



The Burden of Pruritus Associated With CKD: A Mixed Methods Analysis Among Patients Undergoing Dialysis

Frédérique Menzaghi, Margaret K. Vernon, Maria Mattera, Joshua Cirulli, Warren Wen, Robert H. Spencer, and Catherine Munera

Rationale & Objective: Despite its prevalence and distress to patients, chronic kidney disease-associated pruritus (CKD-aP) is poorly characterized, which may contribute to the condition's underdiagnosis and inadequate management. This study aimed to understand the symptom experience of patients with CKD-aP and the extent to which pruritus impacts their lives.

Study Design: Mixed methods study including one-on-one qualitative interviews and completion of the Skindex-10 Questionnaire (measuring itch-related quality of life).

Setting & Participants: A total of 23 patients undergoing hemodialysis and reporting pruritus at 4 dialysis centers in the United States.

Analytical Approach: Interviews followed a semi-structured guide that included targeted and follow-up questions to elicit discussion of patients' symptoms of pruritus, including frequency and variability, impact on activities of daily living, and emotional and social functioning. Interviews were digitally audio-recorded. A coding dictionary was developed from transcripts to analyze themes and concepts.

Results: Participants described their itch with various terms, including "numbness," "pain,"

and "tingling" on their skin. Itch affected multiple areas but especially the back, usually occurred daily, and was often worse at night. For some, itching was a constant experience. Patients relieved their itch through scratching and various off-label treatments; some reported skin damage from excessive scratching and most indicated treatments provided limited relief. Pruritus considerably disrupted physical function, including sleep, daily activities, social functioning and relationships, and emotional and psychological wellbeing. All participants reported being bothered by their itching during the past week on the Skindex-10 Questionnaire.

Limitations: All participants were from the United States, so the findings may not be generalizable to other countries.

Conclusions: Although symptom experience varies considerably, CKD-aP causes severe distress for many patients undergoing hemodialysis and can profoundly impair their quality of life. The results of this study show the impact of itch from patients' perspectives and highlight the need for greater awareness and better management of this condition.

Complete author and article information provided before references.

Correspondence to
F. Menzaghi (imenzaghi@caratherapeutics.com)

Kidney Med. 5(9):100696.
Published online July 1, 2023.

doi: [10.1016/j.xkme.2023.100696](https://doi.org/10.1016/j.xkme.2023.100696)

© 2023 The Authors.
Published by Elsevier Inc.
on behalf of the National
Kidney Foundation, Inc. This
is an open access article
under the CC BY-NC-ND
license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Pruritus, or itch, is a common but overlooked symptom of chronic kidney disease (CKD).¹⁻⁵ The underlying mechanisms causing CKD-associated pruritus (CKD-aP) remain poorly understood.³ More than 60% of patients treated by hemodialysis have some degree of pruritus, and the pruritus is moderate to severe in intensity in up to 40% of cases.⁵⁻⁹ The itching often results in a relentless urge to scratch and can be severely distressing for patients who experience it frequently.¹⁰ The itching sensation is systemic and persistent, and scratching to relieve the itch frequently results in skin damage. Until recently, there was no approved treatment indicated specifically for CKD-aP outside Japan and South Korea.^{5,8,11-14} However, in 2021, intravenous difelikefalin was approved for moderate-to-severe CKD-aP in adults treated with hemodialysis.^{15,16}

A key issue is that despite its prevalence and considerable impact on patients, CKD-aP is not commonly discussed between patients and clinicians and is therefore frequently underdiagnosed and poorly managed.^{17,18} Reasons for this undertreatment may be related to patients' or clinicians' poor awareness of the link between itch and CKD, few effective

treatment options for itch, attitudes that itch is not an important health issue, and lack of itch assessment during routine consultations.¹⁸ However, untreated itch is associated with disturbed sleep, depression, missed dialysis sessions, higher resource use, lower general health, and poorer quality of life (QoL).^{6-8,19-23} Improving itch management and treatment is a priority among patients²⁴ and is advocated for in CKD clinical care recommendations.^{2,25} Thus, it is essential to better understand patients' experience of CKD-aP and how it affects their lives. Most studies that have characterized pruritus have used patient surveys or descriptive designs that do not include a qualitative element based on patient interviews.^{22,26,27} Although these studies show patients are significantly impacted by itch based on patient-reported outcome measures, such as the 5D-Itch and various QoL instruments,^{22,27-29} they generally do not include patients' perspectives and experiences of their pruritus in their own words. In this study, we report the findings from one-on-one qualitative interviews that aimed to understand the symptom experience of patients with CKD-aP and the extent to which pruritus impacts their lives.

PLAIN-LANGUAGE SUMMARY

Patients with chronic kidney disease often experience itching, or pruritus, but its importance to patients is regularly overlooked. This study used one-on-one interviews to investigate patients' experiences of chronic kidney disease-associated pruritus and how it impacts their lives. We found that participants experienced itch on various body areas and used different words to describe their itch (eg, "numbness" and "pain"). Some reported skin damage from excessive scratching, and many used off-label treatments and other interventions (eg, rubbing alcohol and multiple showers daily), which provided limited relief. For many, itching was experienced daily and severely disrupted sleep, daily activities, interactions with others, and mental well-being. These findings reveal chronic kidney disease-associated pruritus severely impacts patients and highlights the need for improved management of this condition.

METHODS

Study Design

One-on-one qualitative interviews were conducted in 23 adult (≥ 18 years old) patients undergoing hemodialysis experiencing CKD-aP of any severity. Interview study protocols were approved by an institutional review board (Advarra Inc; approval numbers available on request), and recruitment procedures complied with Health Insurance Portability and Accountability Act regulations. All participants provided their written informed consent before interviews.

