Prevalence and severity of pruritus amongst patients with chronic kidney disease

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Abstract

Introduction: Skin problems are common and diverse in patients with chronic kidney disease (CKD). Pruritus is a highly prevalent condition in patients with chronic kidney disease. It is associated with poor sleep quality, anxiety and depression which may contribute to reduction in quality of life.

Objective: To study the prevalence and severity of pruritus among patients with chronic kidney disease.

Materials and Methods: An observational study was conducted in 77 consecutive chronic kidney disease patients receiving maintenance hemodialysis for more than 3 months at Manik hospital, Aurangabad, Maharashtra, India were studied during January 2015 to December 2015.

Results: Out of 77 patients, 51 (66.23%) of males and 26 (23.67%) of females were examined. The mean age was 51.17 years. Xerosis was the commonest manifestation (87.01%), followed by pruritus (57.14%). Mild pruritus was reported in 59.09% patients whereas severe pruritus was noted in 22.27% patients. High urea, phosphate and ALP levels were noted in severe pruritus group, but difference not statistically significant. 32 patients with pruritus on maintenance HD were followed over next 6 months. Out of 32 patients followed, 37.5% had no change in pruritus. Pruritus improved in 28.12%, while it actually worsened in 34.37% patients.

Conclusion: In this study, 57.14% of patients with chronic kidney disease experience pruritus. Gender, age, presence of DM, duration of dialysis was not statistically significant between pruritus and non-pruritus group. Also hematocrit was similar in pruritus and non-pruritus groups. There was no significant difference in calcium, phosphorus and alkaline phosphatase levels in pruritus and non-pruritus groups.

Keywords: Pruritus, Skin Disorders, Hemodialysis.

Introduction

Skin problems are common and diverse in patients with chronic kidney disease (CKD), especially among those on hemodialysis. Pruritus is a highly prevalent condition in patients with chronic kidney disease. Pruritus is one of the common cutaneous manifestation of chronic kidney disease (CKD) that is present in 40–84% of end stage renal disease population.[1,2]

It is associated with poor sleep quality, anxiety and depression which may contribute to reduction in quality of life. Pruritus severity is reported variably. As further outlined later, the severity of pruritus generally is assessed by a visual analogue scale (VAS), numeric rating scale, or questionnaire. Pruritus may be extremely difficult to control, as therapeutic options are limited. The most consequential approaches to treatment are: topical treatment with or without anti-inflammatory compounds or systemic treatment with (a) gabapentin, (b) μ-opioid receptor antagonists and κ-agonists, (c) drugs with an anti-inflammatory action, (d) phototherapy, or (e) acupuncture. Although the majority of dermatological disorders in chronic kidney disease (CKD) are relatively benign, a few rare skin diseases have the potential to cause serious morbidity and mortality. Early recognition of these severe skin disorders and prompt initiation of treatment can markedly alter their course and even save a patient's life.[3]

End stage renal disease (ESRD), now abbreviated as CKD – stage V-D by KDOQI, is defined as Renal insufficiency requiring dialysis or kidney transplantation for survival.[4] Nitrogenous by-products of protein catabolism, represented as urea (referred to as blood urea nitrogen), creatinine, and various other uremic toxins commonly accumulate within the serum of these patients due to inadequate renal excretion. Various modalities of renal replacement therapy like hemodialysis (HD), peritoneal dialysis (PD) and renal transplantation are commonly used in modern nephrology practice. Cutaneous disorders are a common manifestation of patients with ESRD. Several studies have examined the prevalence of dermatologic disease in this setting. Nunley J R reported that 50-100% of patients have at least one dermatological disorder.[5] Pico et al. assessed the prevalence of dermatologic problems among 102 patients with chronic renal failure undergoing dialysis. All patients examined had at least one cutaneous lesion with the most prevalent disorder being hyperpigmentation.[6] It has been proposed that many of the cutaneous disorders experienced by patients undergoing dialysis have little to do with the uremic syndrome and are related to the underlying pathologic process that induced the renal disease.[5] On the contrary, others proposed that changes in skin histology were more related to the severity and duration of the renal failure and less with its underlying etiology.[7] Recent advances in the treatment have

improved the quality of life and life expectancy of these patients, resulting in changes in the frequency and types of disorders observed in conjunction with ESRD. With an almost 50-100% prevalence in dialysis populations, skin disorders are frequently the subject of patients' complaints.[5] Skin diseases have a considerable negative effect on a patient's quality of life. Pruritus is a common and distressing symptom that affects patients with chronic kidney disease (CKD).

