A Scoping Review: Factors Associated with Pruritus in CKD (Chronic Kidney Disease) Patients Undergoing Dialysis

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ARTICLE INFO

Article history:
Received 21 November 2022
Accepted 1 April 2023
Published 10 June 2023

Keyword:
Chronic Kidney Disease
Dialysis
Pruritus

Abstract

Chronic Kidney Disease (CKD) is characterized by progressive loss of kidney function over time due to kidney damage or reduced glomerular filtration rate (GFR) <60 mL/min/173m² for >3 months. The increased levels of urea in patients with chronic kidney failure can cause pruritus known as uremic pruritus or chronic kidney disease associated pruritus (CKD-ap). The research method that will be used is PRISMA. These scoping reviews will use a systematic approach and selection process. Library sources were traced from the Proquest, PubMed, Scopus and Google Scholar databases. This scoping review examines the associated factors with pruritus in patients undergoing dialysis. Factors related to uremic pruritus, namely based on analysis through scoping reviews that have been carried out on 8 articles, it was found that the most widely used study design was cross-sectional, the most widely used type of dialysis is hemodialysis with the number of articles is 3 and the number of patients that is male 505 samples (60.4%) and women 331 samples (39.6%) with the Total is 836 samples. Factors associated with uremic pruritus are gender, age, dialysis dose, duration of dialysis, urea/urea, C-Reactive Protein (CRP), and parathyroid hormone (PTH). The conclusion is that the factor that most dominant factor affecting pruritus is the factor of laboratory results, which is a factor that can be modified.

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DOI: 10.30604/jika.v8i2.1763
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INTRODUCTION

Chronic Kidney Disease (CKD) is characterized by progressive loss of kidney function over time due to kidney damage or reduced glomerular filtration rate (GFR) <60 mL/min/173m² for >3 months. CKD is a kidney disease in which there is a gradual decline in kidney function over several months or years (>3 months) (Hasan & Obeed, 2021; Swarna et al., 2019).

The prevalence of CKD worldwide reaches 9.1%, which is estimated at around 700 million. The Riskesda report (2018) shows that the prevalence of chronic kidney disease in Indonesia is 0.38% or 713,783 cases. The Data from PERNEFRI states that the prevalence of kidney disease is quite high, reaching 30.7 million (Nurmansyah & Arofiati, 2019). Data from *Dialysis Outcomes and Practice Patterns Study* (DOPPS), which is an observational study, revealed that 67% of the 23,264 patients undergoing hemodialysis experienced problems, namely chronic pruritus. (Locatelli & Legat, 2021).

Patients with chronic kidney failure will experience an increase in urea and creatinine caused by failure of the kidney function to secrete the remains of metabolic substances in the body (Smeltzer & Bare, 2013). An increased level of urea in the body can cause organ function disorders such as fluid and electrolyte disturbances, skin, endocrine metabolism, neuromuscular, cardiovascular, lung, gastrointestinal, hematological, and immunological (Jameson et al., 2015).

Pruritus is a skin problem that interferes with the quality of sleep and daily activities of patients with chronic kidney failure due to the itchiness that appears (Shaikh et al., 2019). Not only that, Juanda research (2017) states that pruritus gives patients a feeling of discomfort, embarrassment, and lack of confidence. It is feared that things like this can lead to more severe psycho-social problems and also do not rule out the possibility that patients will experience mental disorders (Oxtavia et al., 2017). Apart from the psychological impact, Yonathan & Darmawan (2021) stated that patients with chronic kidney disease with symptoms of pruritus are more at risk of infection, injury, calciphylaxis, acquired perforating dermatosis, and nephrogenic systemic fibrosis.

Considering the high incidence of uremic pruritus and complications resulting from uremic pruritus in CKD patients, this scoping review intends to examine what factors cause pruritus in patients undergoing dialysis.

METHODS

The research method that will be used is PRISMA. This scoping review uses a systematic approach and selection process. Library sources were traced from national and international databases including Proquest, PubMed, Google Scholar, and Scopus. The keywords that will be used in the search are (etiology AND pruritus AND uremic AND patients AND dialysis AND Chronic kidney disease). This *scoping review* aims to examine the associated factors with pruritus in patients undergoing dialysis. Therefore the inclusion criteria used to determine that an article is eligible to be included in the review are as follows: patients experiencing uremic pruritus, CKD patients undergoing dialysis, journal publications for the last 5 years (2018-2022), and the study design, which is cross sectional, cohort, and descriptive studies.