Participants

Purposive sampling was used by clinical site personnel to identify and recruit participants from 4 dialysis centers in the United States, based on a review of patient databases, charts, and daily appointment schedules. Patients had to be receiving hemodialysis 3 times per week for ≥ 3 months before screening, self-report experiencing pruritus within the past month, and be able to speak and understand English. Participants were excluded if they were known to be nonadherent with dialysis treatment, had pruritus unrelated to CKD as assessed by their nephrologist, had localized itch restricted to the palms of the hands, or experienced pruritus only during dialysis sessions. Patients were asked at screening to complete the Self-Categorization of Pruritus Disease Severity questionnaire,⁸ which required them to determine to what extent itch made them feel agitated or sad, interfered with their sleep, and left scratch marks on their skin. This was used to classify patients with mild (A), moderate (B), or severe (C) symptoms (see [Table S1](#)). Each center was encouraged to recruit demographically diverse participants with different

pruritus severities (based on Self-Categorization of Pruritus Disease Severity questionnaire scores).

Data Collection

Interviews followed a semistructured interview guide (see [Item S1](#)) that included targeted questions and probes to elicit further discussion on CKD-aP symptoms, their frequency and variability, and the day-to-day impact of itch. Participants were aware of the research topic and interview goals before the interview. Interviews were completed in-person in English at the clinical sites from June-August 2016. The qualitative element was designed to last approximately 15 minutes. Additional time was allocated for participants to complete the Worst Itching Intensity Numeric Rating Scale (WI-NRS) and the Skindex-10 Questionnaire—validated instruments for measuring itch intensity and itch-related QoL in patients with CKD-aP^{8,30,31} ([Table S1](#)). Experienced scientific staff (from Evidera) were trained on the semistructured interview guide before interviewing participants. Only the participant and the trained interviewer were present during the interviews. Participants did not know the interviewer before the study but were informed briefly about the interviewer's qualifications during the interview.

Participants were asked to describe the characteristics of their itch (eg, nature, location, duration, frequency, severity, and triggers), its impact on their lives (eg, daily activities, relationships with others, and emotions), treatments they had tried, and importance relative to other medical conditions.

Interviews were digitally audio-recorded with the consent of the participants. After the interview, participants completed a brief sociodemographic questionnaire and were remunerated for their participation.

Confirmatory Qualitative Analysis

To confirm themes and concepts of the symptom experience, we analyzed qualitative data collected in 'exit interviews' (n=70) of hemodialysis participants with moderate-to-severe CKD-aP who had completed 1 of 2 phase 3 randomized controlled trials of difelikefalin.^{32,33} Full details of the methodology are provided in [Item S2](#), and the reported itching characteristics are noted in [Table S2](#).

Analysis

Recordings of interviews were professionally transcribed, and transcripts were reviewed for quality assurance purposes and to remove any personal health information. Transcripts were analyzed in ATLAS.ti (version 7.5.12 or higher) using a thematic content analysis approach, with participant statements being the unit of analysis (eg, words and phrases) to capture concepts and themes. Coding dictionaries were developed based on the themes and concepts that emerged during each group of interviews. An initial transcript was independently coded by one

Table 1. Patient Characteristics

Characteristic	Value (N=23)
Age (y)	
Median (range)	61.0 (25.0-82.0)
Sex, n (%)	
Male	14 (60.9)
Female	9 (39.1)
Race, n (%) ^a	
White	10 (43.5)
Black or African American	6 (26.1)
Asian	1 (4.3)
American Indian or Alaskan native	1 (4.3)
Other	8 (34.8)
Ethnicity, n (%)	
Not Hispanic or Latino	15 (65.2)
Hispanic or Latino	8 (34.8)
Years on hemodialysis, mean (SD)	5.4 (5.1)
Years with CKD-aP, mean (SD)	2.9 (3.0)
Self-Categorization of Pruritus Disease Severity, n (%) ^b	
A (mild)	4 (17.4)
B (moderate)	9 (39.1)
C (severe)	10 (43.5)

Full details of the participants' demographics and clinical characteristics are published previously.³¹

Abbreviations: CKD-aP, chronic kidney disease-associated pruritus; SD, standard deviation.

^aNot mutually exclusive.

^bSelf-Categorization of Pruritus Disease Severity questionnaire completed at screening (description of this measure given in Table S1).

researcher using the coding dictionary, and this was reviewed by another researcher to ensure that all relevant responses were captured and that coders were interpreting and using codes consistently, as intended. A postcoding comparison and reconciliation occurred with the coders and a senior staff member, in which all codes were compared, discussed, and reconciled wherever differences occurred, to refine the concepts and respective definitions. The remaining transcripts were then coded by a single coder and quality reviewed by a senior researcher to identify inconsistencies or potential errors requiring clarification, which were then flagged for investigation, with final decisions based on consensus discussion. Qualitative results were summarized and interpreted to assess participants' endorsement of symptom and impact concepts and to identify key themes emerging from the interviews. Participants were not involved in the interpretation stage of this study and did not provide feedback on the transcripts or findings.

RESULTS

Participant Characteristics

The 23 participants had a median age of 61.0 years (range, 25.0-82.0 years), were mostly male (60.9%) and White (43.5%), and had been receiving hemodialysis for a mean

of 5.4 years (standard deviation, 5.1) (Table 1). More than half of the participants (n=12, 52.2%) rated their worst itching experience in the 24 hours preceding the interview as a 7 or higher (equivalent to severe) on the WI-NRS (Table 2).

