

The association between CKD-associated pruritus and quality of life in patients undergoing hemodialysis in Pakistan

A STROBE complaint cross-sectional study

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Abstract

Chronic kidney disease (CKD)-associated pruritus is one of the most common symptoms found in patients who undergo dialysis for CKD, leading to a compromised quality of life. This study aimed to investigate the association between CKD-associated pruritus and the quality of life in patients undergoing hemodialysis in Pakistan.

A cross-sectional multicenter study was carried out from July 2016 to April 2017 in 2 tertiary care hospitals in Pakistan. Patients aged 18 years and above of both genders, undergoing hemodialysis, understood the Urdu language, and were willing to participate; were included.

Of 354 recruited patients with a response rate of 100%, majority (66.1%) of the patients were males. The median (intra-quartile range [IQR]) age of patients was 42.0 [34.0–50.0] years. The prevalence of pruritus was 74%. The median [IQR] score for pruritus was 10.0 (out of possible 25) [8.0–12.0]. Multivariate linear regression revealed a statistically significant association between CKD-associated pruritus with age of patients ($\beta=0.031$; 95% confidence interval [CI]=0.002–0.061; $P=.038$), duration of CKD ($\beta=-0.013$; 95% CI = -0.023 – -0.003; $P=.014$) and quality of life ($\beta=-0.949$; 95% CI = -1.450; -0.449). The median [IQR] score for health-related quality of life was 52.00 [43.00–58.00].

Prevalence of CKD-associated pruritus was reported to be 74% and it negatively affected the patient's quality of life. Patients with moderate to severe CKD-associated pruritus have poor quality of life. With an increase in intensity of pruritus, the QOL score decreased among the patients undergoing hemodialysis.

Abbreviations: CI = confidence interval, CKD = chronic kidney disease, FANLTC = functional assessment for non-life-threatening conditions, IQR = intra-quartile range, KMO = Kaiser-Meyer-Olkin.

Keywords: CKD-associated pruritus, FANLTC, hemodialysis, Pakistan, quality of life

1. Introduction

Chronic kidney disease (CKD)-associated pruritus is one of the common symptoms observed in CKD patients undergoing dialysis. Research has shown higher incidences of CKD-associated pruritus in patients undergoing hemodialysis as compared to those undergoing peritoneal dialysis (68% vs

38% respectively).^[1] There are wide variations in the prevalence of CKD-associated pruritus in patients with CKD ranging from 18% to 97%.^[2] A myriad of metabolic changes that are associated with CKD has been linked to the activation and intensification of CKD-associated pruritus such as xerosis, lower trans-epidermal elimination of pruritogenic factors, hyperparathyroidism, hypercalcemia, hypophosphatemia, increased

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amounts of histamine, transdermal mast cell proliferation, and uremic sensory neuropathy.^[3] Chronic pruritus significantly impairs the quality of life of CKD patients by exerting deteriorating effects on the physical, psychological, social, and functional wellbeing of these individuals.^[4] All these eventually lead to daytime fatigue, depressive symptoms, and insomnia.^[5–7]

The quality of life of patients with CKD deteriorates with the progression and increased severity of the associated pruritus. Research has shown that uremic pruritus is associated with a higher probability of death in patients suffering from CKD.^[8] The quality of life of patients having CKD-associated pruritus is compromised owing to the restricted personal autonomy and control, which in turn is due to the treatment which requires a longer duration. Generally, this loss of freedom or autonomy has a deeper impact on the lives of patients such as impaired marital, family, and social relationships.^[9] Treating CKD-associated pruritus among CKD patients is a huge challenge as it is commonly resistant to oral anti-histamines and centrally acting drugs, such as Gabapentin. As a result, it is necessary to develop an understanding regarding factors linked with CKD-associated pruritus and its intensity. Doing so can assist in the execution of strategies such as dialysis adequacy and metabolic stabilization, which can be adopted along with drug treatment.^[10]

To date, no study is done to determine the prevalence of CKD-associated pruritus and its association with quality of life among hemodialysis patients in Pakistan. This study aimed at investigating the association between CKD-associated pruritus and the quality of life in patients undergoing hemodialysis in Pakistan.