RESULTS AND DISCUSSIONS

Based on the search results for articles through the database, namely Proquest, Pubmed, Google Scholar, and Scopus, 13,081 articles were shows high relevance to the topics reviewed between 2018-2022, totaling 3,149 articles. After article check for duplicates, abstracts, and titles 19 articles were entered the next stage of full text and eligibility studies based on the criteria inclusion and exclusion set by the researcher. The 8 research articles that met the criteria inclusion were then reviewed for quality and synthesized into the final report of this scoping review.
**Table 1** List of research articles in *scoping review* on factors causing pruritus in CKD patients undergoing dialysis

<table>
<thead>
<tr>
<th>No</th>
<th>Author (Year)</th>
<th>Title</th>
<th>Country</th>
<th>Study Design</th>
<th>Dialysis Type</th>
<th>Number Of Samples</th>
<th>Outcome</th>
</tr>
</thead>
</table>
2. Age |
| 2  | (Minato et al., 2020) | Factors associated with uremic pruritus in patients undergoing peritoneal dialysis | Japan    | Cross-sectional | Peritoneal Dialysis | 46 patients | Gender (male) |
| 3  | (Zhao et al., 2021) | Determinants of the intensity of uremic pruritus in patients receiving maintenance hemodialysis: A cross-sectional study | India    | Cross-sectional | Hemodialysis | 148 patients | 1. Duration of dialysis  
2. Total dialysis adequacy (dialysis dose) ≤18 Kt/V  
3. Parathyroid Hormone  
4. C-Reactive Protein (CRP) |
| 4  | (Wu et al., 2018) | Prognostic importance and determinants of uremic pruritus in patients receiving peritoneal dialysis: A prospective cohort study | Taiwan   | Cohort study   | Peritoneal Dialysis | 85 PD patients | |
| 5  | (A Harlim., 2020) | Factors associated with uremic pruritus in chronic kidney failure patients | Indonesia| Cross-sectional | Hemodialysis | 33 patients | Hemodialysis duration |
| 6  | (Kumar et al., 2020) | Uremic Pruritus and associated factors in Chronic Dialysis Patients: An Observational Study in Western Nepal | Nepal    | Cohort study   | Hemodialysis and Peritoneal Dialysis | 59 patients | Urea Serum |
| 7  | (Hu et al., 2019) | Clinical features and risk factors of pruritus in patients with chronic renal failure | China    | Cohort study   | Hemodialysis and Peritoneal Dialysis | 382 patients | PTH (Parathyroid Hormone) |
| 8  | (Mehrkash et al., 2021) | Pruritus Features in Children with End-Stage Renal Disease Underwent Dialysis: A Cross-Sectional Study | Iran     | Cross-sectional | Hemodialysis and Peritoneal Dialysis | 30 patients | 1. Age  
2. PTH (Parathyroid Hormone) |

**Table 2** Characteristics Description

<table>
<thead>
<tr>
<th>No</th>
<th>Characteristics</th>
<th>Frequency (N)</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Design Studies</td>
<td>8 articles</td>
<td>62.5%</td>
</tr>
<tr>
<td></td>
<td>Cross-Sectional Cohort Study</td>
<td>5 articles</td>
<td>37.5%</td>
</tr>
<tr>
<td>2</td>
<td>Dialysis Type</td>
<td>3 articles</td>
<td>37.5%</td>
</tr>
<tr>
<td></td>
<td>Hemodialysis</td>
<td>1 article</td>
<td>25%</td>
</tr>
<tr>
<td></td>
<td>Peritoneal Dialysis</td>
<td>1 article</td>
<td>25%</td>
</tr>
<tr>
<td></td>
<td>Hemodialysis and peritoneal dialysis</td>
<td>1 article</td>
<td>25%</td>
</tr>
<tr>
<td>3</td>
<td>Country</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>West Asia</td>
<td>2 articles</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Iraq</td>
<td>1 article</td>
<td>25%</td>
</tr>
<tr>
<td></td>
<td>Iran</td>
<td>1 article</td>
<td></td>
</tr>
<tr>
<td></td>
<td>East Asia</td>
<td>2 articles</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Japan</td>
<td>1 article</td>
<td>37.5%</td>
</tr>
<tr>
<td></td>
<td>Taiwan</td>
<td>1 article</td>
<td></td>
</tr>
<tr>
<td></td>
<td>China</td>
<td>1 article</td>
<td></td>
</tr>
<tr>
<td></td>
<td>South Asia</td>
<td>1 article</td>
<td></td>
</tr>
<tr>
<td></td>
<td>India</td>
<td>1 article</td>
<td>25%</td>
</tr>
<tr>
<td></td>
<td>Nepal</td>
<td>1 article</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Southeast Asia</td>
<td>1 article</td>
<td>12.5%</td>
</tr>
<tr>
<td>4</td>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Male</td>
<td>505 sample</td>
<td>60.4%</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>331 sample</td>
<td>39.6%</td>
</tr>
</tbody>
</table>