Skindex-10 Questionnaire Quantitative Results

On the Skindex-10 Questionnaire, all participants reported that they were bothered by their itching during the past week (Fig S1). Many indicated they were "always bothered" by the recurrence of their itching over the past week (n=7/21, 33.3%), and many reported they had always felt frustrated (n=7/23, 30.4%) or annoyed (n=7/23, 30.4%) about their itching.

Patients' Symptom Experience

Itch Location

Locations of itch differed between participants. Almost two-thirds of participants indicated that their back was the area most affected by itch (Table 2). Other frequently reported locations included the arms, head, and legs. More than half said that the location of itch on their body would vary (n=16, 69.6%).

Itch Characteristics

Participants used a variety of terms to describe the qualities and sensations of their itch, including "uncomfortable," "painful," "skin felt irritated," "a burning sensation," "numbness," "tingling," "stinging," and "skin feels dry" (Table 3). Many described that their itching was "annoying," "uncontrollable," or something that "drives [them] crazy." Some specified that the severity depended on body location. One participant who self-categorized as having severe CKD-aP stated that her itching was so severe that her hair would fall out from the spot where she was scratching (Table 2).

Eighteen participants (78.3%) described at least one thing that would worsen the intensity of their itching. Triggers included the heat or hot weather (n=7, 30.4%), dialysis (n=4, 17.4%), and sweat (n=3, 13.0%). Participants also explained that certain fabrics could intensify or trigger their itching, such as wool, polyester, long pants/sleeves, or shirts with a "scratchier" material (n=2, 8.7% for each). Other triggers that participants believed would cause or worsen their itch included dry skin, dietary changes, potassium levels, cleaning products (eg, laundry detergents and body soaps), and emotions, such as stress, anxiety, or anger.

When specifically asked about the importance of their itch compared with their other medical problems, many participants (n=10, 43.5%) described their itching as being the most or close to the most important thing relative to their other comorbid conditions.

Frequency and Occurrence

Most participants (n=12, 52.2%) stated that they experienced itching daily, with most of the remainder (n=7, 30.4%) reporting that they experienced itching at least

Table 2. Characteristics of Itching Reported by Interview Participants (N=23)

Characteristic	n (%)	Example Responses
Location		
Back	15 (65.2)	"Well when I first started experiencing it, it was my back [...] I know my back is clean. I get out of the shower, I start scratching." (001-003)
Arms	13 (56.5)	"I think my head. I'll start scratching my head or back." (001-002)
Head	11 (47.8)	"On the back, the stomach, chest, uh, lower abdomen, and, uh, obviously my arms." (002-004)
Legs	10 (43.5)	
Face	–	
Feet	5 (21.7)	
Severity (WI-NRS range)		
Mild (<4)	3 (13.0)	"Oh yeah, real bad. My hair came out because I—I scratch it so much it's irritating." (002-001)
Moderate (≥4 to <7)	8 (34.8)	"It's severe [...] Medication does not help it" (002-004)
Severe (≥7)	12 (52.2)	
Itch frequency		
Daily	12 (52.2)	"It just happens, um, and it's daily. If I get too warm in here my legs will start itching. I will just be itching. You will see me. I start digging." (004-005)
≥1 times per week but less than daily	7 (30.4)	"Very bothersome at times. Sometimes it's really constant, other times it just comes and goes." (001-005)
Timing		
Worse at night	14 (60.9)	"In the daytime I'm more aware of it. But when I'm sleeping, very seldom do I wake out of my sleep to scratch." (001-003)
Worse during day	4 (17.4)	"Well the day of dialysis, it's intense. But the days that you're not like, uh, like yesterday. I still itched, but it wasn't as frequent. Like I had dialysis this afternoon and well, I'm not looking forward to the itching. It's going to happen." (002-007)
Worse during dialysis	7 (30.4)	
Worse after dialysis	7 (30.4)	

Abbreviations: CKD-aP, chronic kidney disease-associated pruritus; WI-NRS, Worst Itching Intensity Numeric Rating Scale.

once per week (Table 2). The duration of itching varied; most participants (n=18, 78.3%) reported that their itching would come and go whereas the remainder (n=5, 21.7%) indicated that their itching was a constant experience. Those who experienced on and off itching reported various durations of itching: for some, their itching typically lasted 3-5 minutes at a time (n=3, 13.0%) whereas, for others, itching usually lasted a couple of hours (n=5, 21.7%). Several participants stated that they would itch

more during dialysis (n=7, 30.4%) or after dialysis (n=7, 30.4%).

Scratching and Other Methods to Relieve Itch

Most participants described scratching to relieve their itch (n=16, 69.6%). Many used their fingernails or a back-scratcher (n=17, 73.9% for each). Several participants mentioned that their frequent scratching could lead to breaks in the skin.

Besides scratching, participants reported using a wide variety of treatments and methods to relieve their symptoms. All but one participant (n=22, 95.7%) reported trying treatments for itching. The most commonly reported treatments included allergy medications (n=7, 30.4%), cortisone (n=4, 17.4%), investigational medications (n=3, 13.0%), and topical creams (n=2, 8.7%). Several participants mentioned trying topical approaches, including rubbing alcohol, calamine lotion, cocoa butter, aloe, and antibiotic ointments (n=2, 8.7% for each). Several commented that showering and bathing helped relieve their itch (n=8, 34.8%), although some described having to take multiple showers a day or waking during the night to shower.

Five participants (21.7%) stated that they felt their medications and other methods of relief did not help at all.

