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Article

Pruritus and Patient Reported Outcomes in Non-Dialysis CKD

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Abstract

Background and objectives Among patients on hemodialysis, pruritus has been associated with poorer mental and physical quality of life, sleep quality, depression, and mortality. We evaluated patients with nondialysis CKD to describe the prevalence of pruritus, identify associated factors, and investigate associations with patient-reported outcomes.

Design, setting, participants, & measurements Using cross-sectional data from patient questionnaires in the CKD Outcomes and Practice Patterns Study (CKDopps), we asked patients with CKD stages 3–5 (nondialysis) from the United States, Brazil, and France to identify how much they were bothered by pruritus. Response options ranged from "not at all" to "extremely." Log-Poisson regression, yielding prevalence ratios, was used to evaluate associations of moderate-to-extreme pruritus with patient characteristics, CKD stage, self-reported depression symptoms, and restless sleep. Mixed linear regression was used to examine associations between pruritus and physical and mental component summary scores, with lower scores indicating poorer quality of life.

Results Of the 5658 CKDopps patients enrolled in the United States, Brazil, and France, 3780 (67%) answered the pruritus question. The prevalence of moderate-to-extreme pruritus was 24%, and more likely in older patients, women, and those with stage 5 CKD, lung disease, diabetes, and physician-diagnosed depression. In adjusted models, patients with moderate pruritus 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 pruritus, and they also had a higher adjusted prevalence of patient-reported 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 pruritus. These patient-reported outcomes were progressively worse with increasing severity of pruritus.

Conclusions Our findings demonstrate high prevalence of pruritus in nondialysis CKD, as well as strong associations of pruritus with poor health-related quality of life, self-reported depression symptoms, and self-reported poor sleep.

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Introduction

Uremic pruritus, defined as itching associated with CKD, causes distress (1) and contributes to restless sleep and depression (2). A large, international study demonstrated the prevalence of moderate-to-extreme pruritus among patients with ESKD on hemodialysis to be approximately 40% and was associated with a higher prevalence of comorbid conditions, worse biochemical profiles, poorer mental and physical quality of life, higher probability of depression, and poorer sleep quality and survival (3). More recently, this prevalence was shown to range from 26% in Germany to 48% in the United Kingdom (2). Other studies have also demonstrated an association between pruritus and worse kidney disease burden scores, poorer health-related quality of life, and greater frequency of sleep disturbances in patients on dialysis (4–7).

However, pruritus is often overlooked by health care providers within dialysis units (8,9). In dialysis facilities where 21%–50% of patients reported having severe pruritus, only 1% of medical directors estimated this same prevalence (2). This may be due, in part, to underreporting by patients, as 17% of patients who were nearly always or always bothered by pruritus had not reported their symptoms to any health care provider (2).

In contrast to the large number of published studies on uremic pruritus in patients with ESKD, few published studies have investigated pruritus in patients with nondialysis CKD. Small, single-center studies in patients with nondialysis CKD have shown wide variation in the prevalence of pruritus, ranging from 12% to 74% (10–15). In a larger international study, over 50% of patients with advanced CKD suffered from itching, which was reported

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as severe among 11% and 18% of men and women, respectively (16).

Taken together, the studies in patients with ESKD have shown that uremic pruritus is a highly prevalent yet underreported symptom, which is inadequately treated and has a detrimental effect on mental and physical quality of life. However, studies are needed regarding the prevalence of pruritus and its effects on patient wellbeing within the nondialysis CKD population. Here, we used a large international sample of patients with nondialysis CKD to (*1*) describe the prevalence of pruritus by patient-reported severity, stratified by country and CKD stage; (*2*) describe associations of patient characteristics with the likelihood of having moderate-to-extreme pruritus; and (*3*) investigate associations of pruritus with self-reported mental and physical domains of quality of life, depression symptoms, and restless sleep.

Materials and Methods

Patients and Data Collection

The CKD Outcomes and Practice Patterns Study (CKDopps) (www.dopps.org) is an international, prospective, nephrology clinic–based cohort study, which gathers and analyzes data on the care provided to patients aged ≥18 years with eGFR≤60 ml/min per 1.73 m^2. The CKDopps study design has been described previously (17). Ethics approval and informed patient consent were obtained as required by national and local ethics committee regulations. As of June 2017, 5658 patients with CKD stages 3–5 (nondialysis) were enrolled in the CKDopps from Brazil (1034 patients; 21 CKD clinics), the United States (1591 patients; 35 CKD clinics), and France (3033 patients; 40 CKD clinics).

