Kidney Medicine

Chronic Kidney Disease-Associated Pruritus Burden: A Patient Survey Study

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Rationale & Objective: Chronic kidney disease-associated pruritus (CKD-aP) is a common, underrecognized condition in patients with chronic kidney disease (CKD), especially those receiving hemodialysis (HD). The present study analyzed the clinical treatment journey and overall burden of pruritus among patients with CKD-aP.

Study Design: Cross-sectional, patient-reported online survey.

Setting & Participants: Data from adult patients undergoing HD (December 2021–May 2022) in the United States.

Exposure: Patients participated in an online survey and responded to questions on validated patient-reported outcome instruments related to CKD-aP.

Outcomes: Self-reported measures analyzed at the end of this survey include itch characteristics; symptom management; health care provider (HCP) engagement; and effect on HD, quality of life (QoL), sleep, and work productivity.

Analytical Approach: Bivariate analysis assessed the association of itch severity with CKD-specific QoL.

Results: Overall, 354 patients with CKD-aP were included in analyses, of which 49% and 30% had moderate and severe itch, respectively (22% were mild). Around 68% reported symptoms to HCPs, most commonly a nephrologist or primary care provider, and 55% received a treatment recommendation. The most common treatments were topical lotions/moisturizers (75%) and corticosteroids (48%); use of oral prescriptions was low (20%), with limited satisfaction with treatments. Overall, 23% of patients reported shortening and 17% reported missing HD sessions because of itch. In bivariate analysis, patients with more severe CKD-aP reported significantly worse disease and function scores (kidney disease score, cognitive function, quality of social interaction, sleep [all, $P < 0.001$], and sexual function [$P < 0.05$]), suggesting a direct effect of CKD-aP on QoL.

Limitations: Possible recall bias, especially for questions with longer recall periods.

Conclusions: CKD-aP is often inadequately treated and disruptive of dialysis treatment, even among patients who report itch to HCPs. Worse itch severity is associated with poorer QoL, sleep quality, and functional/work impairment.

Complete author and article information provided before references.

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Chronic kidney disease-associated pruritus (CKD-aP) refers to itching that is specifically related to kidney disease, often affecting patients on hemodialysis (HD).[1,2] The persistent itching can significantly affect the quality of life (QoL) for individuals with CKD. Patient surveys and epidemiologic studies showed CKD-aP is common and often severe, with an overall prevalence of up to 80% in patients with end-stage kidney disease (ESKD) and a prevalence of up to 40% for moderate-to-severe CKD-aP.[3,4] Gaps in identifying, diagnosing, and treating CKD-aP persist, which can be attributed to patients underreporting and providers under or inadequately treating CKD-aP.[5,6] Real-world data show that 17% of patients on HD who were nearly always or always bothered by itch never reported their symptoms.[5] Furthermore, CKD-aP prevalence is underrecognized based on a study reporting that 65% of dialysis medical directors estimated prevalence in their facility as <5%.[5]

CKD-aP confers a significant burden on patients and society. Pruritus has been associated with poorer health-related quality of life (HRQoL), sleep disorders, depression, exhaustion, hospitalization risk, and mortality[3,7,8]; specifically, poorer HRQoL is noted with increasing itch severity.[9] Pruritus may cause work impairment; however, this needs to be further examined through validated research.

Treatment of CKD-aP remains challenging. The underlying pathogenesis is poorly understood.[6,7,10] As of now, there are no universally established global guidelines for the diagnosis or treatment of CKD-aP.[11-13] Additionally, the available treatments for CKD-aP are limited in their effectiveness.[11] Until recently, commonly used management approaches included topical emollients, oral antihistamines, gabapentinoids, and other neuropathic agents, as well as dialysis optimization or, if appropriate, early referral for kidney transplantation.[6] Previous research has shown the most common treatments as antihistamines (topical or oral) and topical corticosteroids; however, 18% of worldwide and 29% of US patients reported receiving no treatment.[5] Recently, the US Food and Drug Administration and the European Medicines Agency approved the first injectable therapy, difelikefalin, indicated for the treatment of moderate-to-severe CKD-aP in patients receiving HD.[14,15] However,

PLAIN-LANGUAGE SUMMARY

Chronic kidney disease-associated pruritus (CKD-aP) is a common problem in patients with kidney disease, especially in those who are receiving dialysis. There are few approved treatment options for CKD-aP. Understanding how CKD-related itch affects patients may help identify ways to improve CKD-aP symptoms/signs. This patient-reported survey assessed itch characteristics, symptom management attempts and effectiveness, and burdens caused by itch in patients with CKD-aP. Although >60% of hemodialysis patients reported having itch-related symptoms, CKD-aP may be underdiagnosed. Most patients reported that they were not given treatment options and/or were not satisfied with their current treatments. The study also showed that itch intensity affected patient's full participation in prescribed dialysis sessions, quality of life, quality of sleep, and work productivity.

this treatment was not yet available during the time this study was conducted; thus, the current study was conducted to examine unmet needs in the context of existing treatments at the time.

The present study used a patient-reported survey to understand the journey of patients with CKD-aP undergoing hemodialysis. The survey explored various aspects, including the nature and intensity of itching, the degree of burden it imposes on patients' daily lives, understanding communication patterns regarding itchy skin, the effectiveness of different treatments, and whether CKD-aP influences adherence to dialysis treatment protocols.

METHODS

Study Design and Data Source

This study was a cross-sectional, patient-reported survey conducted between December 2021 and May 2022 in the Unites States in adult individuals with CKD-aP undergoing hemodialysis. A convenience sample of participants was recruited through panel companies DISQO,[16] Rare Patient Voice,[17] and Research on Investment[18] and through the American Association of Kidney Patients patient-advocacy group (PAG).

A pretest telephone interview was first conducted with 3 adult participants in the United States to ensure participants' understanding of the survey questions. Following the pretest phase, a quantitative one-time patient-reported online survey was administered. Participants were invited via email or through an online link distributed by American Association of Kidney Patients PAG through their Center for Patient Research and Education. Survey questions included validated patient-reported outcome instruments and custom study-specific questions. The study was reviewed by the Pearl Institutional Review Board (Atlanta, GA) and granted exemption status (according to 45 CFR 46.104(d)(2) Tests, Surveys, Interviews). All research was conducted in accordance with Good Pharmacoepidemiology Practices guidelines issued by the International Society for Pharmacoepidemiology. All participants provided informed consent before study participation.

Study Sample

The present study was targeted to recruit 450 CKD-aP participants. The final study sample included for analysis was 354 respondents who met all eligibility requirements (Fig S1).

Participants were eligible if they (i) were ≥18 years of age, (ii) were residing in the United States, (iii) self-reported as being diagnosed with ESKD by a clinician, (iv) were receiving in-center or home HD scheduled 3 times/week, (v) had an average self-reported itch severity of 1-10 over 28 days via a modified version of the Worst Itching Intensity Numeric Rating Scale (mWI-NRS), and (vi) provided informed consent. Excluded respondents included those who were unable to speak or read English or had a mWI-NRS result of 0, self-reported dementia, hepatitis B, or hepatitis C.

