Medicine®

OPEN

Prevalence of chronic kidney disease-associated pruritus among adult dialysis patients

A meta-analysis of cross-sectional studies

Xinmiao Hu, BN[a], Yan Sang, MN[b], Mei Yang, MPH[c,*], Xue Chen, BA[d], Wenjuan Tang, BN[a]

Abstract

Chronic kidney disease (CKD)-associated pruritus is a common adverse symptom in patients with end-stage renal disease treated by dialysis. Herein, a systematic review and meta-analysis of the prevalence of CKD-associated pruritus among adult dialysis patients was conducted.

An electronic search of PubMed, Web of Science, Elsevier, Wanfang, and Chinese National Knowledge Infrastructure databases was conducted from inception to November 23, 2016, and all cross-sectional studies that reported the prevalence of CKD-associated pruritus in dialysis were collected. The pooled prevalence was estimated by random-effects model. Potential publication bias was evaluated by the funnel plot as well as Begg and Egger tests.

After rigorous screening, a total of 42 studies conducted on 11,800 patients were included in this study. The overall prevalence of CKD-associated pruritus among adult dialysis patients was 55% (95% confidence interval [CI], 49–61, $I^2 = 97.6\%$), the stratification of which was 55% (95% CI, 45–65, $I^2 = 94.7\%$) in men and 55% (95% CI, 46–65, $I^2 = 93.3\%$) in women. In hemodialysis (HD) patients, the prevalence of CKD-associated pruritus was 55% (95% CI, 49–62, $I^2 = 97.9\%$), while in peritoneal dialysis (PD) patients, it was 56% (95% CI, 44–68, $I^2 = 89.9\%$). The prevalence of CKD-associated pruritus for mean dialysis duration <40 months was 56% (95% CI, 48–63, $I^2 = 75.1\%$), while that for mean dialysis duration ≥40 months was 50% (95% CI, 36–64, $I^2 = 99.1\%$).

The prevalence of CKD-associated pruritus is high in HD and PD. The prevalence among adult dialysis patients is comparable between China and foreign countries as well as between females and males. Studies with the similar disease definition and analysis of the effects of risk factors on CKD-associated pruritus are needed.

Abbreviations: AHRQ = Agency for Healthcare Research and Quality, CI = confidence interval, CKD = chronic kidney disease, ESRD = end-stage renal disease, HD = hemodialysis, HRQOL = health-related quality of life, PD = peritoneal dialysis, SF-36 = 36-Item Short Form Health Survey, VAS = visual analog scale.

Keywords: chronic kidney disease-associated pruritus, hemodialysis, meta-analysis, peritoneal dialysis, prevalence

1. Introduction

Chronic kidney disease (CKD) refers to a condition where the kidneys are damaged or the glomerular filtration rate has been <60 mL/min per 1.73 m^2 for >3 months.[1] End-stage renal disease (ESRD) is the terminal stage of various CKDs and its incidence has risen markedly in the past 30 years.[2] Jha et al reported that the highest incidence of ESRD was found in Taiwan (about 410 per million per year), while the lowest was in Paraguay (about 10 per million per year). In general, the majority of countries have a high incidence of ESRD (100–200 per million per year).[1] Over 80% of patients in developed countries received treatment for ESRD[3] and most of them chose to be treated with dialysis to increase their lifespan.

As the most common skin symptom in ESRD, pruritus is widely known as "uremic pruritus." Because there is no true cause–effect relationship with uremia, and pruritus is usually not observed in patients with acute kidney disease, we and others have suggested that the term "CKD-associated pruritus" is more precise.[4,5] In addition, CKD-associated pruritus could be difficult to distinguish from pruritus caused by nonrenal comorbidities typically linked with CKD, for instance, thyroid disease and hematological malignancy.[6] Previous studies have reported variable prevalence rates of 18% to 70% in patients with variable severity.[7,8] Patients with peritoneal dialysis (PD) or hemodialysis (HD) suffer from different CKD-associated pruritus at different rates, which requires further study.[9–11]

As a distressing symptom in ESRD patients, CKD-associated pruritus impairs their health-related quality of life (HRQOL)[12–14] and increases the risks of death and hospitalization.[15] In addition, patients with CKD-associated pruritus have a poorer quality of sleep or more serious depression as compared to patients without CKD-associated pruritus.[16–18] Notably, there is no single study tool for the measurement of CKD-associated pruritus. Many risk factors have been linked with CKD-associated pruritus in dialysis patients with ESRD,[19–21]

Editor: Dominik Steubl.

Xinmiao Hu and Yan Sang contributed equally to this work and should be considered co-first authors.

The authors have no funding and conflicts of interest to disclose.

[a] Department of General Surgery, Shanghai Children's Hospital, Shanghai Jiao Tong University, Shanghai, [b] Department of Nursing, Affiliated Hospital of Nantong University, [c] Department of Ophthalmology, Affiliated Hospital of Nantong University, Nantong, [d] Art College, Nanjing Audit University, Nanjing, Jiangsu, China.

[*] Correspondence: Mei Yang, Department of Ophthalmology, Affiliated Hospital of Nantong University, No. 20 Xisi Road, Nantong, Jiangsu 226001, China (e-mail: jsyangmei@126.com).

Medicine (2018) 97:21(e10633)

Received: 8 August 2017 / Accepted: 11 April 2018

http://dx.doi.org/10.1097/MD.0000000000010633

although with conflicting findings. Hence, the prevalence of CKD-associated pruritus in dialysis patients should be investigated in order to take appropriate measures for reducing the disease burden.

Till date, a limited comprehensive review of the prevalence and associations of CKD-associated pruritus in patients treated with dialysis has been performed. Therefore, a meta-analysis was needed to assess the absolute and relative prevalence, and risk factors for CKD-associated pruritus in dialysis patients.