2. Methodology

In order to ascertain the relationship between CKD-associated pruritus and the quality of life among patients undergoing hemodialysis, a prospective cross-sectional multicenter study was carried out. Data for the present study were collected from 2 tertiary hospitals, namely Pakistan Kidney Patients Association, in Rawalpindi and Institute of Kidney Diseases, in Peshawar. The study was conducted from July 2016 to April 2017.

3. Sample size

Sample size was calculated by using Daniel sample size.^[11] Our pilot study found prevalence of CKD-associated pruritus as 70%.^[12] The minimum sample size required was 322 (with 95% level of confidence and 80% power). However, 354 respondents were recruited to remove the chance of error.

4. Patients recruitment criteria

4.1. Inclusion criteria

Patients aged 18 years and above, both genders, undergoing hemodialysis, understand the Urdu language and willing to participate in the research project.

5. Procedure

5.1. Patient recruitment

Patients were contacted while they were undergoing hemodialysis. The objective of the study was explained to them. A written informed consent form was signed by patients who were willing to participate.

6. Study tools

6.1. Baseline demographic questionnaire

This questionnaire was used to collect demographic data such as socioeconomic status, disease duration, dialysis duration, and comorbidities conditions.

6.2. Validated Urdu 5D-itch scale

In order to measure CKD-associated pruritus, a validated version of the Urdu 5D itch scale in hemodialysis^[12] was administered. The scale has 5 domains, which are duration, degree, direction, disability, distribution.^[12] The overall score of the Urdu 5D-itch scale was calculated by summing all 5 domains; a score below 5 indicates no pruritus; whilst a score of 25 indicates severe pruritus.^[12]

6.3. Urdu FANLTC scale

To assess the aspects of quality of life, the Urdu version of the Functional Assessment for Non-Life-Threatening Conditions (FANLTC) was administered. The FANLTC has 4 subscales (i.e., physical well-being, social/family well-being, emotional well-being, and functional well-being), and the overall quality of life can be assessed by using scoring manual for all 26-items on the scale. In each subscale, each item is scored from 0 which means “not at all” to 4 which means “very much”. The scoring of positively stated items is 4, 3, 2, 1, and 0, while the negatively stated items are reverse scored. In order to score subscales, the scores of all items are summed, multiplied by the number of items in every subscale, and divided by the number of items answered. The overall FANLTC score is calculated by totaling the scores of all 4 subscales.^[13] The overall FANLTC score ranges from 0 to 104. Higher score reveals better quality of life. The reliability and validity of the Urdu version of the FANLTC was checked: Cronbach’s alpha was used to assess the internal consistency of the Urdu FANLTC version. A Cronbach’s alpha value of >0.70 indicates good internal consistency,^[14] and the Cronbach’s alpha for the Urdu FANLTC version was found to be 0.759. To address any concerns about the tool’s content, its adequacy was measured using the Bartlett test of sphericity. The Kaiser-Meyer-Olkin (KMO) measure of sampling adequacy is an effective technique for judging content adequacy. A KMO value greater than 0.6 indicates an acceptable level of compatibility of the variables with the test, while 0.80 indicates a good level.^[15] The KMO for the Urdu FANLTC version was found to be 0.851 and the Bartlett test of sphericity was found to be significant ($df=325$, $P<.001$). These values demonstrate that the contents of the instrument are satisfactory to meet the study’s needs.

7. Ethical considerations

The study was approved by the Monash University Human Research and Ethics Committee (MUHREC Approval No: CF16/1766–2016000890); Institute of Kidney Diseases (IKD Peshawar) Pakistan, committee (Approval No: 844) and Pakistan Kidney Patient Association (Rawalpindi) Pakistan. Written informed consent was obtained from patients. The names and identities of the respondents were kept confidential and were not reported.

Table 1
Demographics of participants (n=354).

