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Uremic pruritus and associated factors in hemodialysis patients: A multi-center study

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Background: Uremic pruritus is a common and disturbing problem in hemodialysis patients. Although its pathogenesis is not completely understood, it is thought to be multifactorial. The aim of this study was to identify risk factors of uremic pruritus in hemodialysis patients.

Methods: A total of 249 patients from four dialysis centers were included in this study. Data were collected using a questionnaire, the visual analogue scale, and the Hospital Anxiety and Depression Scale. We investigated whether socio-demographic and biochemical parameters were correlated to uremic pruritus.

Results: Pruritus was present in 53.4% of the hemodialysis patients. The mean visual analogue scale severity was 6.47 ± 1.56. Patients with white blood cell (WBC) counts > 6.7 × $10^3/\mu L$ had 1.73 times (95% confidence interval [CI], 1.360–2.888; $P = 0.036$) more pruritus than did those with WBC counts < 6.7 × $10^3/\mu L$. Patients with dry skin were 0.2 times (95% CI, 0.070–0.182; $P = 0.028$) more likely to suffer from very severe pruritus than were those with normal skin.

Conclusion: Uremic pruritus remains a serious problem in dialysis patients. The WBC level and presence of dry skin are thought to be among its causes. Therefore, data regarding the possible risk factors of uremic pruritus must be followed closely in patients at risk.

Keywords: Dry skin, Hemodialysis, Pruritus, Uremic, Leukocytes

Introduction

Uremic pruritus (UP) is a common and disturbing problem in patients undergoing hemodialysis (HD) treatment [1,2]. The incidence of UP is 15% to 49% in the predialysis period, and 50% to 90% during dialysis treatment [3]. Although its pathophysiology is not well understood, UP is thought to be multifactorial. Many hypotheses have been proposed regarding the development of UP. Recent hypotheses suggest that changes in the immune and opioid systems are to blame for UP [4].

The immune system hypothesis suggests that an increase in the Th1, Th2 cell ratio causes pruritus. Th1 cells are believed to cause pruritus by activating cytokines and inflammatory cells, and Th2 cells by ensuring the secretion of anti-inflammatory cytokines [2,5]. In contrast, the opioid system hypothesis suggests that irregularities in the opioid receptors cause UP. For example, an increase in μ receptor agonists is reported to trigger itching, while

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an increase in the κ receptor agonist has the opposite effect [6].

Although the pathophysiology of UP is not completely understood, several factors are thought to be involved in its development [7]. These predisposing risk factors include increased blood urea nitrogen (BUN), calcium, phosphorus and β_2-microglobulin [8]. Other contributing factors are as follows: serum magnesium and vitamin A excess; an increased aluminum level; anemia; erythropoietin deficiency; high ferritin levels; low transferrin and albumin levels; secondary hyperparathyroidism; increased calcium, phosphate and magnesium levels; and an increase in substances released from mast cells (histamine, interleukin [IL]-2, protease, etc.) [9]. Dry skin is caused by sweat gland atrophy and dehydration of the skin's stratum corneum layer. These factors are also reported to play a role in UP development [7].

Patients with UP have difficulty coping with it, and develop associated stress [4]. UP is an increasingly important problem among dialysis patients. It has a negative effect on patients' quality of life, sleep, emotional state, and social relations [1,10]. Pruritus also contributes to the development of skin and soft tissue lesions and/or infections [10]. UP affects close to 90% of dialysis patients, and corresponds to increased morbidity and mortality [7]. The mortality risk of UP was found to be > 17% based on 18,000 HD patients in the International Dialysis Outcomes and Practice Patterns Study (DOPPS) [2]. Overall, UP is typically resistant to treatment and difficult to manage.