2. Materials and methods

2.1. Data sources and search strategies

An electronic search of PubMed, Chinese National Knowledge Infrastructure, Elsevier, Web of Science, and Wanfang databases was conducted from inception to November 23, 2016. The search terms, like "dialysis," "hemodialysis," and "peritoneal dialysis," were united with the terms "pruritus," "itch," and "prevalence" to generate the references. We examined references of all retrieved studies and contacted authors to obtain further information, if necessary. The literature search was independently conducted by 2 reviewers (XH and YS) using a study selection form.

2.2. Eligibility criteria

Eligibility criteria were cross-sectional studies reporting the prevalence of CKD-associated pruritus in adult ESRD patients with dialysis. CKD-associated pruritus examined by a trained clinician was defined as an uncomfortable sensation of the skin resulting in the desire to scratch.[22] Editorials, letters, or case reports where no data on prevalence could be evaluated were excluded. Unpublished materials were also excluded.

2.3. Data extraction

Relevant data were independently extracted by 2 reviewers (XH and YS), and a discussion was held to achieve consensus. A third reviewer (MY) was consulted, if necessary. The extracted data included: first author, year of publication, country, study populations, sample size, prevalence, study methods quality, dialysis duration, study tools, and significant correlates of pruritus.

2.4. Study quality assessment

The quality of cross-sectional studies was estimated by Agency for Healthcare Research and Quality (AHRQ) ranging from 0 to 11 scores. Hu et al[23] also assessed the quality of cross-sectional studies using AHRQ. The instrument consisted of 11 points. If the answer was "NO" or "UNCLEAR," the item was scored "0"; conversely, the item was scored "1." According to the summarized scores, the quality of articles was classified into the following 3 levels: 0 to 3 was considered as low quality; 4 to 7 as moderate quality; and 8 to 11 as high quality.

2.5. Statistical analysis

All analyses were performed with STATA (version 12.0). Estimates were expressed as the prevalence and 95% confidence intervals (CIs) for each study.[24] Prevalence estimates from individual studies were pooled using a random-effects model.[25,26] Subgroup analyses were also used to study populations, gender, country, study tools, sample size, and year of publication. The heterogeneity across included studies was analyzed using Cochran Q (heterogeneity χ^2) and I^2 statistics.[27] In the χ^2-based Q test, $P < .10$ indicated no heterogeneity, while $P > .10$ was deemed as vital heterogeneity. Across the study, I^2 was used to evaluate total variation due to heterogeneity rather than chance (<25% was considered as low heterogeneity, 25% to 50% as moderate, and >50% as major heterogeneity). The funnel plot was used to examine potential publication bias.[28] Funnel plot asymmetry was evaluated using Egger linear regression test, where $P < .05$ was considered as statistically significant publication bias.

2.6. Ethics approval

All analyses were based on previously published studies. Hence, ethics approval or patient consent was not required.

3. Results

3.1. Search results

Figure 1 shows the detailed study selection process. A total of 6995 articles were identified by the literature search, of which 634 were from PubMed, 789 from Web of Science, 2684 from Elsevier, 1598 from Wanfang Data, and 1290 from CNKI. A total of 2979 duplicate studies were removed using NoteExpress software. Among the remaining studies, 3682 studies were excluded after screening the titles and abstracts. Therefore, 154 studies were chosen after full-text screening, of which 112 studies were excluded due to the following reasons: 27 studies included adolescent patients; 37 studies did not have data on the prevalence; 8 studies had incomplete data; 40 studies were not cross-sectional studies. Finally, 42 studies were included in the meta-analysis.

3.2. Study characteristics and quality assessment

Table 1 provides a summary of the characteristics of the included studies and detailed quality information. Our analysis included 42 eligible articles, which were all cross-sectional studies. Of these, 11 studies were published in Chinese, and 31 studies in English. The sample size of the included studies was 29 to 1773 patients, while a total of 11,800 patients were included in the 42 studies. A total of 24 studies assessed CKD-associated pruritus with a visual analog scale (VAS), which was reported from 0 to 10 (0=no pruritus and 10=intolerable pruritus). Moreover, 22 studies assessed CKD-associated pruritus by other validated and

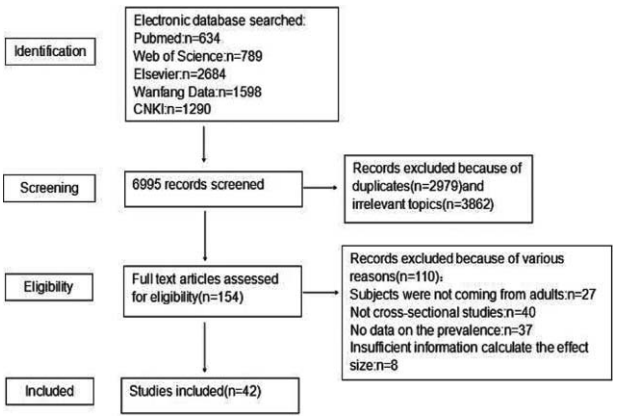

Figure 1. Flow chart of study selection.

Table 1

Basic characteristics of the included studies in the meta-analysis.

