

# Prevalence of Uremic Pruritus, Its Risk Factors and Impact on Health-Related Quality-Of-Life in Patients on Maintenance Hemodialysis

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## Abstract

**Background:** Renal pruritus is one of the most debilitating symptom of chronic kidney disease especially affecting patients on maintenance hemodialysis. **Subjects and Methods:** It was a cross-sectional questionnaire based study. Demographic, dialysis related and biochemical parameters of maintenance hemodialysis patients were recorded, and a pre-defined questionnaire was put to them. Severity was calculated with 12 point pruritus severity scale (PSS), health-related quality of life with SKINDEX-10, and sleep survey with ITCH-MOS. **Results:** The total of 164 patients (mean age  $52 \pm 17$  years, males-57.9%, females-42.1%) completing questionnaire and laboratory analysis were included in the study. Prevalence of pruritus was 53.7% (mild in 31.8%, moderate-45.5%, severe-22.7%). Prevalence was higher in diabetic CKD ( $p=0.0001$ ), and irregularly dialyzed patients ( $p=0.001$ ). The severity of pruritus correlated with older age ( $p=0.004$ ), shorter dialysis vintage ( $p=0.000$ ), irregular dialysis (0.000), higher serum phosphorus (0.003), and parathyroid hormone level (0.000) and higher calcium-phosphorus product (0.001). SKINDEX-10 showed worsening symptoms, emotional and functional quality of life ( $p=0.000$ ), and poorer sleep quality and quantity as per ITCH-MOS (0.000), with increasing severity of itching. **Conclusion:** Renal itch is highly prevalent in maintenance hemodialysis patients, most severely affecting diabetics, elderly, irregularly dialyzed patients, with poorly controlled mineral bone parameters. The severity correlates with worsening sleep and overall quality-of-life.

**Keywords:** Uremia, uremic/renal pruritus, maintenance hemodialysis, health-related quality of life, sleep.

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## Introduction

Pruritus is one of the most bothersome symptom for chronic kidney disease (CKD), with reported prevalence as high as 50–90%.<sup>[1]</sup> It affects patients in all stages of CKD, irrespective of underlying etiology, gender, age or comorbidities, however certain factors are hypothesized to affect its incidence and severity. Uremic pruritus significantly impairs the quality of life in CKD. The gravity of this seemingly trivial complaint can be judged from the fact that uremic pruritus has been an independent predictor of increased mortality, probably because its impact on the patient's quality of sleep.<sup>[2-4]</sup> Despite advances in the care of end-stage renal disease (ESRD) patients, the management of pruritus remains one of the most challenging clinical problems for the treating nephrologist. The present study intended to analyze the prevalence of uremic pruritus in maintenance hemodialysis patients, its relationship with demographic and metabolic parameters, and its impact on their health-related quality-of-life (HR-QOL) and sleep.

## Subjects and Methods

This cross-sectional study was done in a large tertiary care centre in North India, in patients undergoing maintenance hemodialysis (with more than three months of dialysis vintage). The study was approved by the institutional ethical committee and a written informed consent was taken from each patient before inclusion in the study. The demographic details, etiology of CKD, hemodialysis vintage and frequency was recorded for all the patients. All the patients were being dialyzed on B-Braun-Dialog+ slow-flux hemodialysis machines, with formalin sterilized reused dialyzers. The laboratory parameters including hemoglobin, calcium, phosphorus, calcium-phosphorus product and parathyroid hormone levels were done in all the patients. The prevalence, intensity and diurnal variation of pruritus, its correlation with metabolic parameters, and its impact on the health related quality-of-life (HR-QOL) and sleep of the patients was analyzed on the basis of a pre-defined performa including 12 point pruritus severity scale (PSS) for severity,<sup>[5]</sup> SKINDEX-10 for assessment of HR-QOL,<sup>[6]</sup> and sleep survey from the Medical Outcomes Study

(MOS) ITCH-MOS for impact on sleep.<sup>[6]</sup> Data were described in terms of frequencies (number of cases) and relative frequencies (percentages), mean ± standard deviation (± SD), as appropriate. Comparison of quantitative variables between the groups was done using ANOVA. For comparing categorical data, Chi square (χ<sup>2</sup>) test was performed and exact test was used when the expected frequency was less than 5. A probability value (pvalue) less than 0.05 was considered statistically significant. All statistical calculations were done using SPSS (Statistical Package for the Social Science), SPSS-21 version statistical program for Microsoft Windows.