	Total no. of patient (n=354) N (%)	Without pruritus n=92N (%)	With pruritus n=262N (%)	P value
Gender				
Male	234 (66.1)	58 (24.8)	176 (75.2)	.471*
Female	120 (33.9)	34 (28.3)	86 (71.7)	
Median age [IQR] in years	42.0 [34.0–50.0]	40.0 [30.0–48.0]	42.0 [35.0–51.0]	.013 ^{†,‡}
18–30 yr	64 (18.1)	27 (42.2)	37 (57.8)	.012 ^{†,‡}
31–40 yr	108 (30.5)	24 (22.2)	84 (77.8)	
41–50 yr	99 (28)	26 (26.3)	73 (73.7)	
51–60 yr	57 (16.1)	9 (15.8)	48 (84.2)	
61–70 yr	19 (5.4)	3 (15.7)	16 (84.2)	
70 yr and above	7 (2)	3 (42.9)	4 (57.1)	
Median duration of CKD [IQR] in months	36.0 [12.0–48.0]	24.0 [12.0–36.0]	36.0 [24.0–48.0]	<.001 ^{†,‡}
< 1 yr	40 (11.3)	22 (55.0)	18 (45)	<.001 ^{†,‡}
1–2 yr	126 (35.6)	40 (31.7)	86 (68.3)	
3–4 yr	114 (32.2)	15 (13.2)	99 (86.8)	
5–6 yr	37 (10.5)	10 (27.0)	27 (73.0)	
7–8 yr	20 (5.6)	2 (10.0)	18 (90)	
9–10 yr	9 (2.5)	1 (11.1)	8 (88.9)	
11 yr and more	8 (2.3)	2 (25.0)	6 (75.0)	
Median duration on hemodialysis [IQR] in months	24.0 [12.0–36.0]	7.0 [2.25–12.0]	24.0 [12.00–36.0]	<.001 ^{†,‡}
< 1 yr	86 (24.3)	51 (59.3)	35 (40.7)	<.001 ^{†,‡}
1–2 yr	150 (42.4)	31 (20.7)	119 (79.3)	
3–4 yr	97 (27.4)	10 (10.3)	87 (89.7)	
5–6 yr	13 (3.7)	0	13 (100)	
7–8 yr	8 (2.3)	0	8 (100)	
frequency of hemodialysis				
Twice a week	354 (100)	92 (26)	262 (74)	–
Presence of co-morbidities [§]				
Diabetes mellitus	47	11 (23.4)	36 (76.6)	
Hypertension	215	38 (17.7)	177 (82.3)	
Hyperlipidemia	25	7 (28)	18 (72)	
Cardiovascular diseases	7	2 (28.6)	5 (71.4)	

(Low flux and medium flux dialyzers was used).

[‡] Chi-square test.

[†] Mann–Whitney *U* test.

^{*} *P* < .05; NA=not available.

[§] (Diabetes mellitus, hypertension, hyperlipidemia) were the most common comorbidities observed in current cohort of patients. Figures were >100% as patients may be suffering from more than one chronic condition.

8. Statistical analysis

For data analysis, the Statistical Package for Social Sciences version 22.0 was used (SPSS Inc., Chicago, IL). Normality was assessed using the Kolmogorov–Smirnov test. In order to represent continuous variables, median and interquartile range [IQR] “5th” and “75th” percentile were used, whereas, for representing categorical variables, numbers and frequencies were used. Associations between categorical variable were assessed by Pearson chi-square test and continuous variables were assessed using the Mann–Whitney *U* test (shown in Table 1). The potential predictor variables were chosen based on statistical significance from univariate linear regression. The variables with univariate *P* value <.20 were subjected to multivariate linear analysis.^[16] The use of univariate *P* values <.20 has advantage of tending to include more variables in multivariate linear regression while traditional levels of *P* value such as .05 can fail in identifying variables known to be important. The responses from the patients on Urdu 5D-itch scale and Urdu FANLTC were taken as dependent variables while gender, duration of chronic kidney disease and duration of dialysis, co-morbid conditions (hypertension, diabetes, elevated cholesterol), laboratory parameters (WBC, Hb, Na, K, serum creatinine, calcium, and para-thyroid

hormone) were taken as independent variable. A *P* value of less than .05 indicated statistical significance.