Table 3. Symptoms Reported (N=23)

Symptom Descriptors	n (%)
Annoying/drives [them] crazy	6 (26.1)
Skin breaks out from itchiness	3 (13.0)
Comparable to a mosquito bite	2 (8.7)
Irritated skin	2 (8.7)
Uncomfortable skin	2 (8.7)
Painful skin	2 (8.7)
Numbness	2 (8.7)
Tingling	2 (8.7)
Skin feels dry	2 (8.7)
Other ^a	6 (26.1)

^aPrickly (n=1), tender (n=1), unbearable (n=1), like rash from poison oak (n=1), feeling like "bugs crawling and biting in sync" (n=1), skin trying to "reorganize itself" (n=1).

Table 4. Impact on QoL (N=23)

Aspect Impacted by Itch	n	%	Example Responses
Physical function	6	26.1	
Impact on walking	4	17.4	"I know I'm going to look funny walking and trying to scratch my back, plus I have arthritis, I can't—one of my hands don't go all the way to my back, I have to be very careful with it. So, it might impact—you might not go for a walk maybe?" (003-007)
Impact on eating	2	8.7	"it impacts me in such a way that I have to monitor everything—every single thing I do whether it's eat, fluid intake, food intake, snacks, okay? [...] That's probably the main reason why I in most cases do not go out to eat dinner because I don't know what they're cooking it with [...]."
Daily activities	20	87.0	
Choosing clothes to wear	13	56.5	"I try putting on some like cool clothes [...], you know, to help my skin not to be itching so much. [...] like short sleeves. Like, um, soft material like, you know" (002-001)
Impact on bathing	9	39.1	"Sometimes I have to shower like 15 times—that or 10 times. [...] I'll take a shower first to see if [...] that water will relieve the itching. And if that doesn't stop, I put the alcohol on. Like I'll pour a whole bottle of alcohol on my body and just rub it all through my body." (001-004)
Shopping/errands	8	34.8	"if I go shopping and it itches, of course, I have to go to the side so that nobody [laughter] will see me scratching myself" (003-006)
Housework or yard work	6	26.1	
Preparing meals	5	21.7	
Sleep	19	82.6	
Itching wakes them up at night	16	69.6	"if it wakes me at 2:45 the fair chance is that I'm not going to go back to sleep. So, I—I actually literally get up, you know." (002-004)
Harder to fall asleep	14	60.9	"when I was trying to go to sleep it was—it was horrible and I couldn't sleep, I was frustrated, I was hot, it made it worse, I had to get up and take a shower, so I didn't end up going to sleep until like 5:00 in the morning." (003-007)
Social functioning and relationship impact	7	30.4	"Um, a lot of friends' parties and stuff there are certain groups that I just—I won't even bother going to because just the—the level of self-consciousness. [...] So, I would have to say that it—it has a big effect on my life." (002-004) "I mean, it can make you very sad and solemn, you know, which affects others, you know. [...] And they [grandchildren] want to do something, and you can't because, you know, your back feels like it's on fire from itching, [...] You just try to deal the best you can with it, but you know you're not giving it 100%." (002-004)
Emotional and psychological impacts	9	39.1	"Sometimes I get edgy because I'm itching too much. And then, when I scratch too hard I have scars. It leaves scars—Right—on my skin." (001-004) "Sometimes I cry, you know, and sometimes I—it comes out. I cry because I try to figure out, why am I going through all this itchiness and I ain't never, you know. Yeah. I ain't been through nothing like this before." (002-001)
Medical impacts	6	26.1	
Scarring of skin	3	13.0	"And I actually don't use my fingers as much [to scratch] because I've been noticing on my arm. I mean, you'll notice all the scars and, uh, you actually will—it'll get to the point where you don't realize it." (002-004)
Bleeding caused by scratching	3	13.0	"You're just mindlessly scratching and next thing you're bleeding, you know." (002-004)
Pain	2	8.7	"...a lot of people wouldn't understand it, but it is a painful itch. [...] Every time. [...] There's a level of pain" (002-004)
Hair loss	1	4.3	"Oh yeah, real bad. My hair came out because I—I scratch it so much it's irritating. It just—it's itching, just irritating me real, uh, real bad. [...] Yeah. My hair fell out real bad." (002-001)
Financial impacts	2	8.7	"Um, I have to sit there and buy, um, different kinds of things, like [topical cream] or anything to like try to fix the appearance of my skin—that affects me, because [topical cream] is not cheap." (003-007)