Reference, year	Country	Study populations	Study design	Quality*	Sample size	Setting†	Prevalence, %	Dialysis duration, mo	Woman, %	Study tool
Weiss et al, 2016[8]	Germany	HD	CS	7	860	0	18	57.6±55.2	42.8	A 10-cm VAS
Wu et al, 2016[9]	Taiwan	HD	CS	7	296	2	38.2	None	44.6	A 10-cm VAS
Wu et al, 2016[9]	Taiwan	PD	CS	7	84	2	28.6	None	65.5	A 10-cm VAS
Min et al, 2016[10]	Korea	HD	CS	6	425	0	48.3	None	44.2	A 10-cm VAS
Min et al, 2016[10]	Korea	PD	CS	6	223	0	62.8	None	40.8	A 10-cm VAS
Snit et al, 2013[11]	Poland	HD	CS	6	143	0	41.4	54.6±46.44	44.8	A 10-cm VAS
Snit et al, 2013[11]	Poland	PD	CS	6	54	0	46.3	39.48±38.4	44.4	A 10-cm VAS
Susel et al, 2014[16]	Poland	HD	CS	5	200	0	38	Not reported	38	A 10-cm VAS
Weiss et al, 2015[17]	Germany	HD	CS	8	860	0	25.2	58±56.2	42.8	A 10-cm VAS
Duque et al, 2006[18]	USA	HD	CS	7	105	0	57.1	Not reported	45	A 10-cm VAS
Caplin et al, 2011[29]	UK	HD	CS	6	508	3	52	Not reported	46.4	A 10-cm VAS
Kavurmaci, 2015[30]	Turkey	HD	CS	4	130	2	85.4	Not reported	42.3	A 10-cm VAS
Gatmiri et al, 2013[31]	Iran	HD	CS	6	99	2	58.6	Not reported	35.7	A 10-cm VAS
Chiu et al, 2008[32]	Taiwan	HD	CS	8	321	2	62.6	Not reported	50.5	A 10-cm VAS
Chen et al, 2010[33]	Taiwan	HD	CS	7	321	2	63.2	Not reported	50.5	A 10-cm VAS
Ko et al, 2014[34]	Taiwan	HD	CS	5	178	2	34.8	67.2±52.8	47	A 10-cm VAS
Narita et al, 2006[35]	Japan	HD	CS	5	1773	0	72.9	123.6±90.1	41.1	A 10-cm VAS
Malekmakan et al, 2015[36]	Iran	HD	CS	4	241	0	40.2	Not reported	46.9	All the patients were examined by a trained dermatologist
Subach and Marx, 2002[37]	USA	HD	CS	6	70	0	70	Not reported	58.6	A 100-cm VAS
Makhlough et al, 2013[38]	Iran	HD	CS	6	153	2	61.4	Not reported	47.7	A modified detailed scoring system proposed by Duo
Tajbakhsh et al, 2013[40]	Iran	HD	CS	5	100	2	39	Not reported	49	All the patients were examined by a trained dermatologist
Weisbord et al, 2005[41]	USA	HD	CS	7	162	0	54	Not reported	38.3	DSI
Peres et al, 2014[42]	Brazil	HD	CS	4	145	0	53.8	43.3±42.3	35.9	All the patients were examined by a trained dermatologist
Zucker et al, 2003[43]	USA	HD	CS	7	219	3	47.9	48±51.6	38	Interview
Mourad et al, 2014[44]	Egypt	HD	CS	5	93	2	51.6	38.77±10.6	39.8	All the patients were examined by a trained dermatologist
Dyachenko et al, 2006[45]	Israel	HD	CS	6	70	0	74.3	36±28.8	40	Interview
Lopes et al, 2012[46]	Brazil	HD	CS	6	980	0	43.8	Not reported	40.3	KDQOL-SF
Khanna et al, 2010[47]	India	HD	CS	6	200	2	58	17.1±16.3	43.5	A 100-cm VAS
Cengic et al, 2012[48]	Bosnia and Herzegovina	HD	CS	6	200	0	28	62.6±57	39	An 8-scale profile of functional health
Stahle-Backdahl et al, 1988[49]	Sweden	HD	CS	6	29	2	65.5	Not reported	51.7	All the patients were examined by a trained dermatologist
Wang et al, 2007[50]	China	HD	CS	7	190	2	48.9	41±36.1	43.7	A 10-cm VAS
Xia et al, 2009[51]	China	HD	CS	5	238	2	55.5	58.3±37.3	49.2	A 10-cm VAS
Wang et al, 2012[52]	China	HD	CS	6	97	2	55.7	13.9±10.9	40.2	All the patients were examined by a trained dermatologist
Wang et al, 2006[53]	China	HD	CS	7	126	2	73.8	56.37±37.31	50	Interview
Wang et al, 2012[52]	China	HD	CS	7	97	2	55.7	13.9±10.9	40.2	A 10-cm VAS
Hao et al, 2016[55]	China	HD	CS	6	125	2	64.8	Not reported	47.2	DSI
Wang et al, 2016[56]	China	HD	CS	8	301	2	77.7	75.12±66.84	41.2	DSI
Zhou et al, 2013[57]	China	HD	CS	6	280	2	73.2	40.27±30.24	42.1	DSI
Tu et al, 2016[58]	China	HD	CS	6	158	2	62.7	39.8±44.1	39.2	Dirk R Kuypers
Gao et al, 2014[59]	China	HD	CS	8	182	2	97.8	Not reported	51.6	DSI
Liu et al, 2016[60]	China	HD	CS	4	91	2	55	Not reported	44	A 10-cm VAS
Li et al, 2015[61]	China	PD	CS	7	362	0	65.2	Not reported	46.4	A 10-cm VAS
Figueiredo et al, 2012[62]	UK	PD	CS	6	41	0	78	Not reported	44	Questionnaire developed by authors
Tessari et al, 2009[63]	Italy	HD	CS	5	139	0	51.1	Not reported	Not reported	A 10-cm VAS
Tessari et al, 2009[63]	Italy	PD	CS	5	30	0	56.7	Not reported	Not reported	A 10-cm VAS
Hajheydari and Makhlough, 2008[39]	Iran	HD	CS	3	101	0	38.6	36±11	42.6	All the patients were examined by a trained dermatologist

Age and duration of dialysis listed as range or mean±standard deviation, when available. Only studies that reported at least 1 correlate or predictor were included in this table.

CS = cross-sectional study, DSI = Dialysis Symptom Index, HD = hemodialysis, KDQOL-SF = Kidney Disease Quality of Life Short Form, PD = peritoneal dialysis, VAS = visual analog score.

* Quality rated out of 8: 0 to 3=low quality; 4 to 7=medium quality, and 8 to 11=high quality.