Self-Reported Measures

Demographics and Itch Characteristics

We collected demographic variables (eg, age, sex, race, and ethnicity) and prespecified comorbid conditions (eg, anemia, anxiety or depression, and chronic pulmonary disease). We assessed itch characteristics, including the mWI-NRS score, itch duration, perceived burden, Self-Assessed Disease Severity (SADS) score, and 5-D itch score. The WI-NRS is a reliable, valid, and responsive measure of itch intensity for patients with moderate-to-severe CKD-aP. It measures itch severity within the past 24 hours on a scale of 0 (no itch) to 10 (worst itch imaginable), whereas the modified version used in this study extended recall to the last 28 days.[19-21] We considered itch severity based on mWI-NRS scores as mild if 1-3, moderate if 4-6, and severe if 7-10. SADS is a multidimensional score categorizing itch severity based on the bother caused by concomitant itch-related signs/symptoms (eg, scratch marks, sleep disturbance, and agitation), with the categories defined as type A (never), B (sometimes), or C (often).[22] The 5-D itch scale is a 5-item questionnaire that measures degree, duration, direction, disability, and distribution of pruritus within the last 2 weeks.[23]

Itch-Related Interactions With Health Care Providers

We evaluated itch-related interactions through questions such as (1) type of health care provider (HCP) specialty engaged in itch discussion, (2) who started the discussion (patient or provider), (3) whether an HCP diagnosed

Table 1. Demographics, Comorbid Conditions, and CKD/ESKD Characteristics

Demographics	Worst Itch Group				
	Total (N = 354)	Mild (N = 76)	Moderate (N = 173)	Severe (N = 105)	Overall *P* Values
Age					
Mean ± SD	45.8 ± 16.3	52.2 ± 16.4	45.3 ± 17.1	42.0 ± 13.4	<0.001
Median (IQR: q25-q75)	43 (33.0-60.0)	57 (38.5-64.0)	42 (31.0-61.0)	39 (33.0-50.0)	
Missing	.	.	.	.	
Sex, N (%)					
Male	170 (48)	36 (47)	77 (45)	57 (54)	0.3
Female	184 (52)	40 (53)	96 (56)	48 (46)	
Missing	.	.	.	.	
Race, N (%)[a]					
White	247 (70)	55 (72)	119 (69)	73 (70)	0.9
Black or African American	76 (22)	18 (24)	35 (20)	23 (22)	0.8
Asian	11 (3)	3 (4)	6 (4)	2 (2)	0.7
Native Hawaiian or Pacific Islander	5 (1)	1 (1)	2 (1)	2 (2)	0.9
American Indian or Alaskan Native	5 (1)	0 (0)	2 (1)	3 (3)	0.3
Other	13 (4)	0 (0)	8 (5)	5 (5)	0.2
Prefer not to answer	2 (1)	0 (0)	1 (1)	1 (1)	0.7
Missing	.	.	.	.	
Ethnicity, N (%)[b]					
Hispanic or Latino/a/x	62 (18)	7 (9)	27 (16)	28 (27)	0.009
Not Hispanic or Latino/a/x	266 (75)	66 (87)	131 (76)	69 (66)	
Prefer not to answer	23 (7)	2 (3)	14 (8)	7 (7)	
Missing	3	1	1	1	
Education, N (%)					
Less than high school	2 (1)	0 (0)	0 (0)	2 (2)	0.2
Some high school	9 (3)	1 (1)	2 (1)	6 (6)	
High school graduate or equivalent	81 (23)	17 (22)	44 (25)	20 (19)	
Completed some college or technical school, but no degree	76 (22)	16 (21)	43 (25)	17 (16)	
Associates degree or technical school graduate	46 (13)	14 (18)	19 (11)	13 (12)	
College graduate	91 (26)	19 (25)	43 (25)	29 (28)	
Completed some graduate school, but no degree	12 (3)	4 (5)	3 (2)	5 (5)	
Completed graduate school	34 (10)	5 (7)	17 (10)	12 (11)	
Prefer not to answer	3 (1)	0 (0)	2 (1)	1 (1)	
Missing	.	.	.	.	
Household income for 2020, N (%)					
<$15,000	48 (14)	11 (15)	25 (15)	12 (11)	0.8
$15,000-$24,999	58 (16)	12 (16)	32 (19)	14 (13)	
>$25,000	223 (63)	45 (59)	105 (61)	73 (69)	
Prefer not to answer	25 (7)	8 (11)	11 (6)	6 (6)	
Marital status, N (%)					
Single, never married	103 (29)	24 (32)	49 (28)	30 (29)	0.5
Living with partner	40 (11)	7 (9)	23 (13)	10 (10)	
Married	148 (42)	33 (43)	66 (38)	49 (47)	
Separated	13 (4)	0 (0)	10 (6)	3 (3)	
Divorced	32 (9)	9 (12)	14 (8)	9 (9)	
Widowed	12 (3)	3 (4)	7 (4)	2 (2)	
Prefer not to answer	6 (2)	0 (0)	4 (2)	2 (2)	

(Continued)

Table 1 (Cont'd). Demographics, Comorbid Conditions, and CKD/ESKD Characteristics

Demographics	Worst Itch Group				
	Total (N = 354)	Mild (N = 76)	Moderate (N = 173)	Severe (N = 105)	Overall *P* Values
Location, N (%)[b]					
Urban	122 (35)	17 (22)	60 (35)	45 (43)	0.08
Suburban	153 (43)	37 (49)	76 (44)	40 (38)	
Rural	77 (22)	21 (28)	37 (21)	19 (18)	
Missing	2	1	.	1	
Insurance, N (%)[b]					
Commercial	68 (19)	16 (21)	37 (21)	15 (14)	0.04
Medicaid	93 (26)	14 (18)	42 (24)	37 (35)	
Others	179 (51)	44 (58)	87 (50)	48 (46)	
Missing	14	2	7	5	
Currently employed[b]					
Yes (%)	151 (43)	24 (32)	75 (43)	52 (50)	NA
No (%)	202 (57)	52 (68)	97 (56)	53 (51)	
CKD/ESKD characteristics					
Received hemodialysis primarily at home					NA
Yes (%)	89 (25)	9 (12)	40 (23)	40 (38)	
No (%)	265 (75)	67 (88)	133 (77)	65 (62)	
Missing	.	.	.	.	
Year of diagnosis[b]					
N	339	73	165	101	
Median (IQR, q25-q75)	2016 (2011-2019)	2015 (2011-2019)	2016 (2010-2018)	2017 (2014-2019)	
Missing	15	3	8	4	
Years since diagnosis[b]					
N	340	73	166	101	
Median (IQR, q25-q75)	5.5 (3.0-11.0)	7.0 (3.0-11.0)	5.5 (4.0-13.0)	5.0 (3.0-8.0)	
Missing	14	3	7	4	
Time on hemodialysis (y)					
N	354	76	173	105	
Median (IQR, q25-q75)	3.0 (1.5-5.6)	3.3 (1.1-6.4)	3.0 (1.5-5.4)	3.0 (1.6-5.4)	
Missing	.	.	.	.	

Note: % based on N.
Abbreviations: CKD, chronic kidney disease; ESKD, end-stage kidney disease; IQR, interquartile range; q, quartile; SD, standard deviation.
[a]Multiple responses possible.
[b]Missing data are indicated as N or number of participants.

CKD-aP or informed the patient that itchy skin may be related to kidney failure diagnosis, and (4) whether the HCP recommended treatment.

Effect of Itch on Dialysis

We examined the effect of itch on dialysis based on how often (never, rarely, sometimes, and often) participants skipped or shortened dialysis because of itch or received extra, unscheduled dialysis sessions because of skipped or shortened sessions. Patients also self-reported perceived burden from itch (extremely high, high, moderate, some, and none).

Itch-Related Symptom Management

We analyzed itch-related treatment patterns through patient-reported use of itch-related treatments, including current treatment(s), treatment category, duration of use, treatment frequency, and treatment satisfaction.