**Table 3** Factors Associated with Uremic Pruritus

<table>
<thead>
<tr>
<th>No</th>
<th>Characteristics</th>
<th>Results Summary</th>
<th>Frequency (N)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Gender</td>
<td>Male 72 patients (72.7%) Female 27 patients (27.3%)</td>
<td>2 articles</td>
</tr>
<tr>
<td>2</td>
<td>Age</td>
<td>Age ≥ 45 Years</td>
<td>1 article</td>
</tr>
<tr>
<td>3</td>
<td>Dialysis Dosage</td>
<td>HD Adequacy value &lt;1.88 Kt/V</td>
<td>1 article</td>
</tr>
<tr>
<td>4</td>
<td>Duration of dialysis</td>
<td>Duration of dialysis &gt;4.1 Year</td>
<td>1 article</td>
</tr>
<tr>
<td>5</td>
<td>Laboratory Results</td>
<td>Urea/ureum</td>
<td>2 articles</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mean urea 19.95 mmol/L, or in the range of 18.28–21.65 mmol/L</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mean urea 122.4 mg/dl with SD 36.1, 2.00 (1.00–3.00) &gt; 0.16 (mg/L)</td>
<td>2 articles</td>
</tr>
<tr>
<td></td>
<td></td>
<td>C-Reactive Protein (CRP)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Parathyroid Hormone (PTH)</td>
<td>3 articles</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mean 251.2 (pg/ml) with SD 524.12 pg/ml with SD 313.53</td>
<td>3 articles</td>
</tr>
</tbody>
</table>
Patient characteristic factors

a. Gender

The results of a cross-sectional study showed that the male sex experienced the most uremic pruritus, namely 72 patients (72.7%) compared to women (Hasan & Obeed 2021). This is in line with Hasan & Obeed (2021) cross-sectional study which states that gender is associated with uremic pruritus with a value (p<0.017).

b. Age

The results of a cross-sectional study showed that ≥45 years of age experienced uremic pruritus the most, namely 46 patients (80.8%). Hasan & Obeed (2021) cross-sectional study states that age is associated with uremic pruritus with a value (p<0.034).

Most of the uremic pruritus patients are in middle adulthood, aged 41-60 years. This may be due to the unhealthy lifestyle of the middle adulthood group, such as eating fast food, stressful activities, sitting in the office all day, consuming coffee and energy drinks frequently, and rarely drinking water. This bad habit is a risk factor for kidney damage. Kidney damage is the main cause of uremic pruritus. In addition, the decreased ability of the body to metabolize substances that cause uremic pruritus between the ages of 41 and 60 years is also the reason for the high incidence of uremic pruritus in this age group (Fauziah & Soelistyowati, 2018).

c. Dialysis dose

Dialysis doses with HD adequacy values <1.88 Kt/V can be a factor causing pruritus. This is in line with a cross-sectional study conducted by Kossuth Cabrejos et al (2020) which stated that there was a relationship between dialysis dose and uremic pruritus as indicated by the value (p<0.002).