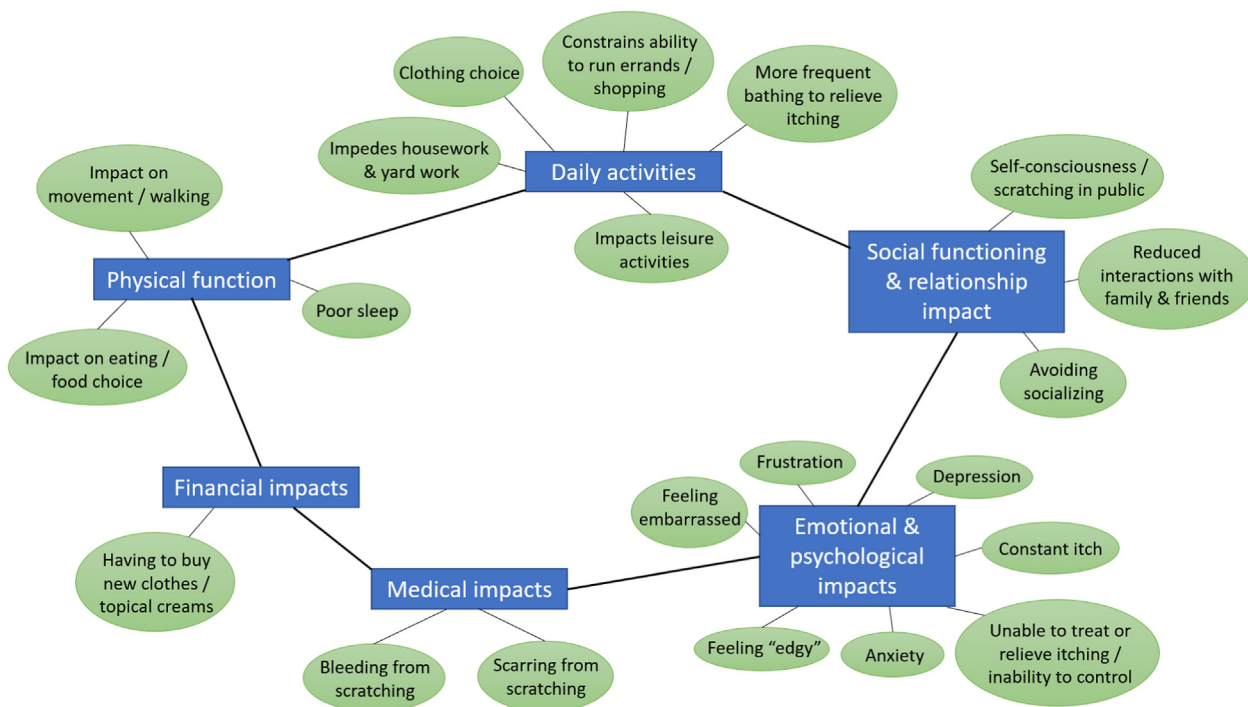


Figure 1. Thematic schema. Themes and subthemes identified from patients' descriptions of how chronic kidney disease-associated pruritus (CKD-aP) impacts their lives.

Others reported that their treatments only helped “temporarily” (n=12, 52.2%), “sometimes” (n=5, 21.7%), or “a little bit” (n=1, 4.3%), and 3 participants (13.0%) reported that they need to “constantly” take medication or use treatment to feel relief from their itching.

Impacts of CKD-aP on Patients' Lives

Physical Function and Daily Activities

Six participants (26.1%) reported an impact on their physical functioning as a result of their itching symptoms, specifically in relation to walking (n=4, 17.4%; eg, “might not go for a walk”) or eating (n=2, 8.7%; eg, having to “monitor” food and fluid intake) (Table 4, Fig 1). Most participants (n=20, 87.0%) reported that their itching impacted daily activities, especially selecting clothes to wear (n=13, 56.5%; eg, having to select “cool clothes” or “soft material” to avoid itching), bathing (ie, needing to bathe more frequently) (n=9, 39.1%), shopping or running errands (n=8, 34.8%), housework or yardwork (n=6, 26.1%), and preparing meals (n=5, 21.7%). Two participants (8.7%) reported having to take 10-15 showers per day to relieve their itching symptoms. Additionally, one woman (4.3%) explained that her daily activities were affected because she would only go out in the morning or the evening to avoid the heat exacerbating her itch. Participants also reported difficulty with toileting, grooming, attending work or school, and taking care of bills because of their itching experience (n=1, 4.3% for each). Other participants (n=4, 17.4%) discussed an impact on their hobbies or

leisure activities, such as watching television, swimming, or gardening.

Sleep

Most participants (n=19, 82.6%) described an impact on their sleep, most stating that itching would wake them (n=16, 69.6%) or that itching would make it harder for them to fall asleep (n=14, 60.9%; eg, “when I was trying to go to sleep it was—it was horrible and I couldn't sleep [...] I didn't end up going to sleep until like 5:00 in the morning”) (Table 4, Fig 1). When asked to elaborate on how their sleep was disturbed, some participants stated that itching made it more difficult to fall back to sleep after being woken up (n=2, 8.7%; eg, “if it wakes me at 2:45 the fair chance is that I'm not going to go back to sleep. So, I—I actually literally get up...”).

Social Functioning

Seven participants (30.4%) indicated that itching interfered with their social functioning. A few participants discussed feeling awkward in public because of their itching, finding it difficult to converse with others when they were intensely itchy, or avoiding social situations altogether because they were self-conscious (n=1, 4.3% for each; eg, “there are certain groups that I just—I won't even bother going to because just the—the level of self-consciousness”). When discussing specifically how they were bothered by their itching, some participants (n=4, 17.4%) mentioned itching in public and feeling worried about what others may think, stating that it is a “nuisance” and “embarrassing” or that people might think they have “cooties” or “bugs” (n=1, 4.3%

for each). Several participants (n=7, 30.4%) also discussed an impact on their relationships with friends and family because of their itching symptoms; for example, 2 participants specifically mentioned struggling to interact with their grandchildren, with 1 participant explaining that her itching prevented her from “giving it 100%.”

Emotional and Psychological Impacts

Nine participants (39.1%) discussed ways in which their itching symptoms affected their mood or emotions. These participants described feeling annoyed by their itching or becoming “edgy” from scratching or leaving scars on their skin (n=2, 8.7% for each). They also reported feeling irritated, frustrated, depressed, embarrassed, or anxious (n=1, 4.3% for each), and one described how her itching would make her cry on occasion.