Work Productivity

Work Productivity and Activity Impairment (WPAI)[24] is a validated 6-question scale measuring work productivity changes over the past 7 days. The WPAI includes scores on 4 parameters: absenteeism (work time missed), presenteeism (time impaired while at work), overall work productivity loss, and activity impairment (time impaired with daily activities). These scores are expressed as percentages, with higher numbers indicating greater impairment and less productivity (worse outcomes).

Quality of Life

The Kidney Disease Quality of Life Instrument (KDQoL-SF, 24 questions on kidney disease-related components) is a validated instrument assessing generic and kidney disease-specific aspects of QoL for individuals receiving dialysis. A majority of the assessment uses a 4-week recall period for domains spanning overall health and kidney

disease-specific impact: daily life, social life, sleep, working life, and satisfaction with care.[25]

The Brief Itching Inventory (BII) includes a single question about sleep[22] adapted from the Medical Outcomes Study[26] and measures sleep disturbance because of nighttime itching on a scale of 0 (not interfered) to 10 (completely interfered with your sleep during the past 24 hours).

Statistical Analyses

We present descriptive statistical analyses in the form of frequencies and percentages for categorical variables and means and standard deviations (SD) for continuous variables. We applied bivariate analyses to compare QoL and sleep quality differences across itch severity subgroups (mild vs moderate, moderate vs severe, mild vs severe). We used χ^2 tests for categorical variables and one-way analysis of variance for continuous variables for comparisons across various itch severity levels. Analyses were performed using SAS software (version 9.4), and P values <0.05 were considered statistically significant.

RESULTS

Cohort Characteristics

A total of 354 patients with CKD-aP undergoing hemodialysis were included with a mean age of 45.8 ± 16.3 years. The majority of the study population were women (N = 184 [52%]), and 247 (70%) were White. Other demographic and patient characteristics are detailed in Table 1 and Table S1. Based on mWI-NRS scores, 76 patients (22%) had mild itch, 173 (49%) had moderate itch, and 105 (30%) had severe itch. Mean age was significantly lower in the group with more severe itch (severe: 42.0 ± 13.4 years, moderate: 45.3 ± 17.1 years, mild: 52.2 ± 16.4 years, overall P < 0.001) (Table 1). For the overall group, 5% (N = 16) patients also reported atopic dermatitis, 9% (N = 31) reported eczema, and 9% (N = 30) reported psoriasis. These itch comorbid conditions were more prevalent among those with moderate or severe CKD-aP than those with mild CKD-aP. Patients who also reported atopic dermatitis represent 0% (N = 0) of patients with mild CKD, 6% (N = 11) of patients with moderate CKD, and 5% (N = 5) of patients with severe CKD. Similarly, patients who also reported eczema represent 4% (N = 3), 8% (N = 14), and 13% (N = 14) of the patients with mild, moderate, and severe CKD, respectively. Finally, 5% (N = 4), 5% (N = 9), and 16% (N = 17) of patients with mild, moderate, and severe CKD, respectively, reported psoriasis. These and other prespecified comorbid condition rates are detailed in Table S1. The median (interquartile range [IQR]) time of itch reporting since CKD diagnosis was 5.5 years (3.0-11.0 years) and since starting HD was 3.0 years (1.5-5.6 years) (Table 1).

Descriptive Analysis: Overall CKD-aP Cohort

Itch Characteristics

Patients reported itch for a median (IQR) duration of 2.1 years (1.1-4.3 years), and 26% (N = 92) of the patients reported that itch was similar during both day and night (worse during the day: 9% [N = 30], worse at night: 13% [N = 46]). Participants' itch bother was predominantly type B (sometimes bothered; 59%, N = 210) based on the SADS, with 22% (N = 77) reporting type A (never bothered), and 18% (N = 65) type C (often bothered). Mean 5-D itch scores were consistently higher among participants in worse itch severity categories (Table 2). Detailed itch characteristics are summarized in Table S2.

Table 2. Itch Characteristics of Patients With CKD-aP

		Total (N = 354)	Mild (N = 76)	Moderate (N = 173)	Severe (N = 105)
Length of time skin has itched (y, [median (IQR, q25-q75)])		2.1 (1.1-4.3)	2.8 (0.8-5.0)	2.0 (1.1-4.0)	2.3 (1.2-4.3)
Time of worst/most intense itch, N (%)[a]	Day	30 (9)	16 (21)	13 (8)	1 (1)
	Night	46 (13)	17 (22)	21 (12)	8 (8)
	Both	92 (26)	18 (24)	47 (27)	27 (26)
	Missing	186	25	92	69
SADS, N (%)[a,b]	Type A	77 (22)	33 (43)	29 (17)	15 (14)
	Type B	210 (59)	40 (53)	116 (67)	54 (51)
	Type C	65 (18)	3 (4)	26 (15)	36 (34)
	Missing	2	.	2	.
5-D Itch[a]	Mean ± SD	14.3 ± 3.2	11.3 ± 2.4	14.2 ± 2.5	16.7 ± 2.8
	Missing	2	.	2	.
mWI-NRS[a]	Mean ± SD	5.6 ± 2.1	2.9 ± 1.1	5.5 ± 1.2	7.8 ± 1.2
	Missing	1	.	1	.

Note: % based on N.
Abbreviations: CKD-aP, chronic kidney disease-associated pruritus; IQR, interquartile range; mWI-NRS, modified Worst Itching Intensity Numeric Rating Scale; q, quartile; SADS, self-assessed disease severity; SD, standard deviation.
[a]Missing data are indicated as N or number of participants.
[b]Patient self-categorization of CKD-aP disease severity based on SADS score that was done depending on severity of concomitant signs and symptoms, ranging from type A (never) to type B (sometimes) to type C (often) patients bothered by scratch marks/sleep disturbances/agitation because of itch.

Table 3. CKD-aP Patient-Reported Experience With HCP and Symptom Management

Health Care Provider Experience		Worst Itch Group			
		Total	Mild	Moderate	Severe
Spoken to health care provider about itchy skin, N (%)[a]	N	354	76	173	105
	Yes	241 (68)	39 (51)	118 (68)	84 (80)
	No	88 (25)	33 (43)	40 (23)	15 (14)
	I do not recall	25 (7)	4 (5)	15 (9)	6 (6)
	Missing	.	.	.	.
Health care provider, N (%)[a,b]	N	241	39	118	84
	Primary care provider or family medicine	126 (52)	13 (33)	64 (54)	49 (58)
	Nephrologist (kidney)	151 (63)	28 (72)	72 (61)	51 (61)
	Dermatologist (skin)	91 (38)	10 (26)	50 (42)	31 (37)
	Dialysis technician	112 (47)	14 (36)	56 (48)	42 (50)
	Nurse practitioner/ physician's assistant	53 (22)	6 (15)	23 (20)	24 (29)
	Social worker	67 (28)	6 (15)	35 (30)	26 (31)
	Dietitian	27 (11)	3 (8)	10 (9)	14 (17)
	Other	40 (17)	9 (23)	19 (16)	12 (14)
	None of the above	1 (0)	0 (0)	1 (1)	0 (0)
	Missing	113	37	55	21
Started discussion about itchy skin, N (%)[b]	N	241	39	118	84
	I started the discussion	185 (77)	30 (77)	95 (81)	60 (71)
	My health care provider	37 (15)	8 (21)	16 (14)	13 (16)
	My family or friend	13 (5)	1 (3)	6 (5)	6 (7)
	My caregiver	4 (2)	0 (0)	1 (1)	3 (4)
	Someone else	2 (1)	0 (0)	0 (0)	2 (2)
	Missing	113	37	55	21
HCP diagnosed you with CKD-aP or itchy skin, N (%)	N	354	76	173	105
	Yes	193 (55)	31 (41)	97 (56)	65 (62)
	No	121 (34)	36 (47)	55 (32)	30 (29)
	I do not recall	40 (11)	9 (12)	21 (12)	10 (10)
	Missing	.	.	.	.
Time Since Diagnosis of Pruritus (y)[a]	N	158	24	74	60
	Median (IQR: q25-q75)	1.5 (1.0-3.0)	1.9 (0.5-5.0)	1.3 (1.0-2.3)	1.8 (1.0-3.2)
	Missing	196	52	99	45
Itchy skin associated with, N (%)[b]	N	161	45	76	40
	CKD/kidney failure	47 (29)	14 (31)	20 (26)	13 (33)
	Dialysis	27 (17)	8 (18)	13 (17)	6 (15)
	Both CKD/kidney failure and dialysis	75 (47)	16 (36)	40 (53)	19 (48)
	Something else	12 (8)	7 (16)	3 (4)	2 (5)
	Missing	193	31	97	65
HCP recommended treatment for itchy skin, N (%)	N	354	76	173	105
	Yes	196 (55)	26 (34)	102 (59)	68 (65)
	No	133 (38)	46 (61)	57 (33)	30 (29)
	I do not recall	25 (7)	4 (5)	14 (8)	7 (7)
	Missing	.	.	.	.
Symptom management					
Treatment used at any time, N (%)[b]	N	354	76	173	105
	Lotion or moisturizers	264 (75)	54 (71)	130 (75)	80 (76)
	Cold, wet cloth	87 (25)	12 (16)	40 (23)	35 (33)
	Corticosteroid creams/ hydrocortisone	168 (48)	29 (38)	79 (46)	60 (57)
	Other creams	76 (22)	15 (20)	32 (19)	29 (28)
	Oral prescription medications	72 (20)	10 (13)	35 (20)	27 (26)