† 0=not stated; 1=community; 2=hospital; and 3=community and hospital.

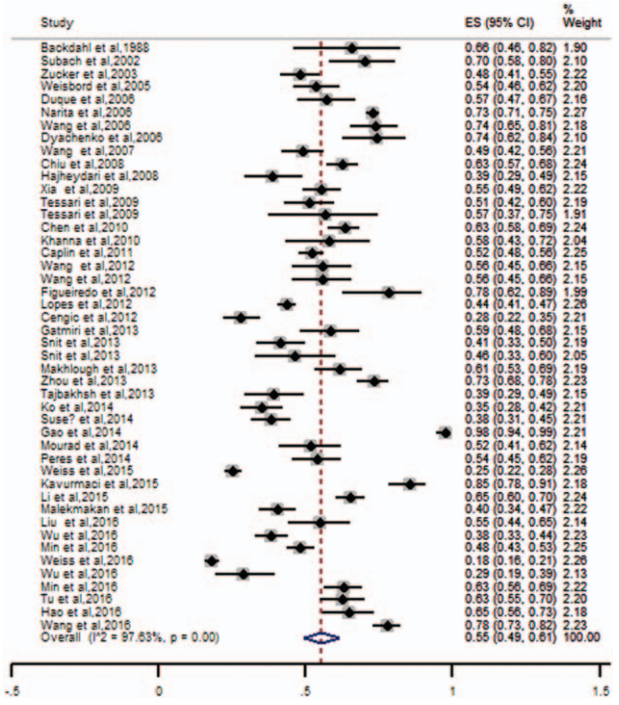

Figure 2. Forest plot of the 42 studies included meta-analysis.

invalid study tools. Thirty-six (85%) studies (10,003 patients)[8,16–18,29–60] only included HD patients, 2 (5%) studies (403 patients)[61,62] only included PD patients, and 4 (10%) studies (1394 patients)[9–11,63] included both HD and PD patients.

The quality scores of cross-sectional studies ranged from 3 to 8. Four studies were high quality, 37 studies were moderate quality, and 1 was low quality. Twenty articles reported the response rate and 15 articles had a sample size >200.

3.3. Prevalence of CKD-associated pruritus among dialysis patients

Among the adult dialysis patients, the prevalence of CKD-associated pruritus in each study ranged between 18% and 97.8% (Fig. 2; Table 1), and the overall prevalence of CKD-associated pruritus was 55% (95% CI, 49–61), with a high heterogeneity among studies (I^2 = 97.6%) (Fig. 2).

3.4. Subgroup analysis

Table 2 shows the results of subgroup analysis, such as gender, study populations, assessment tools, dialysis duration, different countries, and sample size. A total of 15 studies reported the prevalence of CKD-associated pruritus in males and females. The pooled prevalence in males was 55% (95% CI, 45–65), and that in females was 55% (95% CI, 46–65). Forty studies with HD patients showed that the prevalence of CKD-associated pruritus was 55% (95% CI, 49–62), while that in the PD patients was 56% (95% CI, 44–68). The pooled prevalence of CKD-associated pruritus among male HD patients was 54% (95% CI, 44–65), while among females was 55% (95% CI, 44–65). The pooled prevalence of CKD-associated pruritus in dialysis patients assessed with a VAS was 51% (95% CI, 42–60). Meanwhile, the pooled prevalence of CKD-associated pruritus in dialysis patients assessed by other tools was 60% (95% CI, 52–68). The pooled prevalence of CKD-associated pruritus in China was 61% (95% CI, 52–69), whereas in foreign countries, it was 52% (95% CI, 44–60). The prevalence of CKD-associated pruritus was 58%

Table 2

The prevalence of pruritus in different subgroup of adult dialysis patients.

Character	Number of studies	Sample size	Prevalence (95% CI), %	Heterogeneity		
				Q	*P*	I^2
Overall	42	11,800	55 (49–61)	1902.49	<.001	97.63
Gender						
Male	15	1981	55 (45–65)	262.83	<.001	94.67
Female	15	1645	55 (46–65)	208.39	<.001	93.28
Study populations						
Hemodialysis	40	11,326	55 (49–62)	1835.75	<.001	97.88
Peritoneal dialysis	6	474	56 (44–68)	49.46	<.001	89.89
Hemodialysis						
Male	14	1787	54 (44–65)	237.23	<.001	94.52
Female	14	1477	55 (44–65)	191.75	<.001	93.22
Study tools						
Visual analog scale	24	7727	51 (42–60)	1292.55	<.001	98.22
Other tools	22	4073	60 (52–68)	567.81	<.001	96.3
Country						
China	17	3447	61 (52–69)	433.1	<.001	96.31
Other countries	29	8353	52 (44–60)	1287.73	<.001	97.83
Sample size						
<100	13	905	58 (51–65)	54.97	<.001	78.17
100–199	15	2137	59 (48–70)	380.99	<.001	96.33
≥200	18	8758	51 (41–69)	1402.41	<.001	98.79
Dialysis duration						
Mean < 40	8	809	56 (48–63)	28.05	<.0001	75.05
Mean ≥ 40	13	5424	50 (36–64)	1308.80	<.0001	99.08

CI = confidential interval.

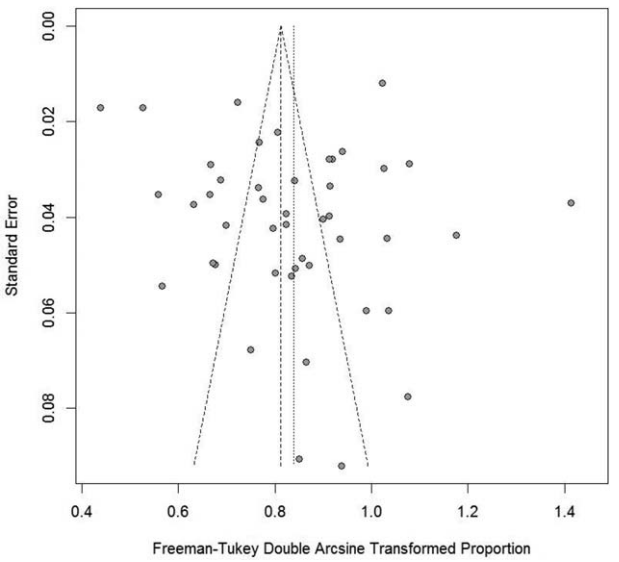

Figure 3. Funnel plot of the 42 studies included in the meta-analysis.