Demographic data, comorbid conditions, laboratory values, and medications, including those prescribed for treating pruritus (*e.g.*, gabapentin, pregabalin, and antihistamines), were abstracted from patient records. Upon enrollment, all participants were asked to complete a patient questionnaire, which collected data on self-reported health measures using validated instruments regarding CKD symptoms, health-related quality of life (Kidney Disease Quality of Life Short Form [KDQOL-SF]) (18–20), and depression symptoms (Center for Epidemiologic Studies Depression Scale [CES-D] short form) (21,22). CKD stage was categorized as stage 3 (combination of stage 3a and 3b because of the small sample size of stage 3a), stage 4, and stage 5 for multivariable analyses.

Using the 36-item version of the KDQOL-SF (18–20) contained within the patient questionnaire, patients were asked the following question: "During the past 4 weeks, to what extent were you bothered by itchy skin?" Response options were (*1*) not at all bothered, (*2*) somewhat bothered, (*3*) moderately bothered, (*4*) very much bothered, and (*5*) extremely bothered. We defined patients who were "not at all," "somewhat," "moderately," "very much," or "extremely" bothered by itchy skin as having no, mild, moderate, severe, or extreme pruritus, respectively.

The mental component summary (MCS) and physical component summary (PCS) scores were calculated using algorithms proposed by Ware *et al.* (20), with a possible score range of 0–100. Higher scores indicate better health-related quality of life. We regarded 3–5 point differences in the MCS and PCS scores as clinically relevant (21,22), which is equivalent to the threshold of discrimination for changes in health-related quality of life for chronic disease of approximately half an SD (23). Patient responses to the ten-item version of the CES-D were used to screen for depression symptoms, with possible scores ranging from 0 to 30. A score ≥10 was used to identify patients with a higher probability of depression (24,25). One specific item from the CES-D asked patients to indicate the frequency during the past week that "my sleep was restless," and this, along with the MCS, PCS, and CES-D scores described above, represent the outcomes in this study.

Data Analyses

For this analysis, data collected upon enrollment in the CKDopps were used. Cross-sectional prevalence of patient characteristics (mean±SD, median [interquartile range], or proportion) was calculated according to the degree of pruritus.

The prevalence ratio and accompanying 95% confidence interval (95% CI) was used to describe the association of particular factors with moderate-to-extreme pruritus and to evaluate how different degrees of pruritus were associated with self-reported depression symptoms or with self-reported restless sleep. Prevalence ratios were assessed using log-Poisson regression, accounting for clustering at the clinic level. It has been recommended to use prevalence ratios instead of odds ratios (from logistic regression) in cross-sectional studies with binary outcomes when the outcome is not rare. Hence, when the proportion experiencing an outcome exceeds 20%, an odds ratio overestimates the strength of the association, whereas the prevalence ratio is a more accurate measure (26,27).

Mixed linear regression was used to examine associations between MCS or PCS scores with each of the five different levels of pruritus. Regression models used generalized estimating equations, assuming a compound symmetry covariance structure and accounting for clustering at the clinic level. Two models were presented: a limited model (adjusted for CKD stage, country, age, and sex) and a full model (additionally adjusted for urine albumin-to-creatinine ratio/protein-to-creatinine ratio and the comorbidities diabetes, hypertension, congestive heart failure, peripheral vascular disease, lung disease, physician-diagnosed depression, recurrent cellulitis/gangrene, and history of cirrhosis of the liver). A secondary analysis was also performed, adjusting for the covariates in the full model in addition to serum phosphate, serum calcium, and hemoglobin.

We used multiple imputations to impute missing covariate values and KDQOL-36 and CES-D scores. We imputed questionnaire scores only for patients who answered at least one item. Overall, missingness was <20% for all covariates except for body mass index (31%) and hemoglobin A1c (37%). Details regarding missing data are presented in Supplemental Table 1. We imputed 20 complete data sets, performed all analyses with each data set, and combined the results using the Rubin rules (28) to reflect the averaged results from these imputations.

From the initial sample of 5658 enrolled patients, 1777 (31%) were excluded because of noncompletion of the patient questionnaire. An additional 101 (2%) patients who did not respond to the question regarding pruritus were also excluded. Consequently, main analyses included 3780 patients.

