



CHRONIC KIDNEY DISEASE–ASSOCIATED PRURITUS (CKD–aP) FACT SHEET

DEFINITION AND BACKGROUND

Chronic kidney disease-associated pruritus (itch) is a common and debilitating condition of itchy skin that is directly related to chronic kidney disease (CKD). For short, it's called CKD-aP. Dialysis patients and those with advanced kidney disease experience it more often, but it also occurs in earlier stages of CKD.

CKD-aP is also known as “uremic pruritus (itch)” because of the association between itching and elevated uremic wastes in the blood such as phosphorus and aluminum in CKD. Current research, however, highlights the concept that uremia may exacerbate underlying pathophysiology, such as that related to the opioid receptor imbalance and immune dysregulation found in CKD.

CKD-aP can present in many ways. Its severity can change in the same person over time from barely noticeable to unrelenting and disturbing; it may be intermittent or persistent; and it may occur before, during, or after/between dialysis sessions. Itch is generalized in up to 50% of patients, and when generalized, it is usually symmetrical, but it can be localized, usually on the face, back, and arm where the vascular access is located. Through clear communication between the patient and the healthcare team, proper diagnosis will help with identifying the most helpful treatments.¹

DIALYSIS OUTCOMES AND PRACTICE PATTERNS STUDY (DOPPS) DATA

- Of 23,264 hemodialysis (HD) patients from 21 countries in the DOPPS phases 4 to 6 (2009-2018), 37% were at least moderately bothered by itch, and 7% were extremely bothered.
- Compared with the reference group of patients not bothered by itch, the adjusted mortality HR for patients extremely bothered by itch was 1.24 (95% CI, 1.08-1.41).
- Cardiovascular and infection-related deaths and hospitalizations were also higher for patients extremely versus not at all bothered by itch (HR range, 1.17-1.44).
- Patients extremely bothered by itch were also more likely to discontinue dialysis and skip HD sessions and were less often employed.
- Associations were observed between itch severity and longer recovery time from an HD session, lower physical and mental quality of life, increased depressive symptoms, and poorer sleep quality.²



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Although many patients with CKD-aP suffer in silence, itch has been identified by patients to be a key research priority. The significant disease burden of CKD-aP is now becoming more widely acknowledged.³

Patient underreporting of CKD-aP is related to their being unaware of its causes, accepting that they must live with it, prioritizing other health issues, and the lengthy and inconvenient timing of consults. Healthcare professionals' assessment and management of pruritus vary and may not be evidence-based.^{1,4}

CHRONIC KIDNEY DISEASE OUTCOMES AND PRACTICE PATTERNS STUDY (CKDOPPS) DATA

- Of the 5658 CKDopps patients enrolled in the United States, Brazil, and France, 3780 (67%) who responded to queries on itch, the prevalence of moderate-to-extreme itch was 24%, occurring more often in older patients, women, and those with stage 5 CKD, pulmonary disease, diabetes, and depression.
- Patients with moderate itch had physical and mental component summary scores 3.5 (95% confidence interval [95% CI], -4.6 to -2.3) and 2.3 (95% CI, -3.2 to -1.5) points lower, respectively, than patients without itch, along with a higher prevalence of depression (prevalence ratio, 1.83; 95% CI, 1.58 to 2.11) and restless sleep (prevalence ratio, 1.69; 95% CI, 1.49 to 1.91) compared with patients without itch.

NATIONAL KIDNEY FOUNDATION (NKF) SURVEY OF HD PATIENTS AND HD CARE TEAM

- Of 692 patients from an NKF survey, itch was common, with 61% self-reporting itch that is at least somewhat intense on a Likert scale, including 25% of patients reporting itch as very or extremely intense.
- Shortening or skipping an HD session because of itch was reported at least some of the time by 55% and 50% of participants, respectively.
- Patients reporting the itch as very or extremely intense were more likely to skip or miss HD treatments.
- Among the members of the HD care team, nephrologists, at 43% of responses, were the most likely professional to be identified by patients to talk with about itchy skin.⁵



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NKF SURVEY OF NON–DIALYSIS CKD PATIENTS

- Of 937 non-dialysis CKD patients from an NKF patient survey, pruritus was common, with 58% stage 2 CKD patients reporting recurring itch at least somewhat intense on a Likert scale, rising slightly to 61%-62% in stages 3, 4, and 5.
- The itch is more severe in later stages, with 57% in stage 4 and 34% in stage 5 rating their worst itch in the past 24 hours as ≥ 7 out of 10 compared to 10%-14% in stages 3 and 2.
- The effect of itch also increases in later stages, with 44% in stage 2 CKD reporting itch that affects them at least somewhat on a Likert scale, rising to 81% in stage 4 and 62% in stage 5.
- Itch interfering with daily activities also increases from 22% in stages 2 and 3 to 50% in stage 4, and 36% in stage 5.⁶

NKF SURVEY OF HEALTHCARE PROVIDERS REGARDING NON–DIALYSIS CKD PATIENTS

- A survey of 203 healthcare professionals (nurses and physicians, physician assistants, and nurse practitioners who specialize in nephrology or primary care) who provide care to adults with CKD who are not on dialysis.
- Healthcare providers (HCPs) estimate that only 24% of their non-dialysis CKD patients have any degree of itch, of which 18% have moderate or severe itch.
- HCPs who have discussed itch with at least half of their non-dialysis patients have higher estimates (40% with any degree of itch and 27% with moderate or severe). Estimates are particularly low when the patient must initiate itch discussions (17% with any degree of pruritus, and 9% moderate or severe).
- Nine out of ten non-dialysis CKD patients report they have itchy skin. Three-quarters say their itch is recurring, indicating their itch is chronic.
- One out of every five patients with non-dialysis CKD report having itchy skin most, if not, all the time. Incidence for all of these is even higher for patients who indicate they are in stage 4 or 5 CKD. This is a longstanding issue, as more than two-thirds of the non-dialysis CKD patients have had itchy skin for a year or more.



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- Three-quarters non-dialysis CKD patients rate their itch as moderate or severe, rising to nine out of ten when in stage 4 or 5. The proportion with moderate or severe itch could be even higher, as patients were rating their worst itch in the last 24 hours and not all experience itchy skin every day.
- Less than half, even in stage 4 or 5, for example, have itchy skin most or all of the time. The HCP estimate for the incidence of moderate or severe itch matches the patient-reported proportion of having itchy skin most of the time.⁷

TREATMENT

Treatment currently involves a stepwise approach that starts with topicals to address dryness and itching. Itching that is resistant to topicals is then treated with antihistamines, and if they are not helpful, then gabapentin or pregabalin may be used. Refractory CKD-aP may be treated with ultraviolet B (UVB) phototherapy but is limited to those not on immunosuppressants or those who do not have lupus nephritis. There is now one Food and Drug Administration-approved drug for HD patients, difelikefalin, which is a non-addictive kappa opioid receptor agonist that is administered intravenously during HD treatments. Other experimental agents have been used with varying degrees of success in refractory cases, such as charcoal and omega-3 fatty acids.¹



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