Despite multiple attempts to identify the risk factors of UP, including calcium and phosphate levels, dialysis adequacy, depression, and anxiety, controversy remains [10–13]. Dry skin, which develops due to reduced sweat gland volume, is thought to play a role in UP development; however, these data are also contradictory [13,14]. UP causes depressive symptoms in dialysis patients, which have been reported to be related to an increase in hospitalization and mortality rates [15]. However, only a few studies have investigated the relationship between UP and depression [2,16] and anxiety [17,18].

In this study, we have two aims: 1) we evaluated the socio-demographic and medical factors and biochemical factors that play a role in pruritus development, the various factors involved in the effect of pruritus on sleep and the social support, and anxiety and depression states all together; and 2) we conducted the study in four dialysis centers in Turkey, a country with an increasing number of patients on HD treatment, so that the results would guide health care professionals in the presentation of health care services.

Methods

Patients and study design

This descriptive study was conducted between November 2015 and June 2016 at four dialysis centers in Ankara, Turkey. The study inclusion criteria were as follows: 1) patients who had been undergoing HD treatments for four hours a day, three days a week for a minimum of six months; 2) patients 18 years old or over; 3) no communication difficulty; 4) no psychiatric disorders that may lead to cognitive deficiencies such as Alzheimer's disease or psychosis; and 5) no diagnosis of active infection, skin disease, acute hepatitis, cholestatic liver disease or cancer. The dialysis technique was HD. There were various dialysis machines and sets used at the four dialysis centers where the study was conducted. The HD water purifying systems were regularly inspected by the relevant authorities. A total of 249 patients met the inclusion criteria and were accepted to participate. Ethical consent was obtained from the hospital ethical committee (session number: 12, registration number: 384). All of the participating dialysis centers gave permission for their participation. The investigators explained the purpose of study to the patients by the investigators. The participants then provided written informed consent to participate.

Data collection and procedure

Data collection forms were completed face-to-face by the investigators during the second hour of an HD treatment session. The patients were verbally informed about the study, and their consent was obtained before data collection began. The patients were asked to answer the questions with regard to the last month. The forms took approximately 15 to 20 minutes to complete. Biochemical parameters from the prior month were obtained from hospital records. The data collection form consisted of the following five sections: 1) Patient characteristics form; 2) Data collection form for pruritus status; 3) Visual

analog scale (VAS); 4) Laboratory parameters form; and 5) the Hospital Anxiety and Depression Scale (HADS).

Identification of uremic pruritus

UP was defined as pruritus lasting for longer than three months with a VAS score of 4 or more (where 0 indicates no pruritus, and 10 unbearable pruritus) [5]. The patients answered the VAS questionnaire by only considering the last month.

Patient characteristics form

The patient characteristics form was developed based on a review of the relevant literature [1,5–9]. It includes data regarding the socio-demographic and clinical characteristics of the patients. The socio-demographic data included age and gender. The medical data included duration of dialysis, interdialytic weight gain (IDWG), causes of chronic renal failure, diabetes, hypertension, cardiovascular or pulmonary disease, erythropoietin and high-flux dialysis use, and anxiety and depression scores. The IDWG was defined as the difference between the predialytic weight and the weight at the end of the previous dialysis session. The skin structure was determined by researchers as "normal" or "dry."

Data collection form for pruritus status

The data collection form for pruritus status evaluated the following parameters: 1) the most involved area, including either head-neck, back, abdomen, arm, leg, or entire body; 2) the period of most intense pruritus, including during dialysis, the day of dialysis, the day after dialysis, or the evening before dialysis; 3) the pruritus severity with VAS; 4) pre-medications used for pruritus; and 5) sleep changes due to pruritus, such as: "I do not wake up, I wake up several times a night, I wake up quite often, or I am always sleepless."

Visual analogue scale

The VAS is the most commonly used scoring system for UP severity [12,14]. VAS is used to convert values that cannot be measured numerically into numerical values. This a 10-point scale in which 0 indicates no pruritus, and 10 indicates very severe pruritus. The numerical values are separated by one cm intervals. We used the categorization by Reich et al [19] as a reference when classifying the VAS score. We classified the severity of pruritus as follows: < 4 points was considered mild; ≥ 4 points but < 7 points was moderate; ≥ 7 points but < 9 points severe; and ≥ 9 points very severe pruritus.