Statistical significance was set as a two-sided P value of 0.05. All analyses were conducted with SAS software, version 9.4 (SAS institute, Cary, NC).

Results

Supplemental Table 2 displays characteristics of patients who completed the patient questionnaire versus those who did not. A higher percentage of patients who completed the patient questionnaire were male, had less advanced CKD, and had fewer comorbid conditions.

Among the 3780 patients (13%, 17%, and 70% from Brazil, the United States, and France, respectively) analyzed, 61% were men and the mean age was 67 years (SD 13). The distribution of patients according to their CKD stage was 15% in stage 3a, 34% in stage 3b, 44% in stage 4%, and 7% in nondialysis stage 5.

Prevalence and Severity of Pruritus

The distribution of severity of pruritus by CKD stage and by country is displayed in Figure 1. The percentage of patients who had at least moderate pruritus was 24% overall, across all stages of CKD (24% in Brazil, 29% in the United States, and 23% in France). The percentage of patients with severe to extreme pruritus across all stages of CKD was 11% in Brazil, 13% in the United States, and 10% in France.

Table 1 displays characteristics of prevalent patients with nondialysis CKD from Brazil, the United States, and France, with moderate-to-extreme pruritus (n=900) versus mild pruritus (n=990) versus no pruritus (n=1890) during the 4 weeks before questionnaire completion.

Of patients with moderate-to-extreme pruritus, 73% also reported moderate-to-extreme dry skin, and 48% had self-reported restless sleep at least 3 days out of the week, compared with 19% and 26%, respectively, for patients without pruritus. Prescription of medications commonly used for treatment for pruritus (antihistamines, gabapentin, and pregabalin) was low at <10%, even among patients with moderate-to-extreme pruritus.

Associations of Patient Characteristics with Pruritus

Multivariable regression analyses indicated older age, female sex, history of lung disease, diabetes, and physician-diagnosed depression were associated with higher prevalence ratios for moderate-to-extreme pruritus, whereas patients

