1.1	10.9 ± 1.7	12.7 ± 2.1*	11.1 ± 1.5	12.9 ± 1.5^{x}	**0.0001**
BUN (mg/dL)	57 ± 11	56 ± 20	22 ± 12^{a}	65 ± 28	12 ± 4^{b}	**0.0001**
Creatinine (mg/dL)	9.1 ± 2.5	9.6 ± 3.5	1.5 ± 0.9^{c}	4.6 ± 2.6^{d}	0.7 ± 0.3^{e}	**0.0001**
Albumin (g/dL)	4.1 ± 0.7	3.6 ± 0.5$^{\alpha}$	4.2 ± 0.5	3.7 ± 0.6$^{\beta}$	4.4 ± 0.3	**0.0001**
IL-31(pg/mL)	0.79 ± 1.15	0.59 ± 0.67	0.90 ± 0.89	0.83 ± 0.69	1.42 ± 2.09	0.135
UGCG (ng/mL)	21.1 ± 9.6	22.0 ± 11.3	19.9 ± 10.5	16.4 ± 6.8	19.5 ± 9.9	0.248

Values are presented as mean ± standard deviation. Group 1: hemodialysis, group 2: peritoneal dialysis, group 3: kidney transplant, group 4: chronic kidney disease, group 5: healthy control. Hb: hemoglobin, BUN: blood urea nitrogen, IL-31: interleukin 31, UGCG: uridine diphosphate glucose ceramide glucosyltransferase, *: group 3 versus groups 1,2, and 4, ^{x}: group 5 versus groups 1,2, and 4, ^{a}: group 3 versus groups 1,2, and 4, ^{b}: group 5 versus groups 1,2, and 4, ^{c}: group 3 versus groups 1,2, and 4, ^{d}: group 4 versus groups 1,2,3, and 5, ^{e}: group 5 versus groups 1,2, and 4, $^{\alpha}$: group 2 versus groups 1,3, and 5, $^{\beta}$: group 4 versus groups 3 and 5.

quencies of nail findings that were significantly different between groups 4 and 5 are presented in Table 7. The frequency of longitudinal nail ridges was not statistically different between groups 4 and 5. However, in group 4, the serum IL-31levels were significantly higher in patients with longitudinal nail ridges than in those without longitudinal nail ridges. Also, in group 3, the serum IL-31 levels were lower in patients with tinea pedis than in those without tinea pedis (Table 8). Furthermore, the patients with pruritus in group 2, those with xerosis in group 4, and those with splinter hemorrhages in group 3 had significantly lower UGCG levels than those without pruritus, xerosis, and splinter hemorrhages, respectively (p =0.045, p =0.01, and p =0.02, respectively; Table 9).

Discussion

The relationship between kidneys and skin is closer than generally considered. Cutaneous manifestations of CKD present unpleasant sensation to patients and impair their quality of life with respect to many aspects[15]. Specifically, pruritus was reported to be associated with poor sleep, anxiety, and depression, even leading to suicide attempts[16].

In the present study, xerosis (51.3 %), hyperpigmentation (43.4 %), alopecia (33 %), and pruritus (26 %) were the most frequently observed cutaneous findings of patients with CKD, in agreement with the previous studies[17]. The reported rate of xerosis is 59-93 % in patients with CKD, and its prevalence is higher in hemodialysis patients, similar to that observed in the present study[18].

Table 7: Differences in the frequencies of nail findings between patients with chronic kidney disease and healthy controls.

Nail findings	Patients with CKD (Groups 1,2,3, and 4)	Healthy controls (Group 5)	p-value
Subungual Hyperkeratosis	76 (66.1)	9 (30)	0.001
Splinter hemorrhages	17 (14.8)	0 (0)	0.024
Onycholysis	32 (27.8)	0 (0)	0.002

Values are presented as the number of patients and percentage in brackets. Group 1: hemodialysis, group 2: peritoneal dialysis, group 3: kidney transplant, group 4: chronic kidney disease, group 5: healthy control. CKD: chronic kidney disease.

Table 8: Comparisons of serum interleukin 31 (IL-31) levels (pg/mL) according to dermatological findings in the study (hemodialysis, peritoneal dialysis, kidney transplant, chronic kidney disease, and healthy control) groups.

Finding		Group 1	Group 2	Group 3	Group 4	Group 5
Longitudinal ridges	present	0.43 (0.01-5.08)	0.28 (0.01-0.89)	0.02 (0.01-3.17)	0.92 (0.46-2.29)	1.02 (0.02-11.53)
	absent	0.38 (0.01-3.92)	0.48 (0.01-3.25)	1.25 (0.01-2.63)	0.5 (0.04-2.52)	0.77 (0.01-2.44)
	p-value	0.8	0.31	0.63	**0.02**	0.3
Tinea pedis	present	0.81 (0.01-1.62)	0.35 (0.02-0.49)	0.006 (0.01-1.19)	0.64 (0.09-2.52)	1.45 (0.06-11.53)
	absent	0.43 (0.01-5.08)	0.48 (0.01-3.25)	1.42 (0.01-3.17)	0.55 (0.04-2.1)	0.87 (0.01-2.04)
	p-value	0.83	0.42	**0.01**	0.4	0.21

Values of IL-31 are presented median and minimum-maximum in brackets. Group 1: hemodialysis, group 2: peritoneal dialysis, group 3: kidney transplant, group 4: chronic kidney disease, group 5: healthy control. CKD: chronic kidney disease. IL-31: interleukin 31.