Data collection form for biochemical characteristics

The following biochemical parameters were recorded: entry and exit values for Kt/V, urea reduction ratio (URR), calcium, white blood cell (WBC), hemoglobin, hematocrit, albumin, phosphorus, calcium-phosphorus (CaxP), parathyroid hormone, C-reactive protein (CRP), ferritin and BUN. These measurements are routinely performed every month at the dialysis centers included in the study. Biochemical parameters of the last month were evaluated. The Daugirdas formula was used in the calculation of the Kt/V value [20].

The patients were divided into two groups according to their WBC level (either $< 6.7 \times 10^3/\mu L$ or $\geq 6.7 \times 10^3/\mu L$) similar to the methods of Pisoni et al [2]. In the study of Pisoni et al [2], the laboratory values with the likelihood of patients having moderate to extreme pruritus vs. mild/no pruritus in the combined DOPPS I and II study sample. The National Kidney Foundation Dialysis Outcomes Quality Initiative (K/DOQI) guide [21] recommends that the CaxP level be $< 55\ mg^2/dL^2$. Therefore, patients were divided into two groups according to a CaxP level $< 55\ mg^2/dL^2$ or $\geq 55\ mg^2/dL^2$. The target values recommended by the Hemodialysis Adequacy 2006 Work Group [22] for Kt/V and URR are 1.4 and 70%, respectively. The patients in this study were divided into two groups according to Kt/V levels of < 1.4 or ≥ 1.4, and URR levels of < 70% or ≥ 70%.

Hospital Anxiety and Depression Scale

The HADS was developed by Zigmond and Snaith [23] in order to identify anxiety and depression risk in patients. The HADS also measures the level and severity of anxiety and depression. Aydemir et al [24] studied the validity and reliability of the HADS scale for Turkey. The HADS is used to quickly diagnose anxiety and depression, and to determine the risk group. However, it is not used

to diagnose patients with other medical disease. Seven of the 14 questions measure anxiety, while the other seven address depression. The responses are scored based on a four-point Likert scale, with each response ranging 0 to 3. The lowest score that a patient can achieve from either subscale is 0, and the highest is 21. The cut-off points of the Turkish HADS are 10 for the anxiety subscale, and 7 for the depression subscale.

Statistical analysis

The SPSS software program for Windows (ver. 15.00; SPSS Inc., Chicago, IL, USA) was used for data evaluation and statistical analysis. The descriptive statistics are shown as numbers and percentages for counted numerical variables (such as gender, marital status), and means ± standard deviations for measured numerical variables (such as age, calcium and albumin value). The Kolmogorov–Smirnov test was used to evaluate the normality of the data. According to the data distribution, either the *t* test for independent groups or Mann–Whitney *U* test was used for comparisons between the two groups. The chi-square test was used for nominal data in pair wise comparisons. The multivariate logistic regression analysis was conducted to determine the factors associated with pruritus development. Variables were included in the regression analysis as candidate variables if they had a *P* value of ≤ 0.25, and demonstrated clinical importance in the single comparisons. *P* values < 0.05 were considered statistically significant.

Results

Patient characteristics

We found that 53.4% of the included patients were experiencing pruritus. Table 1 presents the subjects' descriptive characteristics and presence of pruritus. The mean age of the patients with pruritus was 62.54 ± 12.77 years. A slight majority of the patients were male (54.1%). The mean HD treatment duration was 61.35 ± 43.30 months. There was a low risk of anxiety in 78.2% of patients. However, there was a high of depression in 77.4% of patients. The mean age of patients without pruritus was 62.46 ± 14.31 years, 56.0% of whom were male. The mean HD treatment duration was 66.28 ± 52.81 months in those without pruritus. There was a low risk of anxiety in 87.9% of these patients. Again, however, there was a high risk of depression in 84.5%.