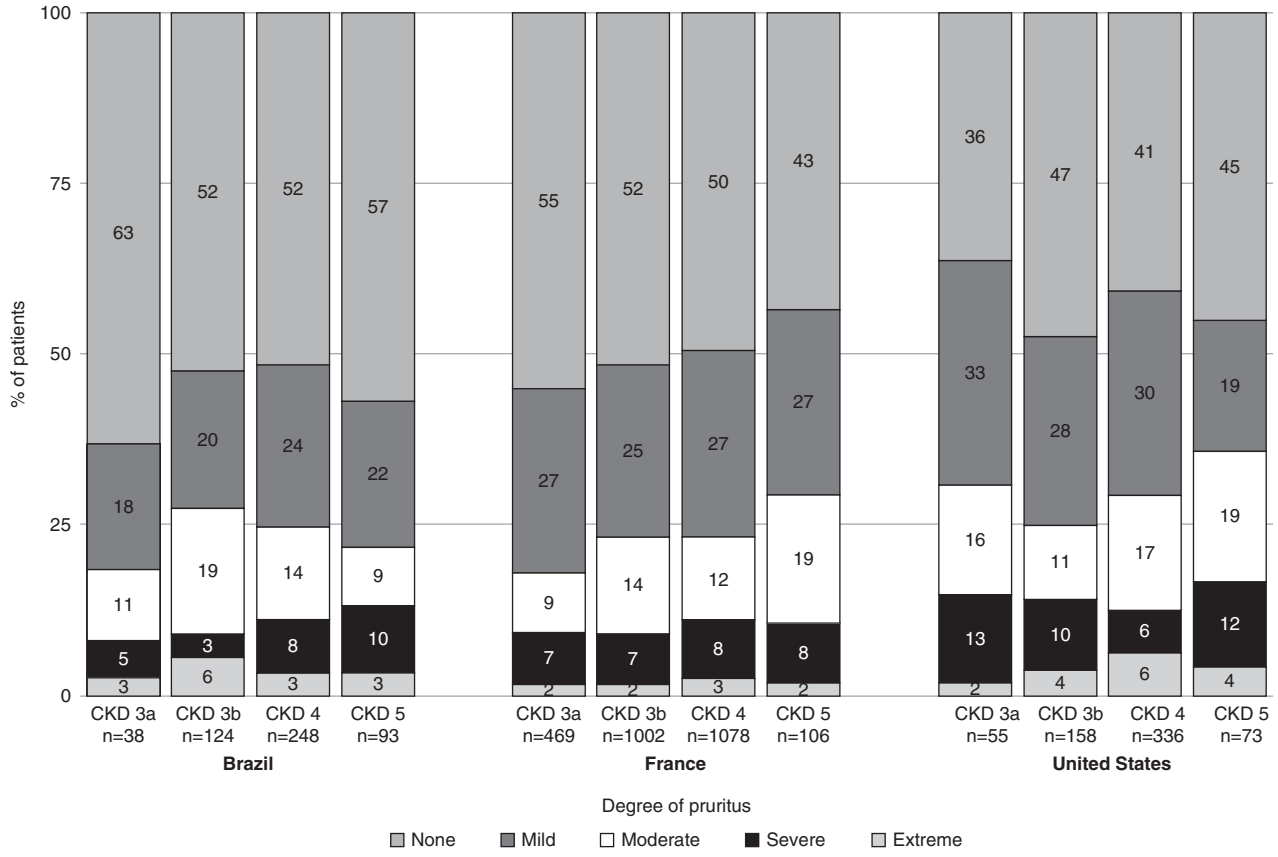

Figure 1. | **Prevalence of patient self-reported degree of pruritus, by CKD stage and country.** Degree of pruritus among patients with CKD across Brazil, France, and the United States, as well as across CKD stages among these countries. The degree of pruritus experienced by patients with CKD during the preceding 4 weeks of patient questionnaire completion is shown, collected from a prevalent cross-section of patients with CKD across nephrology clinics participating in CKDopps.

Table 1. Selected patient characteristics by degree of pruritus

Characteristic	Patients without Pruritus, *n*=1890	Patients with Mild Pruritus, *n*=990	Patients with Moderate–to-Extreme Pruritus, *n*=900
Age, yr	66±13	68±13	69±12
Age, yr, four categories			
<55	18	14	11
55–64	21	18	20
65–74	33	34	36
≥75	28	34	33
Women	38	38	42
History and severity of CKD			
eGFR, ml/min	32±13	31±12	30±12
Albumin- or protein-to-creatinine ratio			
Normal (A1)	31	28	28
High (A2)	28	30	29
Very high or nephrotic (A3)	41	42	43
Cause of CKD			
Diabetes	25	25	28
Glomerular disease	17	13	15
Hypertension	32	32	33
Others	27	30	24
Comorbidities			
Hypertension	87	89	90
Diabetes	40	45	50
Peripheral vascular disease	16	17	21
Congestive heart failure	13	14	17
Lung disease	8	10	15
Depression	8	10	13
Psychiatric disorder	5	7	11
Recurrent cellulitis, gangrene	2	2	4
History cirrhosis of the liver	2	2	3
Laboratory values			
Hemoglobin A1c[a]	7.1±1.2	7.3±1.2	7.2±1.3
Serum calcium, mg/dl	9.4±0.6	9.4±0.5	9.4±0.6
Serum phosphate, mg/dl	3.6±0.8	3.7±0.8	3.8±0.8
Hemoglobin, g/dl	12.8±1.7	12.8±1.7	12.4±1.8
Medication			
Antihistamines	4	3	9
Gabapentin	2	3	3
Pregabalin	2	2	3
Patient-reported outcomes			
Dry skin			
Not at all	58	27	14
Somewhat	24	40	12
Moderately	11	20	30
Very much	6	11	30
Extremely	2	2	13
Restless sleep in the last week			
Rarely/none of the time, <1 d	45	33	25
Some/little of the time, 1–2 d	30	33	26
Occasionally/moderate amount of the time, 3–4 d	17	21	26
Most/all of the time, 5–7 d	9	13	22
SF-12 Physical Component Summary score	42.4±10.3	40.5±10.5	36.6±10.3
SF-12 Mental Component Summary score	48.9±8.7	47.4±8.7	45.3±9.5
CES-D score (0–30)	6.5±4.6	7.5±5.0	9.9±5.7
Depression symptoms (CES-D score ≥10)	22	29	47

Results are shown as prevalence or mean±SD. SF-12, 12-item Short Form Health Survey; CES-D, Center for Epidemiologic Studies Depression Scale.
[a]Hemoglobin A1c is presented only for patients with diabetes mellitus.