Hence the present study was carried out with the objective of to study the prevalence and severity of pruritus among patients with chronic kidney disease.

Materials and Methods

Study Design: A cross-sectional observational study

Study Area: Study was conducted at Manik hospital, Aurangabad, Maharashtra, India which is a tertiary care hospital.

Study Period: Study was conducted period of 1 year during January 2015 to December 2015.

Sample Size: Total 77 consecutive chronic kidney disease patients receiving maintenance hemodialysis for more than 3 months at Manik hospital, Aurangabad, Maharashtra were studied.

Inclusion Criteria: Chronic Kidney Disease patients undergoing maintenance hemodialysis for more than 3 months included in the study.

Exclusion Criteria

1. Patients undergoing hemodialysis following a renal transplant failure.
2. Patients who had undergone peritoneal dialysis.
3. Patients with a history of pruritus or dermatologic disease antedating renal failure.
4. Patients with systemic diseases such as malignancy, cholestatic liver disease, and those with psychiatric disorders or non-compliance to hemodialysis treatment.

Methods

Data Collection: Detailed history regarding duration of CKD, underlying cause of CKD, duration of dialysis, duration of skin ailment, onset of changes with relation to diagnosis of CKD and starting dialysis and improvement noticed following dialysis. Various skin manifestations - xerosis, ichthyosis, pruritus, hyperpigmentation, acquired perforating dermatosis, purpura, calcinosis cutis, bullous dermatosis, skin changes at arterio-venous fistula site, cutaneous infections noted. A questionnaire was prepared to assess severity of pruritus, based on body area involved, duration, frequency of itching and disturbance of usual work and sleep. Oral changes like angular cheilitis, xerostomia, ulcerative stomatitis and macroglossia were noted. Nail changes like half and half nail, onycholysis, onychomycosis and platynychia were noted. Hair changes like dry and lustreless hairs, alopecia noted. Laboratory data in the form of serum creatinine (mg/dl), blood urea (mg/dl), albumin (g/dl), hematocrit (%), i-PTH (pg/ml), calcium (mg/dl), phosphorus (mg/dl), and alkaline phosphatase (IU/L) before the dialysis session was collected. Specific investigations like skin biopsy, culture/ sensitivity for bacterial infections, Gram's stain, and potassium hydroxide mount were carried out as per indication. The severity of pruritus was assessed subjectively and scored as follows:

Mild: Episodic and localized pruritus without disturbance in usual work and sleep.

Moderate: Generalized and continuous pruritus without sleep disturbance.

Severe: Generalized and continuous pruritus with sleep disturbance.

The major emphasis was on the disturbance in usual work and sleep.

Data Analysis

The collected data was compiled in EXCEL sheet and Master sheet was prepared. For analysis of this data SPSS (Statistical Software for social Sciences) software version 20th was used. Qualitative data was represented in form frequencies & percentages. $P<0.05$ was considered statistically significant.

Results

Out of 77 patients, 51(66.23%) of males and 26(23.67%) of females were examined. Male: Female ratio was 1.96: 1. The mean age was 51.17 $\pm$ 15.22 years. The range of age group was between 21-85 years. Age group between 51 to 60 years had highest representation.