(Continued)

Table 3 (Cont'd). CKD-aP Patient-Reported Experience With HCP and Symptom Management

Health Care Provider Experience		Worst Itch Group			
		Total	Mild	Moderate	Severe
	Oral OTC medications	110 (31)	14 (18)	54 (31)	42 (40)
	Phototherapy	14 (4)	3 (4)	6 (4)	5 (5)
	Other	345 (98)	73 (96)	168 (97)	104 (99)
	None of the above	6 (2)	4 (5)	2 (1)	0 (0)
Duration Of prescription medication use (y)[a]	N	58	6	26	26
	Median (IQR: q25-q75)	1.8 (0.8-2.8)	1.1 (0.3-1.4)	2.0 (1.1-2.5)	2.1 (0.7-4.2)
	Missing	296	70	147	79
Current treatment, N (%)	N	354	76	173	105
	Lotion or moisturizers	211 (60)	48 (63)	99 (57)	64 (61)
	Cold, wet cloth	59 (17)	9 (12)	24 (14)	26 (25)
	Corticosteroid creams/ hydrocortisone	103 (29)	13 (17)	52 (30)	38 (36)
	Other creams	43 (12)	7 (9)	17 (10)	19 (18)
	Oral prescription medications	48 (14)	7 (9)	23 (13)	18 (17)
	Oral OTC medications	78 (22)	5 (7)	41 (24)	32 (31)
	Phototherapy	7 (2)	2 (3)	3 (2)	2 (2)
	Other	8 (2)	3 (4)	4 (2)	1 (1)
	None of the above	14 (4)	4 (5)	8 (5)	2 (2)

Note. % based on N.
Abbreviations: CKD-aP, chronic kidney disease-associated pruritus; HCP, health care provider; IQR, interquartile range; OTC, over the counter; q, quartile; SD, standard deviation.
[a]Missing data are indicated as N or number of participant.
[b]Multiple responses possible.

Patients Experience with HCP and Symptom Management

Of 354 participants, 68% reported (N = 241) itch to an HCP, with a still higher frequency among those with more severe pruritus. A majority spoke to a nephrologist (63%, N = 151) and/or a primary care provider (52%, N = 126) about itch. Most participants initiated the discussions with their HCP (77%, N = 185), yet 45% (N = 161) were not given a diagnosis of CKD-aP, and 45% (N = 158) were not given a treatment recommendation (Table 3). Across all itch severity levels, the most common and frequently ever used treatments were lotion/moisturizers (75%, N = 264) and topical corticosteroids (48%, N = 168). Overall, 20% (N = 72) of patients reported ever using an oral prescription medication for itch. Among current users of respective treatments, more than one-third of the participants were not satisfied with their current use of lotions/moisturizers (38%, N = 79) or corticosteroids (34%, N = 34), and 17% (N = 8) were not satisfied with their oral prescription medication. Other treatment types and patterns are summarized in Table S3.

Itch Effect on Hemodialysis

The proportion of participants reporting (often or sometimes) shortening dialysis sessions because of itchy skin was higher among participants with more severe itch (overall: 23%, N = 80; mild: 6%, N = 5; moderate: 22%, N = 37; severe: 37%, N = 38), with a significant overall difference across all itch severity groups (P < 0.001). Similarly, participants who reported extra unscheduled dialysis sessions attributed to having shortened sessions because of itch also differed significantly among the groups (mild: 15%, N = 2; moderate: 35%, N = 32; severe: 57%, N = 37; P < 0.001) (Fig 1).

Similarly, participants with more severe itch skipped dialysis sessions with greater frequency (overall: 17%, N = 61; mild: 5%, N = 4; moderate: 13%, N = 23 severe: 33%, N = 34; P < 0.001), and who attended (often or sometimes) extra, unscheduled dialysis sessions because of skipping sessions (mild: 50%, N = 4; moderate: 37%, N = 23; severe: 64%, N = 35; P = 0.003) (Fig 1). The proportion of patients with CKD-aP reporting high or extremely high itch burden during dialysis was also significantly higher among those in more severe itch group (mild: 5%, N = 4; moderate: 21%, N = 36; severe: 54%, N = 57; P < 0.001) (Fig 2).

Effect on Work Productivity

A total of 151 participants (43%) reported employment or self-employment (Table 1). WPAI-based work productivity showed that participants experienced a mean of absenteeism 21.5% (SD ± 25.4), presenteeism 49.5% (SD ± 25.9), overall work impairment 36.9% (SD ± 21.1), and overall activity impairment 44.2% (SD ± 28.2) of the time. WPAI scores differed significantly across itch severity levels for absenteeism, presenteeism, overall work impairment, and overall activity impairment (all P < 0.001) (Fig 3).