from France were less likely to experience moderate-to-extreme pruritus (Supplemental Table 3, Table 2). When we adjusted for laboratory values, we found a significant association with higher serum phosphate and lower hemoglobin levels (Supplemental Table 4). In the full model, the prevalence of moderate-to-extreme pruritus was 19% higher (prevalence ratio, 1.19; 95% CI, 0.97 to 1.48) for patients with CKD stage 5 than with CKD

Table 2. Association of selected factors with the likelihood of having moderate-to-extreme pruritus in patients with nondialysis CKD

Characteristics	Adjusted Prevalence Ratio of Having Moderate-to-Extreme Pruritus versus No or Mild Pruritus (95% CI)	
	Limited Model	Full Model
Stage 4 versus stage 3	1.06 (0.93 to 1.21)	1.04 (0.91 to 1.19)
Stage 5 versus stage 3	1.21 (0.98 to 1.50)	1.19 (0.97 to 1.48)
Brazil versus the United States	0.89 (0.69 to 1.14)	0.88 (0.69 to 1.13)
France versus the United States	0.82 (0.71 to 0.95)	0.85 (0.74 to 0.99)
55–64 yr old versus <55 yr old	1.38 (1.12 to 1.70)	1.29 (1.05 to 1.58)
65–74 yr old versus <55 yr old	1.53 (1.24 to 1.89)	1.40 (1.13 to 1.74)
≥75 yr old versus <55 yr old	1.50 (1.21 to 1.86)	1.42 (1.14 to 1.76)
Men versus women	0.88 (0.77 to 1.01)	0.87 (0.76 to 0.99)
Albumin- or protein-to-creatinine ratio		
High versus normal		1.07 (0.90 to 1.28)
Very high or nephrotic versus normal		1.09 (0.93 to 1.29)
Comorbidities		
Diabetes versus no		1.17 (1.04 to 1.31)
Hypertension versus no		1.03 (0.84 to 1.26)
Congestive heart failure versus no		1.09 (0.95 to 1.24)
Peripheral vascular disease versus no		1.07 (0.93 to 1.24)
Lung disease versus no		1.37 (1.17 to 1.59)
Physician-diagnosed depression versus no		1.29 (1.10 to 1.52)
Recurrent cellulitis, gangrene versus no		1.17 (0.88 to 1.56)
History cirrhosis of the liver versus no		1.28 (0.92 to 1.78)

Results are on the basis of three countries in the CKD Outcomes and Practice Patterns Study (Brazil, France, and the United States) from a log-Poisson regression analysis adjusted for all factors in the full model. The limited model is adjusted for country, CKD stage, age, and sex. The full model is adjusted for country, CKD stage, age, sex, albumin-to-creatinine ratio, and comorbidities (diabetes, hypertension, congestive heart failure, peripheral vascular disease, lung disease, depression, recurrent cellulitis/gangrene, and history of cirrhosis of the liver). 95% CI, 95% confidence interval.

stage 3. Similar results were seen when patients with CKD stages 3a and 3b were examined separately (Supplemental Table 3) as when they were combined (Table 2), except that the prevalence ratio for more severe pruritus was greater for patients with stage 5 versus stage 3a, compared with patients with stage 5 versus the combined stage 3.

Associations of Pruritus with Health-Related Quality of Life and Depression Symptoms

Different aspects of quality of life were examined to determine their relationship to severity of pruritus in patients with nondialysis CKD. As shown in Figure 2, A and B, as the severity of pruritus increased, patients displayed progressively lower PCS and MCS scores. Patients without pruritus had a mean PCS and MCS score of 46.0 (SD 1.8) and 50.5 (SD 1.5) in the fully adjusted model, respectively. Patients with extreme pruritus had PCS and MCS scores 7.6 points (95% CI, −9.8 to −5.4) and 6.2 points (95% CI, −8.5 to −3.9) lower, respectively, than patients without pruritus in the fully adjusted model.

Figure 3 shows that, compared with patients without pruritus, the adjusted prevalence ratio of patient-reported depression symptoms was almost twice as high for patients with moderate pruritus (prevalence ratio, 1.83; 95% CI, 1.58 to 2.11) and approximately 2.5 times higher for patients with extreme pruritus (prevalence ratio, 2.55; 95% CI, 2.07 to 3.13).

Compared with patients without pruritus (Figure 4), the adjusted prevalence ratio of patient-reported restless sleep was significantly higher in patients with moderate (prevalence ratio, 1.69; 95% CI, 1.49 to 1.91) and extreme (prevalence ratio, 2.10; 95% CI, 1.76 to 2.51) pruritus.