9. Results

9.1. Demographic characteristics

A total of 354 patients were recruited (response rate=100%). The flow on how patients were recruited is shown in Figure 1. The majority were male (66.1%) and the median [IQR] age of patients was 42.0 [34.0–50.0]. The age of patients, duration of having CKD and being on dialysis were significantly higher in patients with pruritus as shown in (Table 1). Hypertension (n=215), diabetes mellitus (n=47), hyperlipidemia (n=25) and cardiovascular diseases (n=7) were the most common co-morbidities observed in CKD patients with pruritus (Table 1).

9.2. Characteristic of CKD-associated pruritus

Among the 354 patients, CKD-associated pruritus was reported in 262 patients. As the objective of the study was to determine the influence of CKD-associated pruritus and its severity on the quality of life of patients undergoing hemodialysis in Pakistan,

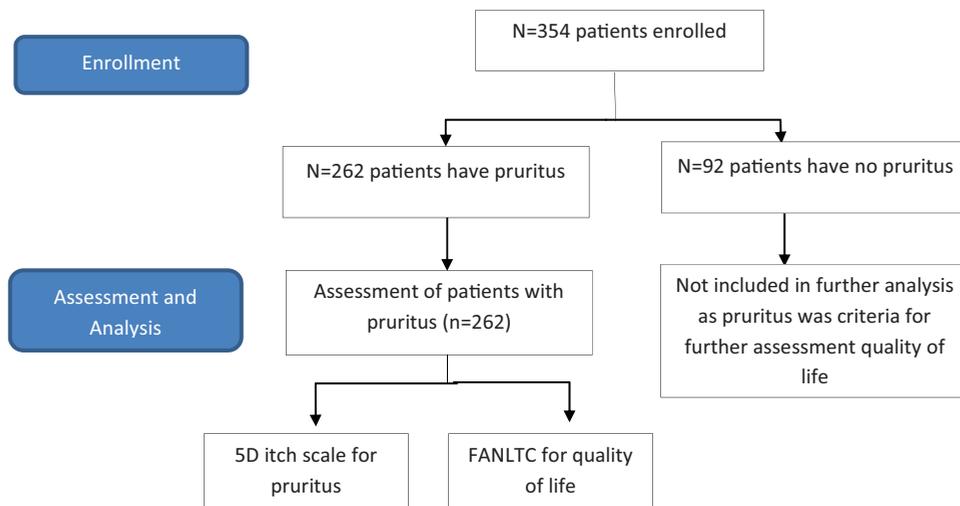


Figure 1. Study flow diagram.

only these 262 patients with pruritus were assessed for severity of pruritus and its impact on quality of life [as shown in Fig. 1]. CKD-associated pruritus was reported in 74% of patients. Most patients (64.5%) reported that they experienced pruritus for <6 hours a day and 53.4% of patients reported that their pruritus was of mild severity. The majority (40.5%) reported that their pruritus has completely resolved, and 30.9% patients had “occasional” delay in falling asleep. Majority of patients 53.8%, 56.1%, 66.8% reported that pruritus did not affect their leisure, housework or work/school respectively. Distribution of pruritus across the extremities, that is, back, forearm, abdomen, lower leg, and thighs, was mostly reported whereas, on basis of severity index, most of patients (52.0%) had mild pruritus (shown in Appendix 1, <http://links.lww.com/MD/D205>). The overall pruritus score with median [IQR] was 10.0[8.0–12.0].

9.3. Characteristics of quality of life

In order to assess the quality of life due to CKD-associated pruritus undergoing hemodialysis, the FANLTC questionnaire was administered. The responses of patients on FANLTC questionnaire [are shown in Appendix 2, <http://links.lww.com/MD/D205>].

The distribution of scores for each domain of the FANLTC tool with median, IQR, and range for the respondents are shown in (Table 2), with the higher score representing better quality of life. Among the patients, the median [IQR] observed was 52.00 [43.00–58.00], with scores ranging from 10 to 86 as shown in (Table 2).