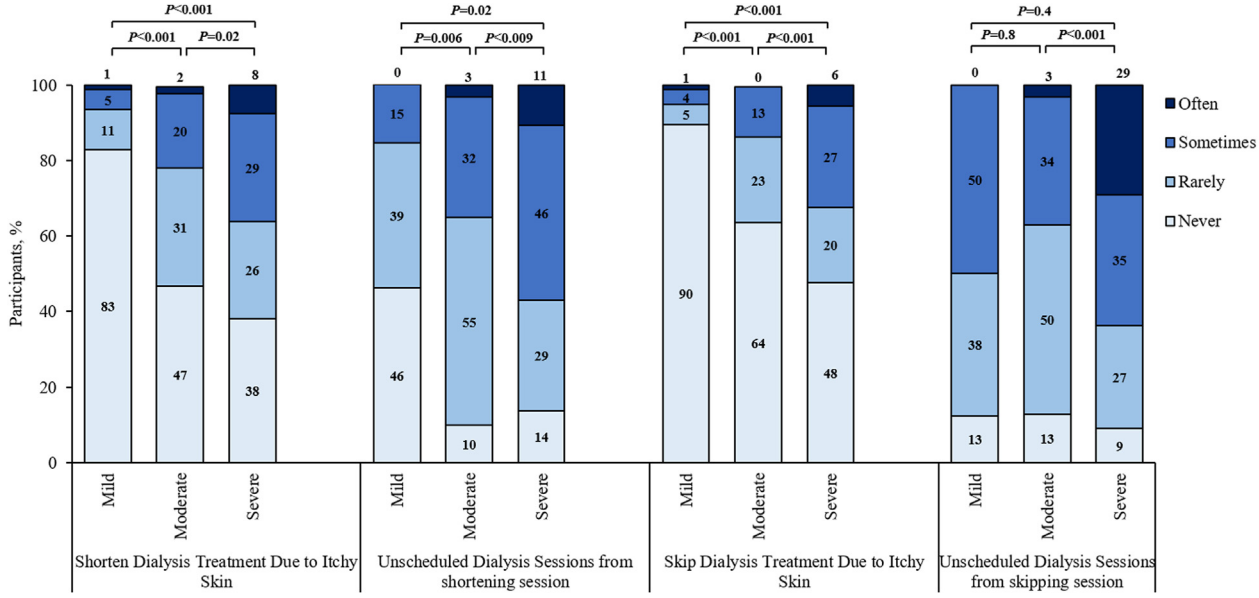

Figure 1. Overview of frequency of participants reporting effect on hemodialysis time.[a]
Note: Missing data were not imputed in the figure. Accordingly, the total of patients for analysis could vary between variables but is computed for each parameter.
P value indicates significant difference in the various parameters in Fig 1, across the itch severity groups.
[a]Overall *P* value < 0.05.

Bivariate Analysis: Quality of Life and Sleep Quality by Itch Severity

Bivariate analysis using KDQoL-SF survey scores showed lower scores among participants with more severe itch. As itch severity worsened, all the parameters evaluated through the KDQoL-SF survey including symptom list scores, effect of kidney disease (KD) score, burden, cognitive function, quality of social interaction, sleep (all $P < 0.001$), and sexual function ($P < 0.05$) were significantly affected, resulting in lower scores (Table 4).

Regarding the mean BII sleep score, on average, participants slept poorly (mean BII score: 5.0 ± 2.7). Those with severe itch had the most sleep disturbance, followed by those with moderate itch, and then those with mild itch. (Fig 4).

DISCUSSION

This cross-sectional survey-based study evaluated the clinical treatment journey and pruritus-related burden among adults with CKD-aP undergoing HD. Study findings elucidate the overall effect of disease burden on HCP engagement, CKD-related QoL, HD participation, and work productivity. We also found that pruritus severity was associated with QoL measures and sleep quality.

Compared with the Dialysis Outcome and Practice Patterns Study (DOPPS),[27] the present study population is younger and had more women and White participants. Inclusion of prior itch as an eligibility criteria, being an online survey, small sample size, and a different scoring system (mWI-NRS) applied for CKD-aP classification in the present study may account for this difference between the current study and the DOPPS study.[8] Present study findings were further strengthened by exclusion of the patients with mWI-NRS score of 0. Additionally, the use of a PAG for recruitment may have resulted in higher recruitment of patients with more severe pruritus.

In the current study, 68% of participants (with mild-to-severe itch) reported speaking to a HCP about itchy skin, leaving almost one-third of patients with unreported itch. The underreporting of itch was also found in the DOPPS study in which 17% of CKD-aP patients who were nearly always or always bothered by itch underreported itch symptoms.[5] Of the patients who spoke to a HCP about itchy skin, 77% initiated the conversation, and almost half (45%) reported not receiving any treatment recommendations. Patients with CKD underreport their pruritus, largely because of a lack of awareness of its link with CKD/ESRD or acceptance of it as a chronic symptom.[28] HCPs often underestimate how common and serious CKD-aP is. This underestimation leads to missed opportunities to improve patients' QoL and reduce the economic burden on society. If HCPs talk to patients about itching or screen them for CKD-aP, they may improve diagnosis and treatment.[28] These findings emphasize the need to establish a checklist or guideline for HCPs for routinely assessing pruritus and to establish general treatment practices to ensure patients are receiving appropriate care. Additionally, health care teams should educate patients about the relationship between their kidney disease and pruritus to encourage self-advocacy.[28]

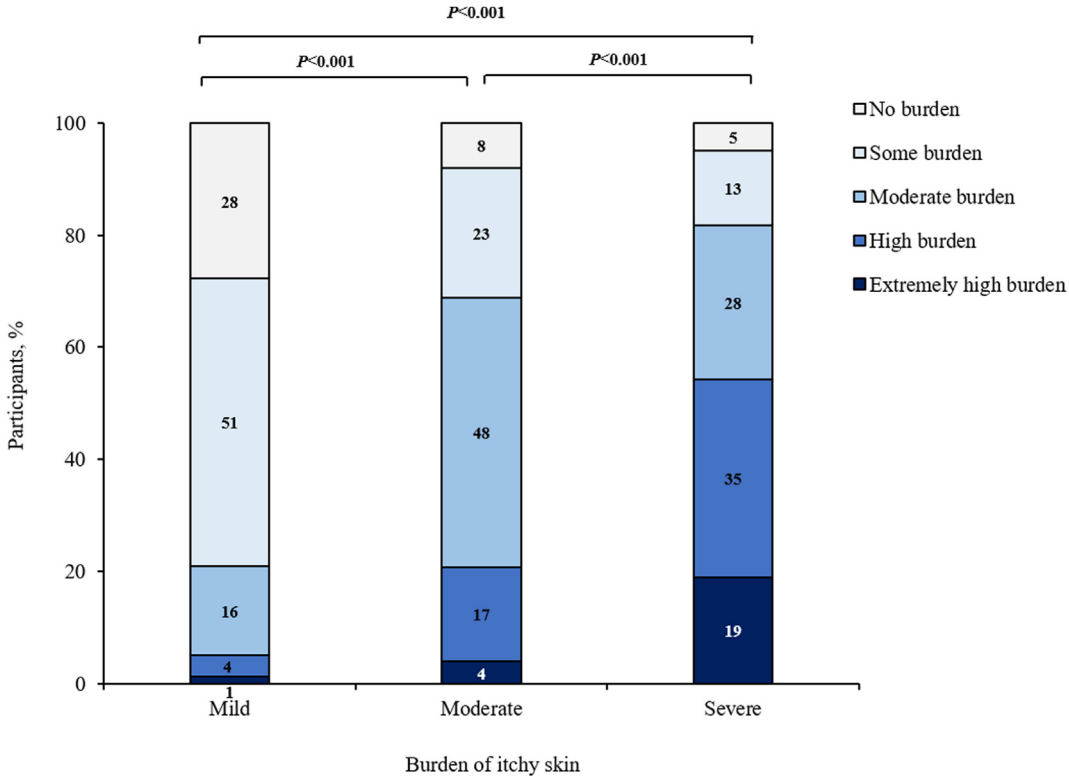

Figure 2. Overview of frequency of participants reporting burden of itchy skin in itch severity groups (mild/moderate/severe).[a]
Note: Missing data were not imputed in the figure. Accordingly, the total of patients for analysis could vary between variables but is computed for each parameter. *P* value indicates significant difference in the various parameters in Fig 2, across the itch severity groups.
[a]Overall *P* value < 0.001.