Discussion

This study is the largest international description of self-reported pruritus among patients with nondialysis CKD and has several major findings. First, the overall prevalence of moderate-to-extreme pruritus was 24%, ranging from nearly 23% in Brazil to 29% in the United States, and was higher in stage 5 than in stage 3 CKD (Table 2). Second, we found certain patient characteristics and comorbidities to be associated with pruritus. Third, more severe pruritus was associated with increasingly poor mental and physical health, self-reported depressive symptoms, and self-reported restless sleep.

In a single-center study of patients with nondialysis CKD, the overall prevalence of pruritus was nearly 19%, but did not significantly differ across CKD stages (14). Our study demonstrated a higher prevalence of moderate-to-extreme pruritus at 24%, but was still lower than the nearly 40% shown among patients with ESKD in the early 2000s (2,3,29).

A study of patients with CKD stage 5 who would have otherwise been on dialysis, but were managed conservatively, reported the overall prevalence of pruritus as 74%, with 32% of these patients describing the symptom as "quite" or "very" distressing, consistent with prior findings of high prevalence of pruritus among patients with ESKD (12). This older population (mean age 82 years) had a higher prevalence of moderate-to-extreme pruritus than our younger CKD population, and echoes prior findings of greater

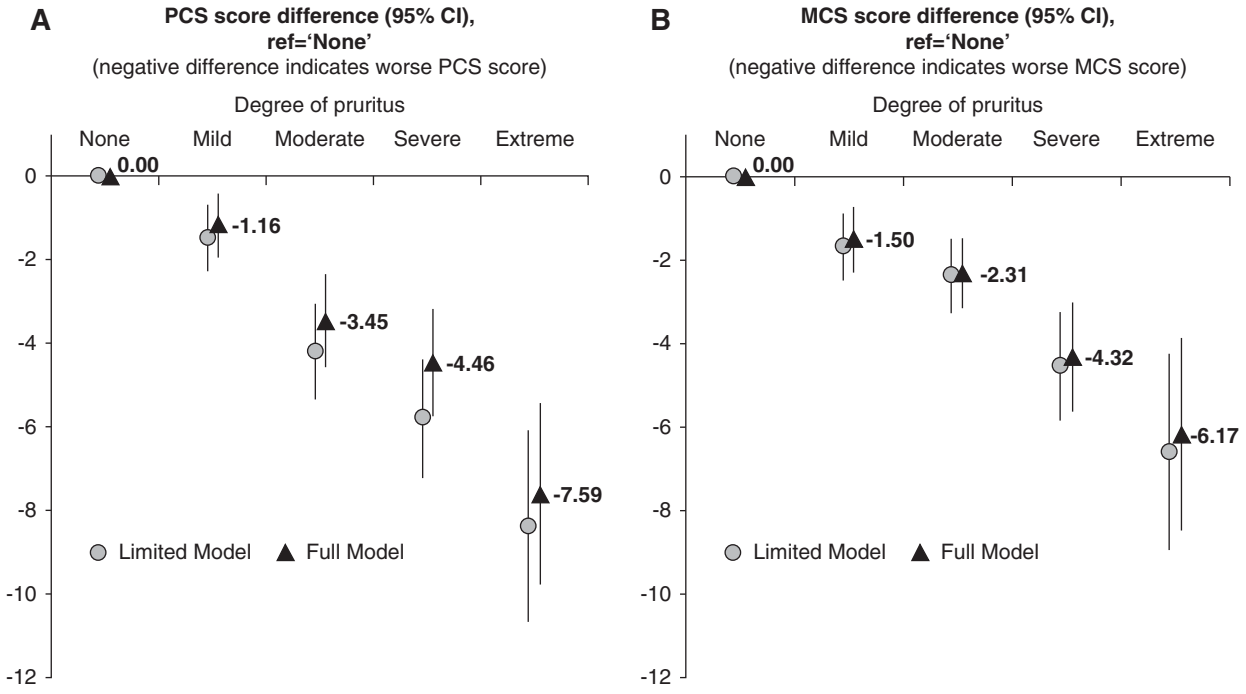

Figure 2. | **Difference in physical and mental summary scores by degree of patient-reported pruritus (compared with "none").** Prior studies have indicated a 3–5 point difference in MCS or PCS scores to be a minimal clinically significant difference (49,50).

intensity of itching in patients on dialysis (compared with patients with nondialysis CKD) (15) and of persistent, widespread itching in at least 50% of people in the seventh decade of life and beyond (30).