In the study, Wu et al (2018) Severity of uremic pruritus was greater in patient with weekly total Kt/V <1.88 (HD work capacity value or urea clearance ratio) than in patients with high solute clearance. According clinical guidelines, target dose of total weekly Kt/V ≥17 Kt/V to ensure adequate clearance of the solution in peritoneal dialysis. The higher the total weekly Kt/V value, it will show that the cleanliness of the solute is higher, so it can remove pruritogenic substances. Pruritogenic substances that can be dialyzed with optimal dialysis targets can reduce uremic pruritus (Wu et al, 2018).

d. Duration of dialysis

The length of the duration of undergoing hemodialysis is one of the factors causing the problem of uremic pruritus. This is supported by the research of Wu et al (2018) which states that there is a relationship between the duration of dialysis and uremic pruritus with an indicated value (p<0.032).

Uremic pruritus is related to the duration of dialysis. This is affected by further damage to kidney function. In theory, it is explained that uremic pruritus usually occurs in patients undergoing dialysis for a long time. The researchers find duration dialysis affected the severity of uremic pruritus symptoms, namely the longer the dialysis treatment was carried out, the more severe the uremic pruritus. This is further exacerbated by impaired kidney function. Therefore, people with CKD are expected to follow and adhere to a predetermined diet so that kidney function does not worsen and uremic pruritus does not get worse (Fauziah & Soelistyowati, 2018).

Laboratory result factor

a. Urea/ureum

Urea levels that exceed normal limits, namely 7-30 mg/Dl or 2.5-10.7 mmol/L, are trigger factors for uremic pruritus. This is in line with the research of Zhao et al (2021) which states that there is a relationship with uremic pruritus, namely a value (p<0.028).

Urea is a substance that is not charged (uncharged), not bound in plasma, soluble in water, easily diffuses between water compartments, easily dialyzed, and dispersed in body fluids. In addition to its low toxicity, urea is a good marker of uremic conditions because it is a product of protein degradation. Uremia is the most common cause of metabolic pruritus in uremic pruritus. Complaints of pruritus are thought to be related to the release of histamine from mast cells in the skin. Histamine is released by mast cells and directly stimulates H1 receptors on specific C fibers. The number of mast cells and basophils increases, resulting in uremic pruritus (Ago Harlim & Yogyartono, 2012; Pardede, 2010; Roswati, 2013).

b. C-Reactive Protein (CRP)

CRP level >0.16 (mg/L) is a factor for uremic pruritus. In line with the prospective cohort study conducted by Wu et al (2018) which states that CRP levels are associated with uremic pruritus as evidenced by the results of the multivariate test with a value (p<0.032).

Uremic pruritus is also known as a systemic disorder associated with inflammation. Inflammation is a marker associated with uremic pruritus in both hemodialysis and peritoneal dialysis patients. Uremic pruritus is considered a skin reaction to an ongoing inflammatory process characterized by increased levels of high-sensitive reactive protein C. The state of uremic inflammation also explains the high number of mast cells in the dermis which eventually results in uremic pruritus (Pardede, 2010; Sarhan et al, 2020; Tseng et al, 2018).

c. Parathyroid Hormone (PTH)

Parathyroid hormone (PTH) affects the occurrence of uremic pruritus. According to Hu et al (2019), there is a relationship between PTH and uremic pruritus as evidenced by the value (p<0.001). Hyperparathyroidism can trigger mast cells to release histamine, causing microprecipitation of calcium and magnesium salts in the skin. However, not all patients with severe hyperparathyroidism experience uremic pruritus. One study reported that pruritus disappeared completely after parathyroidectomy. It was further noted that there was no
relationship between plasma PTH (parathyroid hormone) levels and dermal cell proliferation, nor was there a difference in the number of mast cells or PTH levels between patients with and without pruritus (Roswati, 2013).

LIMITATION OF THE STUDY

This article only uses search sources from four databases and all literature sources obtained in this search are only articles in English.

CONCLUSIONS AND SUGESTIONS

Based on the analysis through scoping review that has been done, it can be concluded that the most dominant factor affecting pruritus is the factor of laboratory results, which is a factor that can be modified. It is recommended to change lifestyles so that the results of the laboratory experience change.

ETHICAL CONSIDERATIONS

Funding Statement

This research was not sponsored or supported by any institution or organization

Conflict of Interest Statement

No conflict of interest

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Smeltzer, S. C., & Bare, B. G. (2013). *Buku Ajar Keperawatan Medikal Bedah*. EGC.