Table 1: Skin manifestations in CKD patients

Skin Manifestation	No. of patients (n=77)	Percentage
Xerosis	67	87.01
Pruritus	44	57.14
Pallor	19	24.67
Pigmentation	14	18.18
Yellowish Tinge	08	10.39
Purpura	06	07.79
Perforating Dermatosis	09	11.69
Gynecomastia	02	2.59

Bacterial Infection	13	16.88
Fungal Infection	21	27.27
Viral Infection	09	11.69
Dermatitis	09	11.69
Bullous Dermatosis	01	1.29
Vasculitis	02	2.59
None	04	5.19

It was seen from Table 1 that majority 73 (94.08%) patients had at-least one skin manifestation. Xerosis was the commonest manifestation (87.01%), followed by pruritus (57.14%). Cutaneous infections were noted in 55.84% patients. Fungal infections were more common with 27.27%. Pallor and hyperpigmentation were noted in 24.67% and 18.18% cases respectively. Perforating dermatosis was observed in 11.68% patients. Bullous dermatosis was noted in only one patient.

Table 2: Varying grades of pruritus (n=77)

Pruritus Grading	No. of patients	Percentage
Absent	33	59.09
Mild	26	33.77
Moderate	08	10.39
Sever	10	12.98
Total	77	100

It was seen from Table 2 that mild pruritus was reported by 59.09% (26/44) patients whereas severe pruritus was noted in 22.27% (10/44) patients.

Table 3: Comparison of demographic parameters in patients with and without pruritus

Clinical Parameters	Pruritic (n=44) (Mean + SD)	Non Pruritic (n=33) (Mean ±SD)	Total (n=77) (Mean±SD)	P-Value
Gender (Male%)	68.18	63.63	66	0.6764
Age (in Years)	50.48+ 13.67	52.09±17.25	51.17+15.22	0.9278
Time on HD (Months)	22.97+ 24.44	29.18± 27.38	25.64±25.74	0.0589
DM (%)	40.90	27.77	35	0.3175
HD Per Week	2.30±0.48	2.27±0.62	2.32±0.54	0.9859

It was evident from Table 3 that demographic characteristics of pruritic vs non-pruritic group were compared. Sex ratio and mean age were similar in both pruritic and non-pruritic group. Presence of DM was however common in pruritic group but was not statistically significant. Duration of dialysis and dialysis frequency were not statistically different in both groups.

Table 4: Laboratory parameters in HD patients with and without pruritus

Parameter	Pruritic (n=44)	Nonpruritic (n=33)	p–value
Hematocrit (%)	31 ±6.41	30.38±6.61	0.9913
Serum Calcium (MG/DL)	8.42+0.98	8.27+0.83	0.9798
Serum Phosphorus	5.44+1.74	5.21+1.21	0.9018
Serum Alkaline Phosphatase (Iu/L)	187.4+108.1	173.8+107.2	0.9015
Blood Urea (Mg/Dl)	104.71+35.35	100.40+40.63	0.9925
Serum Creatinine (Mg/Dl)	7.60+2.19	7.83+2.36	0.9633
Serum Albumin (Mg/Dl)	3.57+0.48	3.68+0.45	0.9873

It was seen from Table 4 that hematocrit was similar in both groups. There was no significant difference in calcium, phosphorus and alkaline phosphatase levels in both groups. No significant difference in Blood urea, creatinine and albumin levels was noted.

Table 5: Patient characteristics and laboratory parameters of various severity of pruritus

Parameter	Pruritus			p-value
	Mild (n=26)	Moderate (n=8)	Severe (n=10)	
Age (in years)	51.72 ±5.46	53.12±10.03	47.2±12.29	0.6875
Time on HD (M)	21 ±21.65	26.62±28.52	17.4±21.90	0.7005
HD PER WK	2.34±0.56	2.37±0.51	2.3±0.48	0.9549

HCT (%)	31.33±7.20	30.41±5.61	29.76 ±6.32	0.8088
UREA (MG%)	101.63±30.46	105.75 ±41.98	118.9±45.67	0.4502
CREAT (MG%)	7.70±2.55	7.75±1.30	7.21±1.79	0.8248
CAL (MG%)	8.44± 0.90	7.75±1.30	7.78±1.12	0.1374
PH (MG%)	5.28±1.63	5.58±1.63	6.33±2.02	0.2774
ALP (IU/L)	162.2± 82.2	201.3±157.8	279.4±209	0.0748
ALB (GM%)	3.69±0.41	3.4 ±0.59	3.36±0.44	0.0901

(CAL – calcium, PH – phosphorus, ALP – alkaline phosphatase, ALB – albumin)

It was seen from Table 5 that high urea, phosphate and ALP levels were noted in severe pruritus group, but difference not statistically significant. Albumin level was lower in severe pruritic group, but not statistically significant.