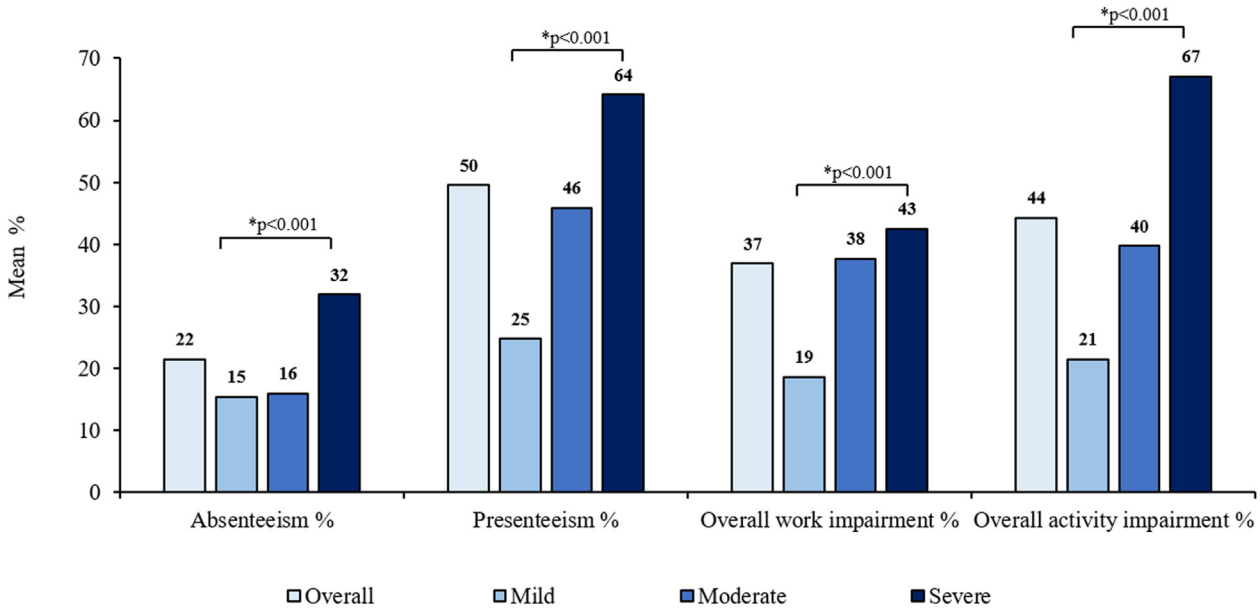

Figure 3. Itch effect on work impairment in patients with CKD-aP.
Note: Missing data were not imputed in the figure. Accordingly, the total of patients for analysis could vary between variables but is computed for each parameter.
*Indicates overall *P* value among the itch severity groups across the WPAI scores (absenteeism, presenteeism, overall work impairment and overall activity impairment).

Table 4. Bivariate Analysis: Quality of Life and Itch Severity

	Total (N = 354)	Mild (N = 76) (a)	Moderate (N = 173) (b)	Severe (N = 105) (c)	a vs b		a vs c		b vs c		Overall *P* Value
					Difference (95% CI)	*P* Value	Difference (95% CI)	*P* Value	Difference (95% CI)	*P* Value	
KDQoL-SF ™											
Symptom List Score[a]											
N	350	76	169	105	8.4 (4.2-12.6)	<0.001	26.9 (21.0-32.9)	<0.001	18.6 (14.0-23.1)	<0.001	<0.001
Mean ± SD	57.6 ± 20.7	69.7 ± 15.3	61.4 ± 15.7	42.8 ± 22.7							
Missing	4	.	4	.							
Effect of KD Score[a]											
N	350	74	172	104	10.6 (5.0-16.2)	<0.001	23.0 (16.2-29.8)	<0.001	12.4 (7.1-17.7)	<0.001	<0.001
Mean ± SD	46.9 ± 23.0	58.9 ± 20.9	48.4 ± 20.3	35.9 ± 23.7							
Missing	4	2	1	1							
Burden of KD Score[a]											
N	352	75	172	105	10.8 (5.0-16.5)	<0.001	17.3 (10.2-24.3)	<0.001	6.5 (1.2-11.9)	0.02	<0.001
Mean ± SD	30.4 ± 22.9	40.8 ± 22.5	30.1 ± 20.6	23.6 ± 24.2							
Missing	2	1	1	.							
Work Status Score[a]											
N	353	76	172	105	−4.2 (−15.2 to 6.9)	0.5	1.1 (−10.3 to12.6)	0.8	5.3 (−4.3 to 14.9)	0.3	0.5
Mean ± SD	38.5 ± 39.6	36.8 ± 40.3	41.0 ± 40.7	35.7 ± 37.2							
Missing	1	.	1	.							
Cognitive Function Score											
N	354	76	173	105	8.2 (3.1-13.3)	0.002	22.1 (14.9-29.2)	<0.001	13.9 (8.2-19.5)	<0.001	<0.001
Mean ± SD	65.2 ± 23.4	75.7 ± 17.1	67.5 ± 19.7	53.7 ± 28.1							
Missing	.	.	.	.							
Quality of Social Interaction Score											
N	354	76	173	105	7.6 (3.0-12.2)	0.001	17.5 (11.2-23.9)	<0.001	10.0 (5.2-14.7)	<0.001	<0.001
Mean ± SD	61.7 ± 20.1	70.6 ± 17.6	63.0 ± 16.7	53.1 ± 23.6							
Missing	.	.	.	.							
Sexual Function Score[a]											
N	127	27	63	37	14.2 (2.1-26.2)	0.02	20.1 (5.4-34.9)	0.008	6.0 (−6.0 to 17.9)	0.3	0.02
Mean ± SD	65.4 ± 28.8	78.2 ± 24.4	64.1 ± 27.2	58.1 ± 32.0							
Missing	227	49	110	68							
Sleep Score[a]											
N	352	76	171	105	2.7 (−1.8 to 7.2)	0.2	10.8 (5.8-15.9)	<0.001	8.1 (3.9-12.4)	<0.001	<0.001
Mean ± SD	48.1 ± 17.5	52.7 ± 15.8	50.0 ± 17.1	41.8 ± 17.9							
Missing	2	.	2	.							
Social Support Score											
N	354	76	173	105	3.1 (−3.6 to 9.7)	0.4	6.1 (−1.9 to 14.1)	0.1	3.0 (−3.5 to 9.5)	0.4	0.3
Mean ± SD	61.8 ± 26.0	65.1 ± 23.1	62.0 ± 25.1	59.0 ± 29.3							
Missing	.	.	.	.							

(Continued)

Table 4 (Cont'd). Bivariate Analysis: Quality of Life and Itch Severity

	Total (N = 354)	Mild (N = 76) (a)	Moderate (N = 173) (b)	Severe (N = 105) (c)	a vs b		a vs c		b vs c		Overall
					Difference (95% CI)	*P* Value	Difference (95% CI)	*P* Value	Difference (95% CI)	*P* Value	*P* Value
Dialysis Staff Score											
N	354	76	173	105	3.4 (−2.7 to 9.5)	0.3	0.4 (−6.4 to 7.2)	0.9	−3.0 (−8.8 to 2.8)	0.3	0.4
Mean ± SD	73.9 ± 23.2	75.7 ± 20.4	72.3 ± 23.4	75.2 ± 24.6							
Missing	.	.	.	.							
Patient Satisfaction Score[a]											
N	352	76	171	105	2.9 (−3.1 to 8.9)	0.3	0.3 (−6.8 to 7.3)	0.9	−2.6 (−8.1 to 2.9)	0.4	0.5
Mean ± SD	63.9 ± 22.6	65.4 ± 23.1	62.5 ± 21.6	65.1 ± 24.1							
Missing	2	.	2	.							