Patients without pruritus had statistically significantly lower risks of cardiovascular disease and anxiety than did those with pruritus ($\chi^2 = 4.649$, $P = 0.031$ and $\chi^2 = 4.110$, $P = 0.043$, respectively). There were no statistically significant differences between the groups with regard to the other variables ($P > 0.05$).

Prevalence and characteristics of uremic pruritus

The descriptive characteristics of patients with pruritus are presented in Table 2. The pruritus affected the whole body in 35.3% of patients, and was most intense on the day after the dialysis in 39.1%. The mean pruritus severity was 6.47 ± 1.56, and 50.4% experienced moderate pruritus. Pruritus led to sleep disturbances in 33.8% of patients. In addition, 60.9% of patients used medications, such as oral antihistamines or topical therapies, for their pruritus. There was no significant relationship between the type of medication and the pruritus severity (data not presented, Z = −0.813; $P = 0.416$).

Table 3 demonstrates the relationship between the VAS level and HADS score in patients with pruritus. There was a weakly positive relationship between the VAS score and the Hospital Depression Score in patients with pruritus ($P = 0.034$).

Univariate regression analysis was used to identify factors potentially correlated to pruritus development. The odds ratio (OR) of WBC was 0.220 (95% confidence interval [CI]). Patients with dry skin were 0.2 times more likely to suffer from very severe pruritus than were those with normal skin (Table 4). None of the other variables had a statistically significant effect on pruritus development.

Multivariate regression analysis was used to identify the factors potentially related to pruritus development. The OR for WBC was 0.225 (95% CI). Patients with dry skin were 0.194 times more likely to suffer from very severe pruritus compared to those with normal skin (Table 5). However, the data in this model had a weak fit ($R2 = 0.11$). None of the other variables were significantly associated with pruritus development.

Table 6 presents the biochemical parameters according to the presence of pruritus. WBC counts ≥ $6.7 \times 10^3/\mu L$ were significantly more common in the group with pru-

Table 1. Descriptive characteristics based on the presence of pruritus

Characteristic	Pruritus present	Pruritus not present	*P* value
Subjects	133 (53.4)	116 (46.6)	
Age (yr)	62.54 ± 12.77	62.46 ± 14.31	0.718
Gender			0.764
Male	72 (54.1)	65 (56.0)	
Female	61 (45.9)	51 (44.0)	
Duration of dialysis (mo)	61.35 ± 43.30	66.28 ± 52.81	0.712
IDWG (kg)*	2.35 ± 0.83	2.22 ± 0.90	0.219
Chronic renal failure cause			0.732
Diabetes	34 (25.6)	30 (25.9)	
Hypertension	36 (27.1)	31 (26.7)	
Glomerulonephritis	12 (9.0)	7 (6.0)	
Unknown	37 (27.8)	30 (25.9)	
Other†	14 (10.5)	18 (15.5)	
Diabetes			0.430
Yes	57 (42.9)	44 (37.9)	
No	76 (57.1)	72 (62.1)	
Hypertension			0.401
Yes	56 (42.1)	55 (47.4)	
No	77 (57.9)	61 (52.6)	
Treatment with erythropoietin			0.251
Yes	42 (31.6)	29 (25.0)	
No	91 (68.4)	87 (75.0)	
Cardiovascular disease			0.031
Yes‡	27 (20.3)	12 (10.3)	
No	106 (79.7)	104 (89.7)	
Lung disease			0.510
Yes§	4 (3.0)	2 (1.7)	
No	129 (97.0)	114 (98.3)	
Use of high-flux dialyzer			
Yes (synthetic)	30 (22.6)	36 (31.0)	0.131
No (polysulfone)	103 (77.4)	80 (69.0)	
Hospital Anxiety Score			0.043
Low (0–10)	104 (78.2)	102 (87.9)	
High (11–21)	29 (21.8)	14 (12.1)	
Hospital Depression Score			0.160
Low (0–7)	30 (22.6)	18 (15.5)	
High (8–21)	103 (77.4)	98 (84.5)	
Skin type			0.239
Normal	73 (54.9)	55 (47.4)	
Dry	60 (45.1)	61 (52.6)	

Data are represented as means ± standard deviation or number (%).