Although studies have demonstrated that males with ESKD on hemodialysis have a higher likelihood of suffering from pruritus (3,29), our data show that males with nondialysis CKD had a lower likelihood of experiencing moderate-to-extreme pruritus. We found that comorbidities such as lung disease, diabetes, and physician-diagnosed depression were associated with a higher prevalence of moderate-to-extreme pruritus. Although lung disease has previously been associated with pruritus among patients on hemodialysis (3), the reason for this association is unclear. It may be related to eosinophilic lung conditions, given the association of pruritus with eosinophilia (14). The association of diabetes with pruritus among patients with nondialysis CKD parallels similar findings for patients on hemodialysis (3) and might potentially be related to peripheral neuropathy (31) linking both disorders. Additionally, pruritus is also common in those with psychiatric disorders, as shown in a study of patients hospitalized in a mental institution with diagnoses ranging from schizophrenia to affective disorders, where 32% reported suffering from itching in the past 6 months or at present (32). Psychogenic pruritus has been associated with depressive disorders (30), and prior findings have shown that feelings of helplessness and hopelessness are also associated with pruritus (30). It is conceivable that the higher prevalence of depression seen among patients with more severe pruritus could be mediated through mechanisms such as restless sleep and fatigue, which are exacerbated by severe pruritus as discussed below.

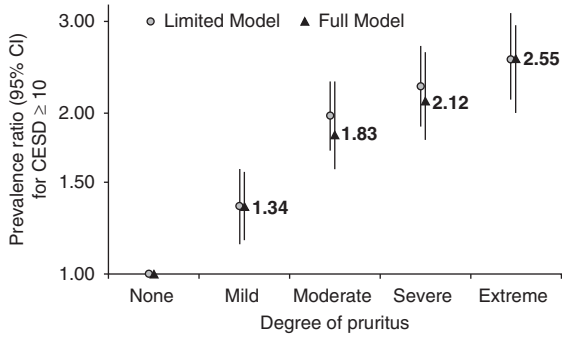

Figure 3. | **Adjusted prevalence ratio of having symptoms of depression (CES-D score ≥10) by degree of patient-reported pruritus (compared with "none").**

Our study identified a higher prevalence of dry skin among those with severe pruritus, similar to prior findings among patients on hemodialysis with pruritus (2,33), but given the high correlation of itching with dry skin, this was not adjusted for in our analyses.

In our analysis of biochemical markers, higher serum phosphate and lower hemoglobin levels were associated with a higher prevalence of moderate-to-extreme pruritus. However, given their strong correlation with advanced CKD (34,35), high serum phosphate and low hemoglobin levels may, to some extent, serve simply as markers of poor kidney function. Therefore, it is difficult to elucidate to what extent the association seen between CKD stage and pruritus may be specifically mediated by these biochemical parameters, if at all. Consequently, interpretation

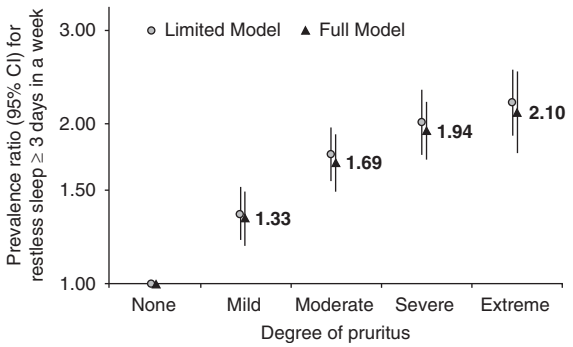

Figure 4. | Adjusted prevalence ratio of having self-reported restless sleep ≥3 days in a week by degree of patient-reported pruritus (compared with "none").

of the relationship of pruritus with serum phosphate and hemoglobin levels should be made with caution. Although one study of patients with nondialysis CKD showed an association between pruritus and higher serum calcium and phosphate levels (11), another did not show an association between pruritus and serum phosphate, vitamin D, parathyroid hormone, or calcium, but did demonstrate a significantly lower hemoglobin level in patients with nondialysis CKD with uremic pruritus than in those without uremic pruritus (14). It should be noted, however, that although there have been conflicting reports across studies with regards to the relationship between pruritus in patients on dialysis and metabolic bone disease parameters, the vast majority have found no relationship between pruritus and phosphate levels (2,10,11,36–39).