(95% CI, 51–65) for sample sizes <100 subjects, 59% (95% CI, 48–70) for samples with 100 to 199 people, and 51% (95% CI, 41–60) for sample sizes >199 people. Given the effects of dialysis duration, the prevalence of CKD-associated pruritus in patients with different dialysis duration was also analyzed. The pooled prevalence of CKD-associated pruritus was 56% (95% CI, 48–63) for mean dialysis duration <40 months and 50% (95% CI, 36–64) for mean dialysis duration ≥40 months.

3.5. Publication bias

Begg and Egger tests were used to evaluate publication bias (Fig. 3). There was no evidence of publication bias in the included studies using STATA (version 12.0).

4. Discussion

CKD-associated pruritus is a common cutaneous change in patients with chronic renal failure.[39,64,65] As a leading factor influencing the quality of life (QOL), CKD-associated pruritus is influenced by dialysis.[66] To the best of our knowledge, this is the first meta-analysis on the prevalence of CKD-associated pruritus among adult dialysis patients. After rigorous screening, a total of 42 studies conducted on 11,800 participants were included in this meta-analysis. The prevalence of CKD-associated pruritus among adult dialysis patients in each study was between 18% and 97.8%. The pooled prevalence of 42 studies was 55% (95% CI, 49–61). Patients suffering from CKD-associated pruritus accounted for a large proportion of dialysis patients. The heterogeneity in the prevalence data may be due to the different study design, selection of participants (e.g., study populations, races, and sample sizes), and the definition of CKD-associated pruritus in the included studies.

This meta-analysis showed that the pooled prevalence of CKD-associated pruritus in HD and PD was 55% and 56%, respectively. While some previous studies[11,63,67] had shown similar results, Min et al[10] found that HD patients had a higher prevalence of CKD-associated pruritus than PD patients. Moreover, Wu et al[9] found that HD patients had a significantly higher severity of CKD-associated pruritus than PD patients, while Mistik et al[68] showed the opposite results. Younger patients, shorter duration of dialysis and greater target dose for dialysis adequacy of solute clearance lead to lower severity of CKD-associated pruritus. However, the optimal treatment for reducing CKD-associated pruritus remains unknown. Therefore, randomized controlled trials are needed.

Previous studies reported that ESRD patients had poor HRQOL as compared to the general population.[69,70] Fei et al[71] evaluated the HRQOL using 36-Item Short Form Health Survey (SF-36) among HD and PD patients, and found that PD patients with HRQOL were better than HD patients, which was consistent with Huarong et al.[72] However, Xing et al[73] suggested no difference between PD and HD patients. These studies measured HRQOL using the SF-36, which is widely validated and applied to assess the QOL of patients and the general population.[74] The most optimal dialysis modality that could be widely used remains unknown.

Differences in the prevalence were observed among countries. For instance, in the United States, Duque et al[18] conducted a cross-sectional study including 105 HD participants and discovered that the prevalence of CKD-associated pruritus was 57.1%. Meanwhile, Gatmiri et al[31] studied 99 HD patients in Iran and found that the prevalence was 58.6%. These studies were consistent with the findings of the present meta-analysis. Nevertheless, other studies yielded different results. Yun and Ying[59] surveyed 182 HD patients in China and found a high prevalence of 97.8%. Another cross-sectional study in Turkey also showed a high prevalence of 85.4%.[30] Other studies found a lower prevalence than our study. For example, Weiss et al[8] conducted a cross-sectional study with 860 HD patients in Germany and found that the prevalence was only 18%. These discrepancies were perhaps due to regional, racial, and economic differences worldwide.

There are many study tools for measuring pruritus, such as a 4-item Itch Questionnaire and VAS.[75] Some patients were examined by a trained dermatologist.[39,40] Because majority of the studies used a VAS for the assessment of CKD-associated pruritus, the included studies were divided into 2 groups: those using a VAS and those using other tools. Patients measured by other study tools had a higher pooled prevalence of CKD-associated pruritus than those evaluated by a VAS (60% vs. 51%). Our study also found differences in classifying the high level of pruritus by a VAS. Thus, a more standardized questionnaire is needed to characterize pruritus.

Gender was related to the prevalence of CKD-associated pruritus in some studies with a small sample size.[30,31] However, our results indicated that the total prevalence rate of CKD-associated pruritus in both males and females was 55%, which was in agreement with the findings of Yun-Feng et al[51] and Malekmakan et al[36] with large sample sizes. Age, depression, quality of sleep, parathyroid hormone (PTH), and dialysis duration were predictors of pruritus in few studies.[17,29,46,50,58,76] Further studies are needed to explore other predictors of CKD-associated pruritus.[77,78]

Dialysis duration is an important factor affecting the prevalence of CKD-associated pruritus. Our findings indicated that the dialysis duration was negatively associated with the prevalence of CKD-associated pruritus, which was different from previous reports[11,17,35,43,45,50–54] that revealed no correlation between the 2. The following reasons could explain this phenomenon. First, most studies had a small sample size, and did not analyze whether dialysis duration was linked to the

prevalence of CKD-associated pruritus. Second, with the improvement of medical and health conditions, and living environment, along with patients' self-care awareness, efficient dialysis could provide a clinical benefit in some aspects. Third, since most studies had a short dialysis duration, we divided the dialysis duration into 2 groups, which may have oversimplified the results. Moreover, the prevalence of CKD-associated pruritus was correlated with the duration of renal chronic disease. Wikstrom[79] and Szepietowski et al[80] reported that dialysis duration was positively correlated with the intensity of CKD-associated pruritus. Future multicenter and large sample size studies are needed to arrive at a definite conclusion.