## Results

The total of 183 patients were included in the study out of which 164 patients completing questionnaire and laboratory analysis were included in the final analysis. The mean age of the cohort was 52 ± 17 years, and it included 95 (57.9%) males and 69 (42.1%) females. Majority of the patient were in 5<sup>th</sup>, 6<sup>th</sup> and 7<sup>th</sup> decades of life. The diabetic kidney disease (n=70, 42.7%) was the most common etiology for end stage kidney disease. Most of them (61%) were undergoing twice a week hemodialysis. [Table-1].

**Table 1: Baseline characteristics of maintenance hemodialysis patients in the study**

Baseline Characteristics	Number Of Patients (N=164)	Percentage
Gender distribution		
Males	95	57.90%
Females	69	42.10%
Age distribution (in years)		
<20	4	2.40%
21-30	24	14.70%
31-40	24	14.60%
41-50	32	19.50%
51-60	42	25.60%
>60	38	23.20%
Causes of Chronic kidney disease		
Diabetic Nephropathy	70	42.70%
Hypertensive Nephrosclerosis	38	23.20%
Chronic glomerulonephritis	30	18.30%
Chronic interstitial nephritis	17	10.40%
Unexplained etiology	9	5.40%
Dialysis Vintage		
Less than 1 year	44	26.80%
1-3 years	76	46.40%
3-5 years	34	20.70%
More than 5years	10	6.10%
Frequency Of Hemodialysis		
Once In 10 Days	16	9.80%
Once Weekly	34	20.70%
Twice Weekly	86	52.40%
Thrice Weekly	28	17.10%
Miscellaneous		
Smokers	8	4.80%
Active alcohol intake present	14	8.50%
Active opium addiction	6	3.70%
Hepatitis C positive	8	4.80%
Hepatitis B positive	4	2.40%
Retrovirus positive	1	0.60%

Out of the total 164 patients, 88 patients (53.7%) had

pruritus, inspite of most of them being on anti-pruritic treatment. Pruritus affected 57.9% males (55/95) and 47.8% (33/69) females (p=0.202). Diabetics had higher prevalence of pruritus than non-diabetic CKD (p=0.0001). Higher prevalence was found in patients on irregular dialysis (p=0.0001). Active smokers, and alcohol and opium users and hepatitis B, C and retro positive patients were found to have high prevalence. Pruritus was divided into mild (n=28, 31.8%), moderate (n=40, 45.5%) or severe (n=20, 22.7%) based on the 12-Item Pruritus Severity Scale (PSS).[Table-2].