Abbreviations: CI, confidence interval; KDQoL-SF ™, kidney disease Quality of Life; KD Score, kidney disease score; SD, standard deviation.
[a]Missing data are indicated as N or number of participants.

Across all levels of pruritus severity, lotions/moisturizers (75%) and corticosteroids (48%) were the most common treatments used for itchy skin at any time, similar to previously published studies.[6] Only 20% of patients reported ever using any kind of oral prescription medication for their itchy skin, similar to the percentage reported in previous studies.[5] Patients reported trying many different treatments for long durations, with use and duration higher among those with more severe pruritus. One-third of the study population reported dissatisfaction with treatment, including almost one-fourth of patients being dissatisfied with oral prescription treatment. Dissatisfaction with treatment, despite or irrespective of high treatment utilization, suggests patients have consequential unmet treatment needs that require further examination.

We examined the burden of pruritus on dialysis treatment adherence. Across all pruritus severity, 23% of patients reported shortening and 17% reported missing HD sessions because of itch. More than one-third (37%) of patients reported shortening and 33% reported skipping dialysis sessions because of severe itch. Moreover, patients with more severe pruritus reported missed dialysis and extra unscheduled dialysis sessions with greater frequency. Adherence to HD schedule is challenging in patients with ESKD for a variety of reasons.[29] Missing or shortening sessions may lead to increased risk of mortality and adverse events.[30] This study highlights a potential disconnect between diagnosing and treating pruritus in these patients. This disconnect may represent a missed opportunity to improve adherence to HD schedules.

Patients with CKD-aP also reported a loss of work productivity and overall work impairment, suggesting not just personal and financial, but also societal economic consequences of CKD-aP. Patients experienced loss of overall work productivity for >30% of the time (20% of which from absenteeism) and overall activity impairment for nearly 50% because of their itch. The loss in work productivity and activity impairments were more common among participants with more severe pruritus. The effect of pruritus on work productivity may contribute to an individual going on disability instead of potentially maintaining some form of employment and being able to support a family, own a home, and/or retire securely.

We estimated the effect of CKD-specific QoL among patients undergoing HD by employing the KDQoL-SF survey and the BII sleep score. The association of CKD-aP with poor HRQoL has been shown in previous studies.[1,3,31] Although there are some studies examining the relationship between pruritus severity and QoL,[9,32,33] the current study further adds to this growing body of research. Findings in the present study showed significantly lower KDQoL scores among participants with more severe pruritus, including mean symptom score, KD scores, burden of KD scores, cognitive function scores, quality of social interaction scores, sleep score, and sexual function score. The previously reported association

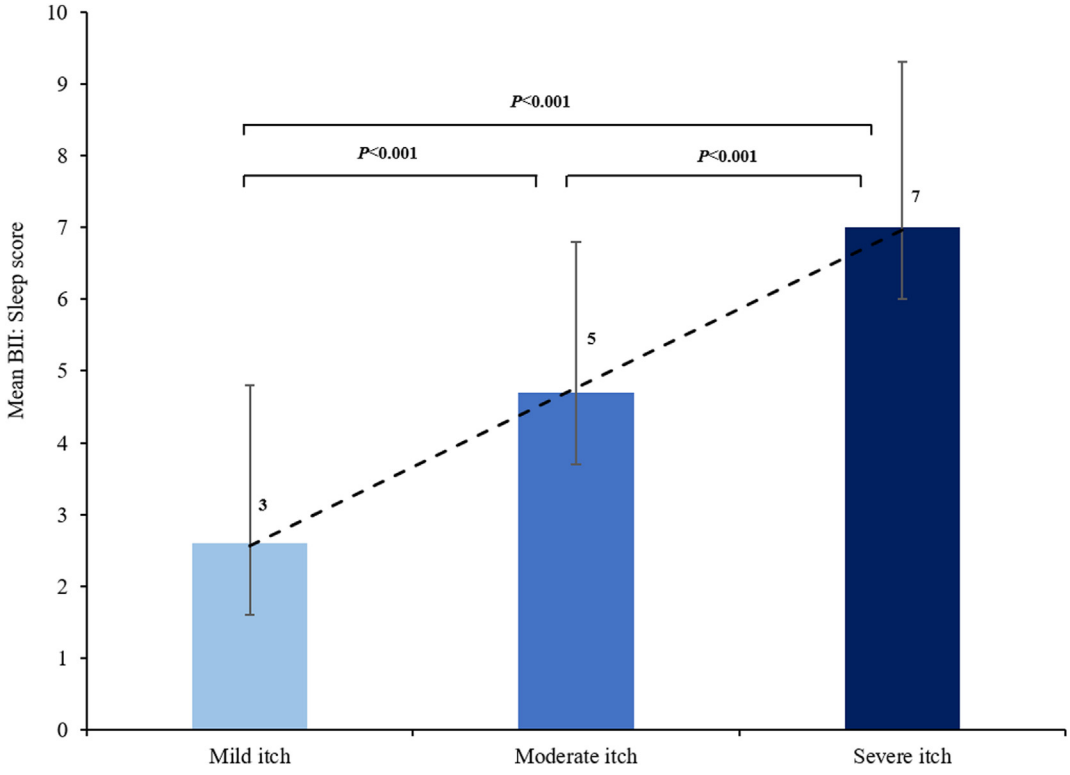

Figure 4. BII: Sleep scores among various itch severity groups. Dotted line indicates a linear trendline. Note: Missing data were not imputed in the figure. Accordingly, the total of patients for analysis could vary between variables but is computed for each parameter. Abbreviation: BII, Brief Itching Inventory.

between severe pruritus and poorer sleep quality was further underlined by the significantly lower sleep quality among participants with more severe pruritus.[34,35] Overall, our study findings demonstrate a strong association between severity of pruritus and CKD-specific HRQoL and sleep, which may be related to patients not being diagnosed or satisfactorily treated earlier during the progression of pruritus severity.

The main strength of the present study is that the findings reflect patients' perspectives on their burden because of CKD-aP. We measured self-reported work impairment and were able to address both employer-based and self-employed work efforts.

Limitations of the study include possible recall bias, especially for questions with longer recall periods. Participants may have underreported their diagnosis as "CKD-aP" because this is a new clinical term that might be recognized by clinicians or patients as different from uremic pruritus. The study assessed itching in all participants, regardless of a diagnosis of CKD-aP or other skin conditions such as atopic dermatitis, eczema, or psoriasis. This approach might have included reports of itching caused by factors other than CKD-aP. This study did not collect data on the type of dialysis (length and number of sessions per week, HD or hemodiafiltration, and type of dialyzer) that may provide more insights around dialysis burden. Any bias attributed to patients volunteering in research efforts and/or engaged in PAGs, convenience sampling and nongeneralizability of the results to the US hemodialysis population (eg, compared with US Renal Data System data, our study population was younger, had lower prevalence of Blacks, and higher levels of education and employment) can also be considered as further limitations.

In conclusion, the present study highlights the significant pruritus-related burden experienced by patients with CKD-aP undergoing HD. Pruritus, which is often underdiagnosed and undertreated, can disrupt necessary dialysis treatment, potentially leading to poor clinical outcomes. Almost half of the study population were not being given treatment recommendations by HCPs. Among patients who were treated, a large proportion were highly dissatisfied. Pruritus has often been considered a less severe symptom to HCPs; however, this study highlighted that pruritus severity closely relates to patients' QoL, cognitive function, and sleep quality. These findings provide additional insights into the effect of CKD-aP on patients' interactions with HCPs, their treatment journey, symptom management, work productivity, and overall QoL; furthermore, it identifies an opportunity for improvement

of HD adherence by diagnosing and treating pruritus earlier and more effectively.