Financial Impacts

Two participants (8.7%) mentioned that their CKD-aP affected them financially. One (4.3%) participant described that he preferred to buy new t-shirts rather than wash t-shirts he had worn because of concern that the detergent might worsen the itch. The other participant (4.3%) mentioned ruining her clothes because of her scratching and also needing to buy topical creams for reducing scars, which she explained “is not cheap.”

Confirmatory Analysis

Themes and concepts were confirmed in a larger cohort of US patients with moderate-to-severe CKD-aP who participated in interventional trials (N=70; see [Item S2](#)).

DISCUSSION

This qualitative study detailed hemodialysis patients’ experiences with CKD-aP and how their itch affects their day-to-day lives. More than half of participants reported severe itch, as indicated by a rating of ≥ 7 on the WI-NRS. The qualities of the itch varied; participants reported that their itch affected different locations but especially the back, head, and limbs, and used different words to describe the itch sensation—from “pain” to “bugs crawling over the skin.” Most participants reported that they experienced itch daily, especially at nighttime, when it would impair their sleep; some reported that they itch constantly. Several reported that they were disturbed by skin damage self-caused by their need to scratch and how their scratching might be perceived by others. Overall, CKD-aP considerably diminished patients’ QoL; it impacted day-to-day activities, impaired relationships and social functioning, and frequently affected their mood and emotions. Many described their itch as a major cause of anxiety (and social anxiety), frustration, and depression.

Increasing emphasis in patient care is placed on incorporating patients’ preferences in regulatory, reimbursement, and prescribing decisions, because patients have different perceptions of how their health conditions and

treatment outcomes affect their QoL.^{34–36} The findings from this study help address the absence of published qualitative data for CKD-aP from the perspective of patients. They also highlight how patients perceive pruritus as an important health issue and how they might prioritize its treatment. Greater awareness of CKD-aP and shared decision-making around its management is important because this symptom often goes unrecognized and untreated despite its considerable impact on patients’ lives.¹⁸

The findings from this study align with earlier descriptive studies and patient surveys for the location of itch,²⁷ disturbed sleep and daily activities,^{7,8,22} and negative social and emotional impacts.^{7,8,22,28,29} However, they build on these studies by uncovering descriptions from patients of the severe impact CKD-aP has on their lives, which has rarely been detailed in earlier work. Specific examples include how some take multiple showers each day to relieve itch, descriptions of the social anxiety and fear of others’ perceptions of their scratching, and physical difficulties preventing interaction with others including grandchildren. Some participants also described a financial impact from managing their itch—which is not well documented in prior studies—for example, through buying topical treatments for damaged skin. A previous qualitative study identified other impacts of CKD-aP that were not mentioned in the interviews, including concentration problems or difficulties focusing because of itching.³⁷ Another study found patients undergoing dialysis with moderate-to-severe pruritus were also 4 times more likely to feel ‘drained’⁷; this was not mentioned specifically by the participants in the present study, possibly because fatigue was attributed to other causes.

Participants described trying various off-label treatments, such as antihistamines and corticosteroids to manage their itch, and many regularly resorted to alternative interventions, including taking multiple showers per day, topical skin lotions, rubbing alcohol, and placing ice cubes on affected skin. Some participants—in this and another qualitative study of hemodialysis patients’ symptoms¹⁰—believed that itching could also be controlled by dietary changes, for example, avoiding foods high in phosphorous (although there is no clear evidence that lowering serum phosphorus alleviates CKD-aP³⁸). Many participants indicated that these treatments did not effectively relieve itching or did so only temporarily. Together, these results highlight the limited effective treatment options for moderate-to-severe CKD-aP^{3,39} and the lengths some may go to for relief.

Almost half of the participants described their itch as the most, or close to the most, important of their existing health conditions. Preventing and treating pruritus has been identified as a clinical priority for patients with CKD receiving or nearing dialysis.²⁴ As we previously reported,³¹ most participants in the exit interview cohort considered improvement in CKD-aP—attained during the clinical trial—as meaningful, and their reasoning for why this was meaningful included reduced frequency, severity,

and duration of their itch; reduced social anxiety; physical improvements on their skin as it healed; and improved QoL or state of mind. These qualitative data give clues to the value patients may place on treatments that reduce their itch and how treatment-induced alleviation of itch may be perceived.

This study had limitations. First, the generalizability of the findings could be limited because all participants were from the United States. Participants from other countries might describe the characteristics of their itch using different phrases and expressions, and there could be different or additional experiences and cultural impacts of CKD-aP not captured in this study. The purposive sampling used to recruit participants might have also introduced selection bias; for example, participants who place more importance on itch as a symptom compared to other health issues might have been more willing to participate. Finally, although we report the number of participants who spontaneously mentioned particular symptoms and aspects, the participants were not systematically questioned about these items, and larger studies would be needed to accurately estimate their prevalence.

In conclusion, this study highlights the impact of CKD-aP on patients treated by hemodialysis and addresses a gap in qualitative data on this prevalent symptom. Although the symptom experience and qualities of CKD-aP varied, the condition causes severe distress for many patients undergoing hemodialysis and can profoundly impair their QoL. The information about the patient experience described here has implications for clinical practice; routine symptom assessments using validated patient-reported outcome measures could be incorporated to detect pruritus earlier in dialysis patients, and greater awareness of CKD-aP could be achieved among clinicians, dialysis organizations, and patients. Such initiatives would promote discussions between clinicians and patients around managing and treating this debilitating symptom from its onset.

SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

Figure S1: Skindex-10 Questionnaire results

Item S1: Semistructured Interview Guide

Item S2: Confirmatory Qualitative Analysis

Table S1: Patient-Reported Outcome Measures Used

Table S2: Characteristics of Itching Reported by Exit Interview Cohort (N=70)

ARTICLE INFORMATION

Authors' Full Names and Academic Degrees: Frédérique Menzaghi, PhD, Margaret K. Vernon, PhD, Maria Mattera, MPH, Joshua Cirulli, PharmD, Warren Wen, PhD, Robert H. Spencer, PhD, and Catherine Munera, PhD.

Authors' Affiliations: Cara Therapeutics, Stamford, CT (FM, JC, WW, RHS, CM); and Evidera, Bethesda, MD (MKV, MM).

Address for Correspondence: Frédérique Menzaghi, PhD, Cara Therapeutics, Inc, 4 Stamford Plaza, 107 Elm Street, 9th Fl, Stamford, CT 06902. Email: fmenzaghi@caratherapeutics.com

Authors' Contributions: Study conception and design: FM, MKV, CM, MM; data interpretation: FM, MKV, CM, MM, JC, WW, RHS; data acquisition and analysis: MM. Each author contributed important intellectual content during manuscript drafting or revision and accepts accountability for the overall work by ensuring that questions pertaining to the accuracy or integrity of any portion of the work are appropriately investigated and resolved.

Support: This study was sponsored by Cara Therapeutics, Inc. The authors employed by the sponsor were involved in the study's design, data interpretation, and preparation of the manuscript. Medical writing was provided by Jonathan M. Pitt, PhD (Evidera, Paris, France) and funded by Cara Therapeutics.

Financial Disclosure: Drs Menzaghi, Cirulli, Wen, Spencer, and Munera are employed by Cara Therapeutics, Inc. Dr Vernon is employed by Evidera. Dr Mattera is a former employee of Evidera.

Data Sharing: The datasets used and analyzed during this study are available from the corresponding author on reasonable request. The data are not publicly available due to privacy or ethical restrictions.

Peer Review: Received September 14, 2022. Evaluated by 2 external peer reviewers, with direct editorial input from the Statistical Editor, an Associate Editor, and the Editor-in-Chief. Accepted in revised form May 19, 2023.

REFERENCES

- 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. doi:10.2147/IJNRD.S108045
- Lipman ZM, Paramasivam V, Yosipovitch G, Germain MJ. Clinical management of chronic kidney disease-associated pruritus: current treatment options and future approaches. *Clin Kidney J*. 2021;14(suppl 3):i16-i22. doi:10.1093/ckj/sfab167
- Mettang T, Kremer AE. Uremic pruritus. *Kidney Int*. 2015;87(4):685-691. doi:10.1038/ki.2013.454
- Nair D, Finkelstein FO. Pruritus as a patient-reported primary trial end point in hemodialysis: evaluation and implications. *Am J Kidney Dis*. 2020;76(1):148-151. doi:10.1053/j.ajkd.2020.01.002
- Verduzco HA, Shirazian S. CKD-associated pruritus: new insights into diagnosis, pathogenesis, and management. *Kidney Int Rep*. 2020;5(9):1387-1402. doi:10.1016/j.ekir.2020.04.027
- Narita I, Alchi B, Omori K, et al. Etiology and prognostic significance of severe uremic pruritus in chronic hemodialysis patients. *Kidney Int*. 2006;69(9):1626-1632. doi:10.1038/sj.ki.5000251
- 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 Transplant*. 2006;21(12):3495-3505. doi:10.1093/ndt/gfl461
- 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. doi:10.2215/CJN.00100110
- Hayani K, Weiss M, Weisshaar E. Clinical findings and provision of care in haemodialysis patients with chronic itch: new results from the German epidemiological haemodialysis itch study. *Acta Derm Venereol*. 2016;96(3):361-366. doi:10.2340/00015555-2280
- Cox KJ, Parshall MB, Hernandez SHA, Parvez SZ, Unruh ML. Symptoms among patients receiving in-center hemodialysis: A