Table 6: Parathyroid hormone levels: among various groups of pruritus

Parameter	Pruritus				p-value
	No Prutitus	Mild (n=7)	Moderate (n=4)	Severe (n=5)	
SR. PTH (pg/ml)	356.76 ±247.90	190.42±141.06	656.95±844.87	464.14±407.54	0.3022

It was seen from Table 6 that serum parathyroid hormone (iPTH) levels were done in 22 patients. Mean parathyroid hormone level was 427.82 ± 448.52 (pg/ml). High levels of serum PTH noted in moderate and severe pruritus group as compared to no or mild pruritus but difference was not statistically significant.

Table 7: Change in uremic pruritus over 6 months follow-up

Uremic Pruritus	No. of Patients (%)
Improved	09 (28.12)
No change	12 (37.5)
Worsened	11 (34.37)
Total	32(100)

It was seen from Table 7 that 32 patients with pruritus on maintenance HD were followed over next 6 months. Out of 32 patients followed, 37.5% had no change in pruritus. Pruritus improved in 28.12%, while it actually worsened in 34.37% patients.

Table 8: Association of nail changes with various causes of CKD

Nail Changes	DM	CIN	CGN	Others	Total
Platynychia	06(50.0%)	04(33.3%)	02(16.7%)	00	12 (15.58%)
Half & Half Nail	03(50.0%)	02(33.3%)	01(16.7%)	00	06(7.79%)
Onycholysis	03(50.0%)	01(16.7%)	02(33.3%)	00	06(7.79%)
Onychomycosis	2 (66.7%)	00	01(33.3%)	00	03(3.89%)

It was seen from Table 8 that Platynychia was the commonest nail change observed, (15.58%). Half and half nail was observed in 6 (7.79%) patients. All the nail changes were mostly noted in diabetic group which was statistically significant (p=0.023). Hair loss was noted in 7/77 (9.09%) and dry luster less hair was noted in 6/77 (7.79%) patients. Specific Skin Investigations: Skin scraping with KOH mount for fungal elements was done in 4 cases out of which 2 were positive for fungal elements. Pus culture and sensitivity including Gram staining was done in 5 cases of suspected bacterial infection and 2 were positive, 1 for staphylococcal aureus and 1 for streptococcus.

Skin Biopsy: In our study, biopsy was done for 5(6.49%) cases. 02 (cases of keratotic lesions showed common features which included perforation of the epidermis, basophilic debris, marked hyperkeratosis, focal prominent parakeratosis, necrotic material in follicles, well defined granular layer and moderate acanthosis. Dermis revealed adnexa with small amount of chronic inflammatory cells. These features were suggestive of perforating dermatosis. One case with a presumptive diagnosis of perforating disorders, showed upper epidermal inflammation on biopsy. However the diagnosis of perforating dermatosis was made based on clinical characteristics. Biopsy of a case with multiple vesiculo-bullous lesions over palms and soles showed subepidermal bulla with immune deposits of IgG along with the basement membrane zone suggesting epidermal bullosa acquisita or bullous pemphigoid.

Discussion

The present study population comprised 77 consecutive patients of CKD on maintenance

hemodialysis at Medwin Hospital, Hyderabad during 1 year period from January 2008 to December 2008.

Prevalance of Dermatologic Manifestations: In the present study, dermatologic manifestations were prevalent in 94.08% patients, who had at least one skin symptom or sign. Only 4 patients (all nondiabetic) were free from skin problems. This was similar to Pico et al[6] and Udayakumar P et al[8] who have reported 100% prevalence of skin manifestations.

Age and Gender Distribution: In the present study, there were 26 (34%) female patients and 51 (66%) male patients. This was comparable to the study by Udayakumar P et al,[8] where men (70%) were more frequently involved than women (30%).