SUPPLEMENTARY MATERIALS

Supplementary File (PDF)

Figure S1: Study population.

Table S1: Comorbid Conditions Associated with CKD-aP Patients.

Table S2: Itch Characteristics in CKD-aP Patients.

Table S3: Symptom Management in CKD-aP Patients.

ARTICLE INFORMATION

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REFERENCES

1. Shirazian S, Aina O, Park Y, et al. Chronic kidney disease-associated pruritus: Impact on quality of life and current management challenges. *Int J Nephrol Renovasc Dis*. 2017;10:11-26.
2. Verduzco HA, Shirazian S. CKD-associated pruritus: new insights into diagnosis, pathogenesis, and management. *Kidney Int Rep*. 2020;5(9):1387-1402.
3. Kim D, Pollock C. Epidemiology and burden of chronic kidney disease-associated pruritus. *Clin Kidney J*. 2021;14(Supplement_3):i1-i7.
4. Pisoni RL, Wikström B, Elder SJ, et al. Pruritus in haemodialysis patients: International results from the Dialysis Outcomes and Practice Patterns Study (DOPPS). *Nephrol Dial Transplantation*. 2006;21(12):3495-3505.
5. Rayner HC, Larkina M, Wang M, et al. International comparisons of prevalence, awareness, and treatment of pruritus in people on hemodialysis. *Clin J Am Soc Nephrol*. 2017;12(12):2000-2007.
6. Wang CCY, Wu HHL, Ponnusamy A, Pye I, Woywodt A. Pruritus in chronic kidney disease: an update. *Allergies*. 2022;2(3):87-105.
7. Sukul N, Speyer E, Tu C, et al. Pruritus and patient reported outcomes in in non-dialysis CKD. *Clin J Am Soc Nephrol*. 2019;7;14(5):673-681.
8. Sukul N, Karaboyas A, Csomor PA, et al. Self-reported pruritus and clinical, dialysis-related, and patient-reported outcomes in hemodialysis patients. *Kidney Med*. 2021;3(1):42-53.e1.
9. Lopes MB, Karaboyas A, Sukul N, et al. Utility of a single itch-related question and the Skindex-10 questionnaire for assessing pruritus and predicting health-related quality of life in patients receiving hemodialysis. *Kidney Med*. 2022;4(6):100476.
10. Makar M, Smyth B, Brennan F. Chronic kidney disease-associated pruritus: a review. *Kidney and Blood Press Res*. 2021;46(6):659-669.
11. Lipman ZM, Paramasivam V, Yosipovitch G, Germain MJ. Clinical management of chronic kidney disease-associated pruritus: current treatment options and future approaches. *Clin Kid J*. 2021;14(Supplement_3):i16-i22.
12. Jha C, Dastoor HD, Holt SG. Obstacles to early diagnosis and treatment of pruritus in patients with chronic kidney disease: current perspectives. *Int J Nephrol Renovas Dis*. 2022;(15):335-352.
13. Mehrotra R, Davison SN, Farrington K, et al. Managing the symptom burden associated with maintenance dialysis: conclusions from a Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference. *Kidney Int*. 2023;104(3):441-454.
14. KORSUVA (difelikefalin) Label. US Food and Drug Administration; Published 2021. Accessed June 20, 2023. https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/214916s000lbl.pdf
15. Kapruvia (difelikefalin). European Medicines Agency; Published 2022. Accessed June 20, 2023. https://www.ema.europa.eu/en/medicines/human/EPAR/kapruvia
16. DISQO homepage. DISQO; 2022. Accessed March 10, 2023. https://www.disqo.com/
17. Rare Patient Voice home page. Rare Patient Voice; 2022. Accessed March 10, 2023. https://rarepatientvoice.com/

18. ROI Rocket home page. ROI Rocket; 2022. Accessed March 10, 2023. https://www.roirocket.com/
19. Storck M, Sandmann S, Bruland P, et al. Pruritus intensity scales across Europe: a prospective validation study. *J Eur Acad Dermatol Venereol*. 2021;35(5):1176-1185.
20. Reich A, Chatzigeorkidis E, Zeidler C, et al. Tailoring the cut-off values of the visual analogue scale and numeric rating scale in itch assessment. *Acta Derm Venereol*. 2017;97(6):759-760.
21. Verweyen E, Ständer S, Kreitz K, et al. Validation of a comprehensive set of pruritus assessment instruments: The chronic pruritus tools questionnaire PRURITOOLS. *Acta Derm Venereol*. 2019;99(7):657-663.
22. Mathur VS, Lindberg J, Germain M, et al. A longitudinal study of uremic pruritus in hemodialysis patients. *Clin J Am Soc Nephrol*. 2010;5(8):1410-1419.
23. Elman S, Hynan LS, Gabriel V, Mayo MJ. The 5-D itch scale: a new measure of pruritus. *Br J Dermatol*. 2010;162(3):587-593.
24. Reilly MC, Zbrozek AS, Dukes EM. The validity and reproducibility of a work productivity and activity impairment instrument. *Pharmacoeconomics*. 1993;4(5):353-365.
25. Hays Ron D, Kallich Joel D, Mapes Donna L, et al. *Kidney Disease Quality of Life Short Form (KDQOL-SF™), Version 1.3: A Manual for Use and Scoring*. RAND. 1997::7994
26. Hays RD, Stewart AL. Sleep measures. In: Stewart AL, Ware JE, eds. Measuring Functioning and Well-Being: The Medical Outcomes Study Approach. Duke University Press: 1992:235-259. Duke University Press.
27. Young EW, Goodkin DA, Mapes DL, et al. The Dialysis Outcomes and Practice Patterns Study (DOPPS): An international hemodialysis study. *Kidney International*. 2000;57(74):74-81.
28. Aresi G, Rayner HC, Hassan L, et al. Reasons for underreporting of uremic pruritus in people with chronic kidney disease: a qualitative study. *J Pain Symptom Manage*. 2019;58(4):578-586.e2.
29. Kammerer J, Garry G, Hartigan M, Carter B, Erlich L. Adherence in patients on dialysis: strategies for success. *Nephrol Nurs J*. 2007;34(5):479-486.
30. Foley RN, Gilbertson DT, Murray T, Collins AJ. Long interdialytic interval and mortality among patients receiving hemodialysis. *N Engl J Med*. 2011;365(12):1099-1107.
31. Weiss M, Mettang T, Tschulena U, Weisshaar E. Health-related quality of life in haemodialysis patients suffering from chronic itch: results from GEHIS (German Epidemiology Haemodialysis Itch Study). *Qual Life Res*. 2016;25(12):3097-3106.
32. Hernandez Alava M, Sasso A, Hnynn Si PE, et al. Relationship between standardized measures of chronic kidney disease-associated pruritus intensity and health-related quality of life measured with the EQ-5D questionnaire: a mapping study. *Acta Dermato Venereol*. 2023;103:1-8.
33. Poku E, Harnan S, Rooney G, et al. The relationship between chronic kidney disease–associated pruritus and health-related quality of life: a systematic review. *Clin Kidney J*. 2022;15(3):484-499.
34. Ur Rehman I, Chohan TA, Bukhsh A, Khan TM. Impact of pruritus on sleep quality of hemodialysis patients: A systematic review and meta-analysis. *Medicina*. 2019;55(10):1-11.
35. Daraghmeh M, Badran M, Janajreh A, et al. Prevalence of pruritus associated with hemodialysis and its association with sleep quality among hemodialysis patients: a multicenter study. *BMC Nephrol*. 2022;23(1):213.