IDWG, interdialytic weight gain.

*IDWG was calculated as the difference between the predialytic weight and the weight at the end of the previous dialysis session. †Drug intoxication, polycystic kidney, pyelonephritis, renal artery stenosis, post-surgery, urinary tract infection. ‡Ischemic heart disease, hearth failure, atrial fibrillation, coronary artery disease, valve disease, atherosclerosis. §Chronic obstructive pulmonary disease, asthma.

P values were calculated using the Pearson chi-square test for categorical data and Mann–Whitney *U* test for continuous data.

Table 2. Descriptive characteristics of patients with pruritus

Characteristic	Data
Pruritus area*	
Head-neck	17 (12.8)
Back	31 (23.3)
Abdominal area	12 (9.0)
Arm-leg	32 (24.1)
Entire body	47 (35.3)
Period of most intense pruritus	
During dialysis	13 (9.8)
The day after dialysis	52 (39.1)
The evening before dialysis	34 (25.6)
After dialysis (on the day of hemodialysis)	17 (12.8)
Constantly	17 (12.8)
Pruritus severity†	
Mild	4 (3.0)
Moderate	67 (50.4)
Severe	49 (36.8)
Very severe	13 (9.8)
Use of medication for pruritus	
Yes	81 (60.9)
No	52 (39.1)
Type of the medication used for pruritus‡	
Oral antihistamine	16 (19.8)
Cream-lotion	65 (80.2)
Pruritus-related sleep disturbance	
"I do not wake up"	88 (66.2)
"I wake up several times a night"	22 (16.5)
"I wake up quite often"	8 (6.0)
"I am always sleepless"	15 (11.3)

Data are presented as number (%).

*Participants marked more than one item. †Pruritus severity was evaluated with visual analog scale; pruritus severity (0–10) 6.47 ± 1.56 (minimum, 3; maximum, 10). ‡Data reflects the people who used the drugs (n = 81).

ritus (χ^2 = 3.883, P = 0.049) than in that without pruritus. However, there was no statistically significant difference between the groups with regard to other variables (P > 0.05).

Determinants of the prevalence and intensity of uremic pruritus

Logistic regression analysis was used to identify factors that are potentially related to pruritus development. The OR for WBC count was 1.730 (95% CI), as shown in Table 7. The other variables did not have a statistically significant effect on the possibility of pruritus development.

Discussion

This study sought to identify the risk factors of UP in HD patients. UP is a common symptom in HD patients that can cause severe discomfort. It is difficult to treat, as its underlying pathophysiological mechanism is not precisely known [10]. The prevalence of UP varies between 30% and 64% in the literature [2,5,25–28]. We found that 53.4% of our patients had UP, which is comparable to

Table 3. Relationship between VAS level and HADS score in pruritic patients

Variable	Hospital Anxiety Score		Hospital Depression Score	
	r*	*P*	r*	*P*
VAS	0.050	0.565	0.184	0.034

HADS, Hospital Anxiety and Depression Scale; VAS, visual analog scale.

*Pearson correlation analyses.

Table 4. Severity of uremic pruritus by univariate regression

Variable (reference value)	β	OR	95% CI	*P* value
Age	−0.005	0.038	−0.027 to 0.017	0.678
Gender (female, 1/male, 0)	−0.034	0.011	−0.622 to 0.554	0.908
Skin type (dry, 1/normal, 0)	0.626	0.200	0.070 to 0.182	0.028
Hospital Anxiety Score	0.005	0.011	−0.076 to 0.087	0.898
Hospital Depression Score	0.054	0.111	−0.032 to 0.141	0.216
Kt/V	−2.510	0.303	−5.077 to 0.778	0.149
Urea reduction ratio	0.062	0.261	−0.033 to 0.157	0.199
White blood cell	−0.152	0.220	−0.274 to −0.030	0.015
Calcium, albumin adjusted	0.023	0.013	−0.325 to 0.370	0.896
Phosphorus	0.211	0.155	−0.119 to 0.540	0.208
Parathyroid hormone	6.14	0.014	−0.001 to 0.001	0.879

CI, confidence interval; OR, odds ratio.