The pathogenesis of uremic pruritus is not well elucidated, although it is theorized that inflammation may play a role. Elevated levels of C-reactive protein (CRP) (2,40), IL-6 (40), and IL-2 (41) have been found among patients on hemodialysis suffering from pruritus, which may also partly explain the association we found between low hemoglobin levels and a higher prevalence of pruritus, given the association between low hemoglobin and inflammatory states (42).

We found progressively poorer mental and physical health, as well as progressively higher prevalence of depression symptoms with increasing severity of pruritus. We showed that patients with extreme pruritus had PCS and MCS scores 7 and 6 points lower, respectively, than patients without pruritus, in the fully adjusted model. In addition to being statistically significant, we considered even a 4- and 5-point change to be clinically relevant in the PCS and MCS scores, respectively, on the basis of the SD for these scores, as shown in Table 1 (23).

Patients with extreme pruritus had more than twice the prevalence of having self-reported restless sleep when compared with those with no pruritus. The strong association of pruritus with these patient-reported outcomes in patients with nondialysis CKD parallels previous findings of the important associations seen between pruritus and psychologic functioning in patients with ESKD (3–7,43,44). Similar to our findings in patients with nondialysis CKD, Pisoni *et al.* (3) demonstrated that sleep quality is much poorer among patients on hemodialysis with more severe pruritus. Studies have shown that disturbed sleep is also related to an impaired quality of life (45), depression (46), and mortality (3), underscoring the effect of poor sleep—and thereby pruritus—on patient outcomes. Future studies should investigate the broader ramifications of optimal management of pruritus, such as possible lower cardiovascular morbidity, perhaps mediated through improved sleep.

There are several limitations worth noting. First, this is a cross-sectional analysis and therefore does not allow conclusions about possible causal relationships. Second, serum albumin and CRP measurements were not included in the analyses because of infrequent measurement, thereby limiting the interpretation of the association between low hemoglobin and pruritus because hemoglobin, albumin, and CRP are all associated with inflammation (42,47,48). Third, the modest sample size of patients with stage 5 CKD may have resulted in a prevalence ratio that was underpowered, affecting the interpretation of this result. Fourth, the patient questionnaire contained only one question pertaining to itching, limiting the details of itching in the data collected, such as duration, timing, frequency, or location. Fifth, although many patients with kidney disease suffer from itchy skin disease (33), we did not collect data on dermatological conditions such as eczema, which may directly cause itching, and therefore were unable to assess how this may have influenced our results. And finally, as shown in Supplemental Table 2, patients who completed the patient questionnaire were different from those who did not complete the patient questionnaire, as more nonresponders were women, typically had more comorbid conditions, and had more advanced CKD, limiting the generalizability to other patients with CKD.

This study is the first of its kind to evaluate the prevalence of pruritus, as well as factors and patient-reported outcomes associated with pruritus, in such a large, international sample of patients with nondialysis CKD. Future studies with longitudinal assessment of particular factors and other patient-reported outcomes associated with pruritus in patients with nondialysis CKD will allow for the study of pruritus severity across the course of CKD. Future studies may also evaluate potential contribution of medications to pruritus and benefits of treatment options for pruritus. This study demonstrates the high prevalence of pruritus as well as the degree to which pruritus is associated with quality of life, self-reported depression symptoms, and self-reported sleep quality. These findings underscore the importance of identifying patients who suffer from pruritus in an effort to target who may benefit from therapies that could potentially provide relief, thereby improving quality of life and the patient experience (2).

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Supplemental Material

This article contains the following supplemental material online at http://cjasn.asnjournals.org/lookup/suppl/doi:10.2215/CJN.09600818/-/DCSupplemental.

Supplemental Table 1. Proportion of missingness for covariate variables.

Supplemental Table 2. Patient characteristics of those who completed the patient questionnaire (PQ) and those who did not.

Supplemental Table 3. Association of selected factors (with CKD stage 3 split into stage 3a and stage 3b) with the likelihood of having moderate-to-extreme pruritus in patients with nondialysis CKD.

Supplemental Table 4. Association of selected factors and laboratory values with the likelihood of having moderate-to-extreme pruritus in patients with nondialysis CKD.

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