There were limitations to several studies on CKD-associated pruritus. Most patients had ESRD, were undergoing dialysis,[81,82] and were adults. Children also had a higher prevalence of CKD-associated pruritus.[75,83] There was no unique definition of the measured time point of CKD-associated pruritus in the majority of studies. Further studies are needed on this important and large subgroup of patients with CKD.

The present study had several notable limitations. First, the heterogeneity among the studies was high both in the total population and in the subgroups. Factors, such as age, gender, and disease duration might contribute to the risks of CKD-associated pruritus among dialysis patients. Second, all included studies were published only in English and Chinese. Third, sample sizes of the included studies were small. More than half of the studies included <200 people. Therefore, multicenter studies with a large sample are required to investigate the prevalence, severity, and association of CKD-associated pruritus among adult dialysis patients.

5. Conclusion

This meta-analysis demonstrated that more than half of adult dialysis patients suffered from CKD-associated pruritus. Both HD and PD patients had a high prevalence of CKD-associated pruritus. The prevalence of CKD-associated pruritus among adult dialysis patients was higher in China than in other countries. A multidisciplinary team would be indispensable for improving CKD-associated pruritus among dialysis patients in the future.

Author contributions

Conceptualization: Xinmiao Hu, Yan Sang.
Data curation: Xinmiao Hu, Yan Sang.
Formal analysis: Mei Yang.
Investigation: Xinmiao Hu, Mei Yang.
Methodology: Yan Sang, Mei Yang.
Project administration: Xinmiao Hu.
Supervision: Xue Chen.
Validation: Wenjuan Tang.
Visualization: Wenjuan Tang.
Writing – original draft: Xinmiao Hu.
Writing – review & editing: Xinmiao Hu, Yan Sang, Mei Yang, Xue Chen.

References

[1] Jha V, Garcia-Garcia G, Iseki K, et al. Chronic kidney disease: global dimension and perspectives. Lancet 2013;382:260–72.
[2] Hallan SI, Vikse BE. Relationship between chronic kidney disease prevalence and end-stage renal disease risk. Curr Opin Nephrol Hypertens 2008;17:286–91.
[3] White SL, Chadban SJ, Jan S, et al. How can we achieve global equity in provision of renal replacement therapy? Bull World Health Organ 2008;86:229–37.
[4] Patel TS, Freedman BI, Yosipovitch G. An update on pruritus associated with CKD. Am J Kidney Dis 2007;50:11–20.
[5] Murphy M, Carmichael AJ. Renal itch. Clin Exp Dermatol 2000;25: 103–6.
[6] Lonsdaleeccles A, Carmichael AJ. Treatment of pruritus associated with systemic disorders in the elderly: a review of the role of new therapies. Drugs Aging 2003;20:197–208.
[7] Kimata N, Fuller DS, Saito A, et al. Pruritus in hemodialysis patients: results from the Japanese Dialysis Outcomes and Practice Patterns Study (JDOPPS). Hemodial Int 2014;18:657–67.
[8] Weiss M, Mettang T, Tschulena U, et al. Health-related quality of life in haemodialysis patients suffering from chronic itch: results from GEHIS (German Epidemiology Haemodialysis Itch Study). Qual Life Res 2016;25:3097–106.
[9] Wu HY, Peng YS, Chen HY, et al. A comparison of uremic pruritus in patients receiving peritoneal dialysis and hemodialysis. Medicine (Baltimore) 2016;95:e2935.
[10] Min JW, Kim SH, Kim YO, et al. Comparison of uremic pruritus between patients undergoing hemodialysis and peritoneal dialysis. Kidney Res Clin Pract 2016;35:107–13.
[11] Snit M, Gawlik R, Lacka-Gazdzik B, et al. Substance P and intensity of pruritus in hemodialysis and peritoneal dialysis patients. Med Sci Monit 2013;19:723–32.
[12] Ibrahim MK, Elshahid AR, El BT, et al. Impact of uraemic pruritus on quality of life among end stage renal disease patients on dialysis. J Clin Diagn Res 2016;10:C1–5.
[13] Yngman-Uhlin P, Johansson A, Fernstrom A, et al. Fragmented sleep: an unrevealed problem in peritoneal dialysis patients. Scand J Urol Nephrol 2011;45:206–15.
[14] Szepietowski JC, Balaskas E, Taube KM, et al. Quality of life in patients with uraemic xerosis and pruritus. Acta Derm Venereol 2011;91:313–7.
[15] Mapes DL, Lopes AA, Satayathum S, et al. Health-related quality of life as a predictor of mortality and hospitalization: the Dialysis Outcomes and Practice Patterns Study (DOPPS). Kidney Int 2003;64:339–49.
[16] Susel J, Batycka-Baran A, Reich A, et al. Uraemic pruritus markedly affects the quality of life and depressive symptoms in haemodialysis patients with end-stage renal disease. Acta Derm Venereol 2014;94:276–81.
[17] Weiss M, Mettang T, Tschulena U, et al. Prevalence of chronic itch and associated factors in haemodialysis patients: a representative cross-sectional study. Acta Derm Venereol 2015;95:816–21.
[18] Duque MI, Thevarajah S, Chan YH, et al. Uremic pruritus is associated with higher kt/V and serum calcium concentration. Clin Nephrol 2006;66:184–91.
[19] Fallahzadeh MK, Roozbeh J, Geramizadeh B, et al. Interleukin-2 serum levels are elevated in patients with uremic pruritus: a novel finding with practical implications. Nephrol Dial Transplant 2011;26:3338–44.
[20] Ko MJ, Wu HY, Chen HY, et al. Uremic pruritus, dialysis adequacy, and metabolic profiles in hemodialysis patients: a prospective 5-year cohort study. PLoS ONE 2013;8:e71404.
[21] Xiang Q, Chu XL, Sun LY, et al. Uremia puritus of 59 uremic patients with hemodialysis. J Clin Dermatol 2002;7:430–1.
[22] Savin JA. How should we define itching? J Am Acad Dermatol 1998; 39:268–9.
[23] Hu J, Dong Y, Chen X, et al. Prevalence of suicide attempts among Chinese adolescents: A meta-analysis of cross-sectional studies. Comprehensive Psychiatry 2015;61:78–89.
[24] Wang D, Mou ZY, Zhai JX, et al. Application of Stata software to test heterogeneity in meta-analysis method. Zhonghua Liu Xing Bing Xue Za Zhi 2008;29:726–9.
[25] Pace NL. Research methods for meta-analyses. Best Pract Res Clin Anaesthesiol 2011;25:523–33.
[26] Cheung MW, Vijayakumar R. A guide to conducting a meta-analysis. Neuropsychol Rev 2016;26:118–21.
[27] Higgins JP, Thompson SG, Deeks JJ, et al. Measuring inconsistency in meta-analyses. BMJ 2003;327:557–60.
[28] Neyeloff JL, Fuchs SC, Moreira LB. Meta-analyses and Forest plots using a Microsoft excel spreadsheet: step-by-step guide focusing on descriptive data analysis. BMC 2012;5:52.
[29] Caplin B, Kumar S, Davenport A. Patients' perspective of haemodialysis-associated symptoms. Nephrol Dial Transplant 2011;26:2656–63.
[30] Kavurmaci M. Prevalence of uremic itching in patients undergoing hemodialysis. Hemodial Int 2015;19:531–5.
[31] Gatmiri SM, Mahdavi-Mazdeh M, Lessan-Pezeshki M, et al. Uremic pruritus and serum phosphorus level. Acta Med Iran 2013;51:477–81.