Table 2	
FANLTC score for n=262 patients having pruritus.	
FANLTC scale	Median [IQR]
Physical well-being	17.00 [13.00–21.00]
Social/family well-being	16.00 [13.00–19.25]
Emotional well-being	11.00 [8.00–13.00]
Functional well-being	14.00 [10.00–17.00]
Total FANLTC score (Quality of life score)	52.00 [43.00–58.00]

9.4. Multivariate linear regression for pruritus and quality of life

To determine the factors associated with CKD-associated pruritus (measured using Urdu 5D-itch scale); we developed a series of linear regression analyses. The multivariate linear regression analysis revealed that there was a statistically significant association between CKD-associated pruritus with age of patients ($\beta=0.031$; 95% confidence interval [CI]=0.002–0.061; $P=.038$) and duration of CKD ($\beta=-0.013$; 95% CI= -0.023 – -0.003 ; $P=.014$)^[17]; however, no other factors were found to be associated with CKD-associated pruritus.

Similarly, to determine the factors independently associated with quality of life; we developed a series of linear regression analyses. The result of multivariate linear regression revealed statistically significant association between CKD-associated pruritus and quality of life ($\beta= -0.949$; 95% CI= -1.450 ; -0.449). The intensity of pruritus was significantly associated with poor quality of life among patients on hemodialysis having CKD-associated pruritus.

Non-parametric tests like Kruskal–Wallis test and Mann–Whitney test, were performed to compare the pruritus score with quality of life. The results showed that there was a statistically significant difference between groups as determined by the Kruskal–Wallis test. The median and IQR score for FANLTC were poor in respondents suffering from moderate pruritus and severe pruritus as shown in (Table 3). Similarly, the results showed that there was a statistically significant difference between groups as determined by the Kruskal–Wallis test. However, when the Mann–Whitney test was run, results revealed no statistically significant differences between both genders, while the FANLTC score was lower in males as compared to females as shown in (Table 3).

10. Discussion

CKD-associated pruritus is a troublesome and a widely prevalent complication among advanced CKD patients. The prevalence rate of CKD-associated pruritus in this study was 74%, however, the pilot study done by the same author to validate the 5D itch

Table 3
FANLTC scores association with chronic kidney disease associated pruritus severity and gender (n=262).

	N	FANLTC Median [IQR]	P value
Pruritus severity			
Mild pruritus	90	55.00 [47.00–63.00]	<.001* [†]
Moderate pruritus	148	51.00 [40.00–57.00]	
Severe pruritus	24	48.00 [35.25–56.50]	
Gender			
Male	176	51.00 [46.50–58.00]	.485 [‡]
Female	86	54.00 [41.00–58.00]	

* Kruskal–Wallis Test was performed.

[†] Mann–Whitney Test was performed.

[‡] statistically significant <0.05.

scale in Urdu found a prevalence rate of 70% in Pakistan.^[12] The intensity of pruritus as observed in this study was mild pruritus (34.4%), moderate pruritus (56.5%), and severe pruritus (9.2%), whereas in that pilot study moderate pruritus was 50%, while severe pruritus was 14%.^[12] In the present study, the severity of pruritus was slightly higher in males as compared to females. Similar findings were observed in another study in which males had a 1.1 greater adjusted odds of having moderate to severe pruritus.^[5]