The backward LR method was used.

Table 5. Severity of uremic pruritus by multivariate regression

Variable (reference value)	β	SE	OR	95% CI	*P* value
Skin type (dry, 1/normal, 0)	0.607	0.265	0.194	0.081 to 0.132	0.024
White blood cell	−0.156	0.059	0.225	−0.273 to −0.038	0.010
Hospital Depression Score	0.055	0.041	0.113	−0.026 to 0.137	0.182
Kt/V	−2.629	1.290	0.371	−5.182 to 0.076	0.54
Urea reduction ratio	0.073	0.043	0.306	−0.013 to 0.158	0.095

CI, confidence interval; OR, odds ratio; SE, standard error.

R2 = 0.11 (*P* = 0.04)

The backward LR method was used.

Table 6. Comparing biochemical parameters according to the presence of pruritus

Characteristic	Pruritus present (n = 133)	Pruritus not present (n = 116)	*P* value
Calcium, albumin adjusted (mg/dL)	9.00 ± 0.90	8.84 ± 0.87	0.196
Albumin (g/dL)	3.84 ± 0.40	3.75 ± 0.34	0.063
CRP (mg/dL)	26.14 ± 45.75	19.84 ± 31.77	0.087
Parathyroid hormone (pg/mL)	417.55 ± 348.72	390.76 ± 319.14	0.655
Ferritin (ng/mL)	615.48 ± 439.34	646.59 ± 424.60	0.436
White blood cell			
< 6.7 × 10^3/μL	50 (37.6)	58 (50.0)	0.049
≥ 6.7 × 10^3/μL	83 (62.4)	58 (50.0)	
Kt/V			
< 1.4	36 (27.1)	33 (28.4)	0.808
≥ 1.4	97 (72.9)	83 (71.6)	
Urea reduction ratio (%)			
< 70	40 (30.1)	35 (30.2)	0.987
≥ 70	93 (69.9)	81 (69.8)	
CaxP (mg^2/dL^2)			
< 55	108 (81.2)	99 (85.3)	0.384
≥ 55	25 (18.8)	17 (14.7)	
Hemoglobin (g/dL)	11.62 ± 1.31	11.69 ± 1.31	0.679
Hematocrit (%)	35.82 ± 4.66	35.81 ± 4.52	0.988
BUN (mg/dL)			
Before hemodialysis	109.95 ± 44.00	121.10 ± 46.66	0.054
After hemodialysis	31.63 ± 13.73	34.53 ± 14.83	0.096
Phosphorus (mg/dL)	5.11 ± 1.14	4.85 ± 1.15	0.068

Data are presented as means ± standard deviation or number (%).

BUN, blood urea nitrogen; CaxP, product of albumin-adjusted serum calcium and serum phosphorus; CRP, C-reactive protein.

P values were calculated using the Pearson chi-square test for categorical data, and the Mann–Whitney *U* test and Student *t* test for continuous data.

prior reports. The UP severity was 7/10 in more than half of studies that evaluated its severity. Similarly, the mean pruritus severity was 6.47 (0–10) in this study.