[32] Chiu YL, Chen HY, Chuang YF, et al. Association of uraemic pruritus with inflammation and hepatitis infection in haemodialysis patients. Nephrol Dial Transplant 2008;23:3685–9.
[33] Chen HY, Chiu YL, Hsu SP, et al. Elevated C-reactive protein level in hemodialysis patients with moderate/severe uremic pruritus: a potential mediator of high overall mortality. QJM 2010;103:837–46.
[34] Ko MJ, Peng YS, Chen HY, et al. Interleukin-31 is associated with uremic pruritus in patients receiving hemodialysis. J Am Acad Dermatol 2014; 71:1151–9.
[35] Narita I, Alchi B, Omori K, et al. Etiology and prognostic significance of severe uremic pruritus in chronic hemodialysis patients. Kidney Int 2006;69:1626–32.
[36] Malekmakan L, Malekmakan A, Sayadi M, et al. Association of high-sensitive C-reactive protein and dialysis adequacy with uremic pruritus. Saudi J Kidney Dis Transpl 2015;26:890–5.
[37] Subach RA, Marx MA. Evaluation of uremic pruritus at an outpatient hemodialysis unit. Ren Fail 2002;24:609–14.
[38] Makhlough A, Emadi N, Sedighi O, et al. Relationship between serum intact parathyroid hormone and pruritus in hemodialysis patients. Iran J Kidney Dis 2013;7:42–6.
[39] Hajheydari Z, Makhlough A. Cutaneous and mucosal manifestations in patients on maintenance hemodialysis: a study of 101 patients in Sari, Iran. Iran J Kidney Dis 2008;2:86–90.
[40] Tajbakhsh R, Dehghan M, Azarhoosh R, et al. Mucocutaneous manifestations and nail changes in patients with end-stage renal disease on hemodialysis. Saudi J Kidney Dis Transpl 2013;24:36–40.
[41] Weisbord SD, Fried LF, Arnold RM, et al. Prevalence, severity, and importance of physical and emotional symptoms in chronic hemodialysis patients. J Am Soc Nephrol 2005;16:2487–94.
[42] Peres LA, Passarini SR, Branco MF, et al. Skin lesions in chronic renal dialysis. J Bras Nefrol 2014;36:42–7.
[43] Zucker I, Yosipovitch G, David M, et al. 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;49:842–6.
[44] Mourad B, Hegab D, Okasha K, et al. Prospective study on prevalence of dermatological changes in patients under hemodialysis in hemodialysis units in Tanta University hospitals. Egypt Clin Cosmet Investig Dermatol 2014;7:313–9.
[45] Dyachenko P, Shustak A, Rozenman D. Hemodialysis-related pruritus and associated cutaneous manifestations. Int J Dermatol 2006;45:664–7.
[46] Lopes GB, Nogueira FC, de Souza MR, et al. Assessment of the psychological burden associated with pruritus in hemodialysis patients using the kidney disease quality of life short form. Qual Life Res 2012; 21:603–12.
[47] Khanna D, Singal A, Kalra OP. Comparison of cutaneous manifestations in chronic kidney disease with or without dialysis. Postgrad Med J 2010;86:617–41.
[48] Cengic B, Resic H, Spasovski G, et al. Quality of sleep in patients undergoing hemodialysis. Int Urol Nephrol 2012;44:557–67.
[49] Stahle-Backdahl M, Hagermark O, Lins LE. Pruritus in patients on maintenance hemodialysis. Acta Med Scand 1988;224:55–60.
[50] Wang YM, Ding XQ, Chen LM, et al. Clinical study of skin pruritus in 190 hemodialysis patients. Fudan Univ J Med Sci 2007;2:292–5.
[51] Xia YF, Shi W, Liang XL, et al. Clinical analysis of uremic pruritus in patients maintaining hemomalysis. J Fourth Mil Med Univ 2009;8: 719–22.
[52] Wang Y, Yang XL, Wang YJ. Analysis of factors related to pruritus and xeroderma in patients with chronic renal failure with hemodialysis patients. China J Lepr Skin Dis 2012;2:84–7.
[53] Wang Y, Li Y, Ding F, et al. Analysis of factors affecting frequency and intensity of pruritus in maintaining hemodialysis patients with end stage renal failure. Shangha Med J 2006;2:71–4.
[54] Wang Y, Yang XL, Wang YJ. Clinical and etiological analysis of skin complications in maintenance hemodialysis patients. Chin J Lepr Skin Dis 2012;3:171–3.
[55] Hao YH, Jiang YF. Symptom experiences among maintenance hemodialysis patients: a cross-sectional study. Chin J Nurs 2016;3: 299–303.
[56] Wang RP, Chen XF, Tang CY. Investigation of demographic characteristics and related factors of symptomatic disorder in maintenance hemodialysis patients. Nurs Pract Res 2016;18:4–7.