Table 9: Comparisons of serum uridine diphosphate glucose ceramide glucosyltransferase (ng/mL) according to dermatological findings in the study (hemodialysis, peritoneal dialysis, kidney transplant, chronic kidney disease, and healthy control) groups.

Finding		Group 1	Group 2	Group 3	Group 4	Group 5
Pruritus	present	18.3 (9.3-45.4)	15.7 (1-29.4)	19 (13-25.2)	13.5 (8.7-22)	39.8 (16-41)
	absent	20.3 (6.4-37.7)	25.4 (5.1-42.7)	16.4 (5.9-39.5)	15.4 (8.8-40.5)	15.5 (7-41)
	p-value	0.79	**0.045**	0.86	0.18	0.06
Xerosis	present	19.6(6.3-45.4)	17.1(5.1-40.9)	25.2(8.1-39)	13.8(8.7-17.1)	20.4(20.4)
	absent	16.1(8.4-30.8)	24.5(1-42.7)	16.3(5.8-39.5)	16.7(10-40.5)	16(7-41)
	p-value	0.35	0.3	0.23	**0.01**	0.45
Splinter hemorrhages	present	18.3 (14.2-24.3)	22.9 (6.5-40.9)	12.5 (5.8-17.9)	14.6 (14.5-14.6)	
	absent	19.6(6.3-45.4)	22.2(1-42.7)	19.1(7.8-39.5)	15.1(8.7-40.5)	16.3(7-41)
	p-value	0.71	0.88	**0.02**	0.93	

Values of UGCG are presented median and minimum-maximum in brackets. Group 1: hemodialysis, group 2: peritoneal dialysis, group 3: kidney transplant, group 4: chronic kidney disease, group 5: healthy control. UGCG: uridine diphosphate glucose ceramide glucosyltransferase.

Additionally, we found that the serum ferritin, potassium, phosphorus, and creatinine levels were significantly higher in patients with xerosis than those without xerosis. Dogramaci et al also found a significant relationship between xerosis and high ferritin levels[19]. We suggest that the unwanted presentation of xerosis and the associated unpleasant symptoms such as pruritus might be mitigated with the optimal control of these parameters. Conversely, the presence of xerosis should raise the suspicion of elevated serum ferritin, potassium, phosphorus, and creatinine levels in these patients.

Diffuse brown hyperpigmentation was the second most common cutaneous finding in the present study. In one study, the prevalence of pigmentary changes was 17.5 %[20]. There was no significant difference in the frequency of pigmentary changes among groups 1, 2, 3, and 4. Hyperpigmentation is considered to associate with the duration of dialysis, and β2-microglobulin levels[21,22]. We also found that the dialysis time was significantly longer in patients with hyperpigmentation than in those without hyperpigmentation in group 2. In the present study, the pruritus frequency was highest in group 2 and lowest in group 3. The frequency of anemia was higher among patients with pruritus than those without pruritus. Similarly, pruritus was reported to be related to anemia among predialysis patients in other studies[23].

Regarding nail changes, some studies reported that half and half nail was the most common nail disorder in patients with CKD[24]. In the present study, subungual hyperkeratosis as the most common nail disorder (66.1 % of the patients with CKD), followed by longitudinal ridges, onycholysis, and leukonychia in 41.7 %, 27.8 %, and 20.9 % of the patients with CKD, respectively. These nail disorders were more frequent among patients with higher serum creatinine levels.

There were no differences in serum IL-31 and UGCG levels among the study groups. We also found that IL-31 was significantly associated with only longitudinal ridges and tinea pedis. Previous studies reported that pruritus was associated with IL-31 levels in patients undergoing hemodialysis patients[4], whereas no study to date reported an association between nail disorders and IL-31 levels. However, a novel cytokine that controls signaling and regulates a wide range of biological functions such as the induction proinflammatory cytokines and, regulation of cell proliferation and tissue remodeling, IL-31 might play a role in genesis of longitudinal nail ridges based on the higher IL- 31 levels observed in patients with longitudinal nail ridges than in those without longitudinal nail ridges among the patients with CKD in group 4[25]. These differences in results among the study groups might be due to the relatively small sample size of the study groups.

We found that the patients with pruritus in group 2, those with xerosis in group 4, and those with splinter hemorrhages in group 3 had significantly lower UGCG levels than those without these dermatological manifestations. Therefore, it is possible that high serum UCGC levels might provide protection from xerosis and pruritus in patients with CKD by supporting the integrity of the epidermis and the epidermal water barrier, which should be investigated in future studies based on the lack of studies to date on this.

The present study has several limitations that should be acknowledged, including the lack of homogeneity with respect to age, sex, eGFR, and duration of CKD.

In conclusion, dermatological manifestations associated with CKD are common, with the highest rates observed in patients with end-stage CKD. Awareness of these manifestations can aid in the accurate diagnosis and prognosis. Examination of skin and nails can provide clues about albumin, urea, ferritin, and phosphorus levels. Conversely, IL-31 might play a role in the development of longitudinal nail ridges, whereas UGCG might provide protection from pruritus and xerosis in patients with CKD. The findings of the present study should be validated in future studies with larger cohorts.

Conflict of interest

All authors declare that there are no conflicts of interest related to the study.

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