In our study population, the frequency of hemodialysis was twice a week with 3-hour dialysis sessions. Shaldon proposed that short dialysis sessions, and under dialysis lead to patient malnutrition and death, and indeed a dialysis time of less than 3 hours and 30 minutes has been associated with a doubled rate of patient mortality as compared to patients dialyzed for 4 hours and being dialyzed thrice weekly.^[18] Similarly, among dialysis patients, clearance was strongly associated with an increased duration time of dialysis.^[19] In our study, it was noted that due to lack of availability of a nephrologist in the dialysis unit, inadequate dialysis staffing, and patient's refusal; there was no record keeping of the dialysis (dialysis registry with pre-dialysis weight, post-. In our study it was dialysis weight, and frequent laboratory parameters measurements) for individual patients. Similar points were highlighted by other authors in Pakistan, and multiple factors were accountable for poor outcomes during dialysis including late referral, malnutrition, anemia, inadequate dialysis, and the lack of availability of qualified nephrologists at dialysis units.^[20–23] In our study, the patients were undergoing ultrafiltration on their choice while communicating with dialysis staff without following the standard protocol, thus contributing to inadequate dialysis. In our study, it was also revealed that dialysis machines were limited, and pressure from too many patients was a contributing factor to inadequate dialysis. Similar findings by Chauhan et al in India (being neighbors and having same socioeconomic status country) were facing same problem of increasing patient number and inadequate hemodialysis machines.^[24] The increase in frequency and longer duration of dialysis sessions improve patients quality of life, as a result there is reduction in chances of mortality.^[25]

In this study, all patients underwent low flux hemodialysis. Hemodialysis, especially high-flux hemodialysis, is currently the most commonly used blood purification method worldwide, but in China and other developing countries, due to the low level of economic development, low-flux dialysis is the main method of extracorporeal blood purification therapy. However, this method is not very effective at removing the middle-molecule uremic

toxins to provide relief from Uremic Pruritus.^[26] Similarly, another study also supports the notion that the use of low-flux dialyzer is significantly associated with the aggravation of pruritus.^[27] The high flux dialyzers efficiently remove average-sized molecules.^[28] In our study, we found an association between CKD-associated pruritus and age of patients; which is similar to findings of other studies in which increase in age of patient found to be significantly related to pruritus.^[28–30] However, other studies found no association with age of patient and CKD-associated pruritus.^[31,32] In our study we found significant association between duration of suffering CKD and CKD-associated pruritus but in literature review we could not find any association between them; however, significant association is reported between CKD-associated pruritus and serum levels of parathormone (PTH),^[28,33] blood urea nitrogen (BUN),^[28,34,35] serum calcium,^[28,36] hyperphosphatemia,^[28] hypertension^[37] and diabetes.^[38] CKD-associated pruritus can adversely affect the medical outcomes and the quality of life of patients.^[8,39,40] In our study, males were observed to have higher impaired quality of life, while a study by Joanna et.al reported that female patients having CKD-associated pruritus have a negative impact on the social and emotional well-being as compared to male patients.^[1] Similarly, other studies also reported that CKD-associated pruritus had a negative impact on both mental and physical composites of the quality of life.^[5,41] Kosmadakis et al reported that 54% of patients with CKD-associated pruritus in the United Kingdom had seriously affected quality of life.^[42] Tessari et al also reported that pruritus was associated with a statistically significant decreased quality of life with regard to social function, emotion, and symptoms.^[43] Few randomized controlled trials have also been performed to improve the quality of life of patients suffering from CKD-associated pruritus. They revealed that the treatment of patients with Nalfurafine versus placebo significantly reduced itching intensity, and also decreased the number of days of non-disturbing itching and increased the number of nights of sound sleep,^[44] while Pregabalin significantly improved sleep and mental health as compared to placebo.^[45] In our study, a weak association was observed between pruritus and quality of life. Hence, by reducing the pruritus, the quality of life of patients can be improved.

11. Strength and limitations

The strength of this study is that it is the first study in Pakistan to assess the impact of CKD-associated pruritus on quality of life among hemodialysis patients and secondly it has a response rate of 100%, indicating minimal selection bias. Limitation of our study is that due to small sample size, the findings are not generalizable to whole population of Pakistan as data were only collected from 2 centers in Pakistan. Future research can focus on pharmacological or non-pharmacological interventions to improve the management of CKD-associated pruritus.

12. Conclusion

There was a high prevalence of CKD-associated pruritus among the study population undergoing hemodialysis. Pruritus is a common and distressing symptom in patients with CKD and is associated with a negative impact on the patient's quality of life which includes their physical, social, mental/emotional, and functional wellbeing.

Author contributions

Conceptualization: Inayat ur Rehman, Tahir mehmoood Khan.
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Writing – original draft: Inayat ur Rehman.
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