[57] Zhou XJ, Zhao QH, Liu LP. Symptom clusters among patients with maintenance hemodialysis. J Chongqing Med Univ 2013;7:697–700.
[58] Tu XW, Chen J, Tang DX, et al. Analysis of Related Factors of Skin Pruritus in Maintenance Hemodialysis Patients. J Jilin Med Sci 2016; 10:2496–8.
[59] Gao Y, Zhou Y. Investigation of symptom distress in maintenance hemodialysis patients. Modern Prevent Med 2014;15:2872–4.
[60] Liu QM. Analysis of skin pruritus in hemodialysis patients with chronic renal failure. World 's Latest Med Inform Digest 2016; 12:163.
[61] Li J, Guo Q, Lin J, et al. Prevalence and associated factors of uraemic pruritus in continuous ambulatory peritoneal dialysis patients. Intern Med 2015;542:827–33.
[62] Figueiredo AE, Goodlad C, Clemenger M, et al. Evaluation of physical symptoms in patients on peritoneal dialysis. Int J Nephrol 2012;2012: 305–424.
[63] Tessari G, Dalle Vedove C, Loschiavo C, et al. The impact of pruritus on the quality of life of patients undergoing dialysis: a single centre cohort study. J Nephrol 2009;222:241–8.
[64] Onelmis H, Sener S, Sasmaz S, et al. Cutaneous changes in patients with chronic renal failure on hemodialysis. Cutan Ocul Toxicol 2012;31: 286–91.
[65] Murtagh FE, Addington-Hall J, Higginson IJ. The prevalence of symptoms in end-stage renal disease: a systematic review. Adv Chronic Kidney Dis 2007;14:82–99.
[66] Weiss M, Weisshaar E. Qualitative interviews on chronic pruritus in haemodialysis patients. Acta Derm Venereol 2014;94:713–4.
[67] Berger TG, Steinhoff M. Pruritus and renal failure. Semin Cutan Med Surg 2011;30:99–100.
[68] Mistik S, Utas S, Ferahbas A, et al. An epidemiology study of patients with uremic pruritus. J Eur Acad Dermatol Venereol 2006;20:672–8.
[69] Zhang HL, Lu Q, Wen CJ, et al. Study on physical activity level and quality of life for young and middle-aged patients undergoing hemodialysis. J Nurs Training 2012;4:293–6.
[70] Lou YJ, Yang LJ, Song XJ, et al. A study on the emotion and quality of life of the maintenance hemodialysis patients and their families. Chin J Clin Psychol 2010;2:196–7.
[71] Deng F, Hong DQ, Feng J, et al. Analysis of the quality of life the related factors of patients with hemodialysis and peritoneal dialysis. Med Front 2016;6:102–3.
[72] Yang Z, Bo QU, Lun SS. Economic burden and quality of life of renal replacement therapy. J Clin Nephrol 2012;12:459–61.
[73] Wu X, Ye RG, Wang T, et al. The relationship between quality of life and nutritional status in dialysis patients. J Sun Yatsen Univ 2003; 24:401–3.
[74] Zhang Y, Qu B, Lun SS, et al. The 36-item short form health survey: reliability and validity in Chinese medical students. Int J Med Sci 2012;9:521–6.
[75] Wojtowicz-Prus E, Kilis-Pstrusińska K, Reich A, et al. Chronic kidney disease-associated pruritus in children. Acta Derm Venereol 2016;96: 938–42.
[76] Narita I, Iguchi S, Omori K, et al. Uremic pruritus in chronic hemodialysis patients. J Nephrol 2008;21:161–5.
[77] Tajbakhsh R, Joshaghani HR, Bayzayi F, et al. Association between pruritus and serum concentrations of parathormone, calcium and phosphorus in hemodialysis patients. Saudi J Kidney Dis Transpl 2013; 24:702–6.
[78] Akhyani M, Ganji MR, Samadi N, et al. Pruritus in hemodialysis patients. BMC Dermatol 2005;5:7.
[79] Wikstrom B. Itchy skin—a clinical problem for haemodialysis patients. Nephrol Dial Transplant 2007;22(suppl 5):v3.
[80] Szepietowski JC, Szepietowski T, Reich A. Efficacy and tolerance of the cream containing structured physiological lipids with endocannabinoids in the treatment of uremic pruritus: a preliminary study. Acta Dermatovenerol Croat 2005;13:97–103.
[81] Lugon JR. Uremic pruritus: a review. Hemodial Int 2005;9:180–8.
[82] Bednarova V, Hruskova Z, Motan V, et al. Peritoneal dialysis and its modification in the treatment of chronic renal failure. Vnitr Lek 2011;57:635–9.
[83] Senturk N, Ozkaya O, Aytekin S, et al. Characteristics of pruritus in children on peritoneal dialysis. Nephron Clin Pract 2008;109:c168–72.