We found that WBC counts ≥ 6.7 × 10^3/μL were also relevant to UP development, and increased its risk by 1.73 times. Prior literature has emphasized the importance of inflammation and proinflammatory factors in the development of UP [29]. We found that the levels of serum pro-inflammatory cytokines (such as IL-6) and CRP were higher in UP patients than in those without UP. The WBC count is also thought to be an important marker, with a WBC count > 6.7 × 10^3/μL particularly significant for UP development [2,5]. Kimata et al [30] found that higher WBC counts increased the risk of UP development by 1.04-fold. Similarly, Pisoni et al [2] found that a WBC count > 8.4 × 10^3/μL increased the risk of UP develop-

Table 7. Multivariate logistic regression of potential risk factors for pruritus

Variable (reference value)	β	OR	95% CI	*P* value
WBC, ≥ 6.7 × 10^3/μL	0.548	1.730	1.360–2.888	0.036
Age	–0.003	0.997	0.976–1.018	0.785
Gender, male	0.123	1.131	0.631–2.026	0.680
Smoking status, yes	–0.257	0.773	0.313–1.912	0.578
Treatment with erythropoietin, yes	0.038	1.039	0.541–1.997	0.909
High-flux dialyzer use, yes	–0.123	0.884	0.474–1.650	0.699
Hospital Anxiety Score	0.039	1.040	0.950–1.138	0.400
Hospital Depression Score	–0.075	0.928	0.846–1.018	0.114
Kt/V	–1.184	0.306	0.025–3.710	0.352
Urea reduction ratio	0.060	1.062	0.972–1.160	0.183
Calcium, albumin adjusted	0.121	1.129	0.802–1.589	0.487
BUN before hemodialysis	–0.006	0.994	0.986–1.001	0.096
Phosphorus	0.108	1.114	0.751–1.653	0.591
CaxP	0.022	1.022	0.981–1.066	0.294
Parathyroid hormone	0.000	1.000	0.999–1.001	0.720

BUN, blood urea nitrogen; CI, confidence inverval; CaxP, product of albumin-adjusted serum calcium and serum phosphorus; OR, odds ratio; WBC, white blood cell.
The backward LR method was used.

ment by 1.20-fold.

UP frequently causes significant mood impairment, including depression and anxiety [16]. Similarly, patients with depressive symptoms have significantly higher odds of developing severe pruritus [31]. Depression was reported to develop 1.3 to 1.7 times more commonly in UP patients [2,15] In addition, Araujo et al [16] reported a significant relationship between depressive symptoms and UP. Other groups have not identified a statistically significant correlation between pruritus and depression using the HADS [17,18]. We also did not find that depression was a risk factor for UP development, although the depression score increased with increasing VAS scores. This discrepancy with the findings in the literature may be a result of the use of a self-administered questionnaire to assess anxiety and depression. Prior studies have mandated psychiatric consultation in cases in which depression or anxiety is suspected based on the self-administered questionnaires [32]. In contrast, psychiatric involvement was not included in our protocol. Therefore, further studies are needed in which a definite diagnosis (of a psychiatric disorder) is made by a physician once it is suspected by self-administered questionnaires. Prior studies of HD patients have focused more on depression than on anxiety. Therefore, the relationship between anxiety and UP development must be studied further.

Dry skin, caused by sweat gland atrophy and dehydration of the stratum corneum layer, is thought to play a role in the development of UP. Dry skin has previously been suggested as a potential causative factor for UP [7]. Kiliç Akça and Taşci [25] reported that the incidence of UP in patients with dry skin is 3.9 times higher than in those without dry skin. We similarly found that dry skin is a risk factor for UP.

The study has several limitations. For instance, the study was inherently subject to recall bias and false declarations based upon its design. In addition, we were unable to measure eosinophil levels in our patients with pruritus. Eosinophils produce multiple substances that are relevant to pruritus. Therefore, future studies ought to investigate whether the eosinophil level is associated with the prevalence of UP.

In conclusion, we found that a WBC count ≥ 6.7 × 10^3/μL was a risk factor for UP development in HD patients. Overall, despite its high prevalence and negative impact on quality of life, UP is disregarded by many health care professionals. Therefore, we recommend that providers monitor the potential risk factors for UP, such as the WBC count, in their HD patients who are at risk.

Conflicts of interest

All authors have no conflicts of interest to declare.

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