**Table 2: Characteristics of patients with uremic pruritus in Maintenance Hemodialysis**

Parameters studied	Number of patients with problem/ total number of patients	Percentage of patients
Prevalence of Uremic Pruritus	88/164	53.70%
Gender distribution of uremic pruritus patients		
Males	55/88	62.50%
Females	33/88	37.50%
Anti-pruritic treatment		
Presently on treatment	65/88	73.90%
Past history of treatment	77/88	87.50%
Compliance with treatment	43/88	48.90%
Topical applications on skin	77/88	87.50%
Oral anti-histaminics	35/88	39.8% %
Opioid analogues for pruritus	Nov-88	12.50%
Gabapentin or pregabalin use	Jun-88	6.80%
Skin rash or itch marks present	69/88	78.40%
One area of body	24/69	34.80%
Multiple areas of rash	45/69	65.20%
Diurnal variation present	49/88	55.70%
Nocturnal exacerbation	44/49	89.80%
Day time exacerbation	May-49	10.20%
Correlation with dialysis session	32/88	36.40%
Increases during session	30/32	93.80%
Decreases during session	2 out of 32	6.20%
Severity of pruritus (12-point PSS)*		
Mild	22/88	25.00%
Moderate	41/88	46.60%
Severe	25/88	28.40%
Etiology of CKD with pruritus		
Diabetic CKD	57/88	64.80%
Non-diabetic CKD	31/88	35.20%
Frequency Of Hemodialysis		
Once In 10 Days	16/16	100%
Once Weekly	34/34	100%
Twice Weekly	28/86	32.60%
Thrice Weekly	10.0/28	35.70%
Miscellaneous		
Smoker	05-08	62.50%
Alcohol intake	01-05	35.70%
Opium addiction	06-06	100%
Hepatitis C positive	04-08	50%
Hepatitis B positive	03-04	75%
Retrovirus positive	01-01	100%

\*PSS- pruritus severity scale

The severity of pruritus was correlated with various patient parameters (Table-3). Severity was higher in older hemodialysis patients (p=0.004), with shorter dialysis vintage (p=0.000), and irregular dialysis (p=0.000). Gender or diabetes did not affect the severity of pruritus. Among the

metabolic parameters, pruritus significantly correlated with higher serum phosphorus (p=0.003), and parathyroid hormone (p=0.000) level. Most of the patient with severe pruritus had higher calcium-phosphorus product (p=0.001). Hemoglobin and calcium levels did not impact the severity.

SKINDEX-10 showed significantly worse health-related quality of life, with respect to symptoms, emotions and functionality in patients with severe pruritus (p=0.000). The ITCH-MOS score worsened significantly with severity of itching (p=0.000).

**Table 3: Correlation of parameters with severity of pruritus in Maintenance Hemodialysis patients**

Parameter	Mild Pruritus (n=22)	Moderate pruritus (n=41)	Severe pruritus (n=25)	Chi-square value/F	p-value
Age (years)	48 ± 12	54 ± 21	65 ± 14	6.005	0.004
Gender					
Males (n=55)	12/55 (13.6%)	28/55 (31.8%)	15/55 (17.0%)	1.247	0.536
Females (n=33)	10/33 (11.4%)	13/33 (14.8%)	10/33 (11.4%)		
Dialysis Vintage (in months)	26 ± 14	45 ± 38	12 ± 13	11.351	0.000
Etiology of CKD					
Diabetic CKD with pruritus (n=57)	12	27	18	1.602	0.449
Non-Diabetic CKD (n=31)	10	14	7		
Dialysis compliance					
Once In 10 Days	0	5	11	36.684	0.000
Once Weekly	5	15	14		
Twice Weekly	11	17	0		
Thrice Weekly	6	4	0		
Hemoglobin (g/dl)	9.6 ± 2.7	10.1 ± 3.1	8.7 ± 2.1	2.012	0.140
Calcium (mg/dL)	8.5 ± 1.9	8.1 ± 2.1	8.8 ± 2.4	0.861	0.426
Phosphorus (mg/dL)	4.7 ± 2.3	6.3 ± 3.7	7.9 ± 2.7	6.121	0.003
Calcium-phosphorus product (mg <sup>2</sup> /dl <sup>2</sup> )	Number of patients	Number of patients	Number of patients		
< 55	17	25	5	17.191	0.001
>55	5	16	20		
PTH (pg/mL)	149.6 ± 40.4	178 ± 32.6	328 ± 92.5	70.687	0.000
SKINDEX-10					
Symptoms	23.9 ± 17.6	32.4 ± 18.4	48.3 ± 20.5	10.466	0.000
Emotions	32.6 ± 11.7	44.7 ± 11.9	52.7 ± 16.4	13.524	0.000
Functioning	21.3 ± 11.6	44.7 ± 18.5	60.8 ± 7.6	43.643	0.000
ITCH-MOS score					
	33 ± 12.2	43 ± 22.7	59 ± 9.8	13.434	0.000