The mean age of studied population was 51.17±15.22 years (range 21 – 85 years). The common age group in this study was 51 to 60 years. Narita et al[9] observed mean age of 60.27 ± 12.8 years. Sex ratio and age distribution was similar to present study.

Prevalance of Pruritus: Pruritus was noted in 57.14% of patients. Similar observations were made by Dialysis Outcomes and Practice Patterns Study [DOPPS], which revealed that UP is still present in 42–52% of adults with CKD.[11] Pavel D et al[12] reported pruritus in 74.3% patients. Udayakumar P et al[8] reported 53% prevalence.

Severity: Mild pruritus was noted by 59.09% patients whereas severe pruritus was noted in 22.27% patients. Pisoni et al[13] (DOPPS) observed generalized pruritus in 20-50% patients. Similar observations were made by Akhyani M et al[14] who reported mild, moderate and severe in 51.4%, 11.4%, and 37.1% (n = 26) of patients, respectively.

Effect of Hemodialysis: Out of 32 patients followed, 12 had no change in pruritus. Pruritus improved in 9, while it actually worsened in 11 patients. Udayakumar P et al[8] noted effect of dialysis on pruritus, 33 out of 53 patients (72%) found no improvement following dialysis, 5 (9.4%) showed improvement and 10 patients (18.8%) reported aggravation after hemodialysis. No significant improvement or worsening was noted in our study. Narita I et a[9] reported higher incidence of severe pruritus in patients on dialysis of longer duration (mean duration of dialysis, 123.67 ± 90.1 months). Present study had short duration follow up, we could not correlate duration of dialysis and severity of pruritus. There was no significant difference in levels of calcium, phosphorus, alkaline phosphatase and iPTH in pruritic and non-pruritic group in this study ($p > 0.05$). Similar observations were noted when theses parameters were compared between various pruritus grades. Similar observations were reported by Akhyani M et al[14] who observed no significant difference in calcium, phosphorus, alkaline phosphatase and parathyroid levels between pruritic and non-pruritic groups. Narita I et al[9] observed higher levels of intact-parathyroid hormone (i-PTH), calcium, phosphate in pruritus group.

Nail Changes: In present study, platynychia was the commonest nail change observed, (15.58%). Half and half nail was observed in 6 (7.79%) patients. Onycholysis was also noted in 6 (7.79%) patients. All the nail changes were mostly noted in diabetic group and difference was significant when compared to non-diabetic group ($p = 0.0233$). Udayakumar P et al[8] noted half and half nails in 21% patients and was significantly more prevalent in diabetic patients. Several other studies have reported an incidence ranging from 16 to 50.6%.[14] Other nail changes reported by Udayakumar P et al[8] included koilonychia (18%), subungual hyperkeratosis (12%), and onycholysis (10%).

Hair Changes: In present study hair loss with sparse body hair was noted in 9.09% and dry lustreless hair was noted in 7.79% patients. Udayakumar et al[8] reported 30 patients with sparse body hair, 11 with diffuse alopecia and 16 with dry, luster less hair. Singh et al.[15] have reported a prevalence of sparse body hairs in 30% CRF patients not on dialysis. Sparse body hair and diffuse alopecia with dry, lusterless hair may be present due to lack of skin hydration.

Conclusion

Pruritus was common among chronic kidney disease patients. 57.14% of patients with chronic kidney disease experience pruritus. Gender, age, presence of DM, duration of dialysis was not statistically significant difference between pruritus and non-pruritus group. Also hematocrit was similar in pruritus and non-pruritus groups. There was no significant difference in calcium, phosphorus and alkaline phosphatase levels in pruritus and non-pruritus groups. No significant difference in blood urea, creatinine and albumin levels was noted. High levels of serum PTH noted in moderate and severe pruritus group as compared to no or mild pruritus but difference was not statistically significant.

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How to cite this article: Kadam M, Kadam P. Prevalence and severity of pruritus amongst patients with chronic kidney disease. Ind J Clin Exp Dermatol. 2018;4(3):215-220.