- qualitative study. *Hemodial Int*. 2017;21(4):524-533. doi:10.1111/hdi.12521
11. Inui S. Nalfurafine hydrochloride to treat pruritus: a review. *Clin Cosmet Invest Dermatol*. 2015;8:249-255. doi:10.2147/CCID.S55942
 12. Gilchrist BA, Stern RS, Steinman TI, Brown RS, Arndt KA, Anderson WW. Clinical features of pruritus among patients undergoing maintenance hemodialysis. *Arch Dermatol*. 1982;118(3):154-156. doi:10.1001/archderm.1982.01650150016012
 13. Hercz D, Jiang SH, Webster AC. Interventions for itch in people with advanced chronic kidney disease. *Cochrane Database Syst Rev*. 2020;12(12):CD011393. doi:10.1002/14651858.CD011393.pub2
 14. Westby EP, Purdy KS, Tennankore KK. A review of the management of uremic pruritus: current perspectives and future directions. *Itch*. 2020;5(3):e38. doi:10.1097/itx.0000000000000038
 15. US Food and Drug Administration. KORSUVA (difelikefalin) injection, for intravenous use. Initial U.S. Approval: 2021. Accessed May 18, 2022. https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/214916s000lbl.pdf
 16. European Medicines Agency. Summary of Product Characteristics. Kapruvia (INN-Difelikefalin) 50 micrograms/mL solution for injection. Accessed May 18, 2022. https://www.ema.europa.eu/en/documents/product-information/kapruvia-epar-product-information_en.pdf
 17. Weisshaar E, Mattered U, Mettang T. How do nephrologists in haemodialysis units consider the symptom of itch? Results of a survey in Germany. *Nephrol Dial Transplant*. 2009;24(4):1328-1330. doi:10.1093/ndt/gfn769
 18. 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. doi:10.1016/j.jpainsymman.2019.06.010
 19. Yosipovitch G, Zucker I, Boner G, Gafter U, Shapira Y, David M. A questionnaire for the assessment of pruritus: validation in uremic patients. *Acta Derm Venereol*. 2001;81(2):108-111. doi:10.1080/00015550152384236
 20. Zucker I, Yosipovitch G, David M, Gafter U, Boner G. Prevalence and characterization of uremic pruritus in patients undergoing hemodialysis: uremic pruritus is still a major problem for patients with end-stage renal disease. *J Am Acad Dermatol*. 2003;49(5):842-846. doi:10.1016/s0190-9622(03)02478-2
 21. Plewig N, Ofenloch R, Mettang T, Weisshaar E. The course of chronic itch in hemodialysis patients: results of a 4-year follow-up study of GEHIS (German epidemiological hemodialysis itch study). *J Eur Acad Dermatol Venereol*. 2019;33(7):1429-1435. doi:10.1111/jdv.15483
 22. 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. doi:10.1016/j.xkme.2020.08.011
 23. 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. doi:10.1093/ckj/sfab218
 24. Manns B, Hemmelgarn B, Lillie E, et al. Setting research priorities for patients on or nearing dialysis. *Clin J Am Soc Nephrol*. 2014;9(10):1813-1821. doi:10.2215/CJN.01610214
 25. Davison SN, Levin A, Moss AH, et al. Executive summary of the KDIGO Controversies Conference on Supportive Care in Chronic Kidney Disease: developing a roadmap to improving quality care. *Kidney Int*. 2015;88(3):447-459. doi:10.1038/ki.2015.110
 26. Lebwohl MG, Bachelez H, Barker J, et al. Patient perspectives in the management of psoriasis: results from the population-based multinational assessment of psoriasis and psoriatic arthritis survey. *J Am Acad Dermatol*. 2014;70(5):871-881.e1-e30. doi:10.1016/j.jaad.2013.12.018
 27. Altınok Ersoy N, Akyar İ. Multidimensional pruritus assessment in hemodialysis patients. *BMC Nephrol*. 2019;20(1):42. doi:10.1186/s12882-019-1234-0
 28. Satti MZ, Arshad D, Javed H, et al. Uremic pruritus: prevalence and impact on quality of life and depressive symptoms in hemodialysis patients. *Cureus*. 2019;11(7):e5178. doi:10.7759/cureus.5178
 29. Suseł J, Batorycka-Baran A, Reich A, Szepietowski JC. Uraemic pruritus markedly affects the quality of life and depressive symptoms in haemodialysis patients with end-stage renal disease. *Acta Derm Venereol*. 2014;94(3):276-281. doi:10.2340/00015555-1749
 30. Vernon M, Ständer S, Munera C, Spencer RH, Menzaghi F. Clinically meaningful change in itch intensity scores: an evaluation in patients with chronic kidney disease-associated pruritus. *J Am Acad Dermatol*. 2021;84(4):1132-1134. doi:10.1016/j.jaad.2020.06.991
 31. Vernon MK, Swett LL, Speck RM, et al. Psychometric validation and meaningful change thresholds of the Worst Itching Intensity Numerical Rating Scale for assessing itch in patients with chronic kidney disease-associated pruritus. *J Patient Rep Outcomes*. 2021;5(1):134. doi:10.1186/s41687-021-00404-z
 32. Fishbane S, Jamal A, Munera C, Wen W, Menzaghi F; KALM-1 Trial Investigators. A phase 3 trial of difelikefalin in hemodialysis patients with pruritus. *N Engl J Med*. 2020;382(3):222-232. doi:10.1056/NEJMoa1912770
 33. CR845-CLIN3103: A Global Study to Evaluate the Safety and Efficacy of CR845 in Hemodialysis Patients With Moderate-to-Severe Pruritus (KALM-2). [ClinicalTrials.gov](https://clinicaltrials.gov/ct2/show/NCT03636269) identifier: NCT03636269. Updated April 26, 2022. Accessed January 8, 2022. <https://www.clinicaltrials.gov/ct2/show/NCT03636269>
 34. Hoos A, Anderson J, Boutin M, et al. Partnering with patients in the development and lifecycle of medicines: a call for action. *Ther Innov Regul Sci*. 2015;49(6):929-939. doi:10.1177/2168479015580384
 35. Smith MY, Hammad TA, Metcalf M, et al. Patient engagement at a tipping point—the need for cultural change across patient, sponsor, and regulator stakeholders: insights from the DIA conference, “Patient Engagement in Benefit Risk Assessment Throughout the Life Cycle of Medical Products.”. *Ther Innov Regul Sci*. 2016;50(5):546-553. doi:10.1177/2168479016662902
 36. Baumgart A, Craig JC, Tong A. Qualitative research in CKD: how to appraise and interpret the evidence. *Am J Kidney Dis*. 2021;77(4):538-541. doi:10.1053/j.ajkd.2020.12.011
 37. Weiss M, Weisshaar E. Qualitative interviews on chronic pruritus in haemodialysis patients. *Acta Derm Venereol*. 2014;94(6):713-714. doi:10.2340/00015555-1823
 38. 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. doi:10.2215/CJN.03280317
 39. Simonsen E, Komenda P, Lerner B, et al. Treatment of uremic pruritus: a systematic review. *Am J Kidney Dis*. 2017;70(5):638-655. doi:10.1053/j.ajkd.2017.05.018