**Discussion**

The prevalence of uremic pruritus among patients undergoing hemodialysis is reported as 22–84%, to as high as 90% in some older series.<sup>[2-4,7-10]</sup> The itching may be mild to severe, continuous or episodic, localized or generalized, often with nocturnal exacerbation,<sup>[11]</sup> and it affects patient’s sleep and overall quality-of-life. The prevalence of sleep disturbances has been 9–76% in different series.<sup>[12]</sup> Although the association of uremia with pruritus has been recognized for many years, the precise pathophysiologic mechanism remains obscure. It is possibly linked to inadequate removal of uremic toxins and abnormal calcium-phosphate metabolism in dialysis patients. Some other reasons being higher rate of xerosis, increased inflammatory cytokines and endogenous opioids.<sup>[2]</sup> Several patient characteristics, biochemical and dialysis parameters have been reported by various investigators to affect uremic pruritus.

In this study we found the prevalence of uremic pruritus to be 53.7% in our maintenance hemodialysis patients, more in older age patients, with diabetic CKD, on irregular hemodialysis, and shorter dialysis vintage. No gender predisposition was found. The severity of pruritus correlated directly with increasing age, possibly due to age related dryness of skin exacerbating the condition. Patients on recently initiated dialysis therapy had tendency to avoid hemodialysis until severely symptomatic for azotemia. These irregularly dialyzed and shorter dialysis vintage patients had

uncontrolled mineral bone parameters like higher phosphorus, parathyroid levels and calcium-phosphorus product and thus increased severity of pruritus. Hemoglobin and calcium did not correlate with severity of pruritus in our study.

Similar correlations with phosphorus levels,<sup>[13-15]</sup> and older age,<sup>[13]</sup> have been reported by other studies, but few other have also found higher serum calcium, male sex, low serum albumin level, current or recent smoking, dialysis adequacy, use of low-(versus high-) dialyzer, hepatitis C positivity and higher serum C-reactive protein levels to correlate with occurrence of pruritus.<sup>[13-17]</sup>

The SKINDEX-10 showed worsening symptom related, emotional, and functional quality of life parameters with increasing severity of pruritus. Similarly ITCH-MOS showed them to have poorer sleep quality and quantity, with worsening renal itch. Many other studies have reported presence of pruritus to correlate with decreased quality of life, and poor sleep with consequent depression, and an independent predictor of mortality, and other poor patient outcomes.<sup>[15,18,19]</sup> However very few have systematically correlated the severity of pruritus with different parameters as our study. Lopes et al<sup>[20]</sup> also reported patients with severe pruritus to have 25% decrease in kidney disease burden-related QoL and this decrease being primarily related to sleep disturbances, depressive symptoms, and dry skin. Mathur et al<sup>[6]</sup> also found a statistically significant relationship between the intensity of pruritus and health-related QoL, particularly with regard to mood, social relations, and sleep. Similar such

observations were seen in studies by Kosmadakis et al<sup>[21]</sup> and Tessari et al<sup>[22]</sup>

Likes any other study, our study too had its limitations. It was a single centre, observational study. There could be innumerable other parameters which can influence pruritus, testing for all was not practically feasible. Therapeutic interventions were intentionally not taken into consideration, as compliance could not be ascertained, due to limited subjective benefits, and multi-therapy. A large multi-centric study in this regard can provide further insight in this regard.

## Conclusion

Renal itch is one of the most debilitating symptom of patient on maintenance hemodialysis, affecting more than half of them. Old aged and irregularly dialyzed patients, with poorly controlled mineral bone parameters, are more severely affected. Measures for aggressive management of uremic pruritus can significantly improve their sleep parameters and overall quality-of-life.

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