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Original Research Article

Study of dermatological manifestations amongst patients with chronic kidney disease

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ABSTRACT

Background: The number of patients with end-stage renal disease (ESRD) in India is increasing with an estimated annual incidence of about 100 per million populations. Hemodialysis is one of the therapeutic modalities which can improve the survival in these patients. About 50–100% of patients with ESRD have at least one associated cutaneous change Skin problems are common and diverse in patients with chronic kidney disease (CKD), especially among those on hemodialysis. Objective was to study dermatologic manifestations among patients with chronic kidney disease on maintenance hemodialysis.
Methods: A descriptive 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.
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±15.22 years. Seventy three (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%. Mild xerosis was noted in 55.84% patients, 24.67% patients were moderate and whereas severe xerosis was noted in 6.49% patients.
Conclusions: Chronic kidney disease patients have prolonged life expectancy due to hemodialysis, hence they should be looked for presence of various skin manifestations which can affect the usual work and cause sleep disturbance which adds to the morbidity and mortality.

Keywords: Hemodialysis, Dermatosis, Skin problems, Xerosis

INTRODUCTION

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.[1] 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. Chronic kidney disease (CKD), defined as progressive and irreversible kidney dysfunction that lasts longer than 3 months has been recognized as significant medical problems for most of the last 2 centuries and, until recent century, as uniformly fatal. Scientific and technologic improvements during the second half of the 20th century have provided renal replacement therapy as a life-

sustaining option for many individuals, giving time to various dermatological changes to manifest. Cutaneous disorders are a common manifestation of patients with ESRD. Several studies have examined the prevalence of dermatologic disease in this setting. Nunley et al reported that 50–100% of patients have at least one dermatological disorder.[2] Pico et al assessed the prevalence of dermatologic problems among 102 patients with chronic renal failure undergoing dialysis.[3] All patients examined had at least one cutaneous lesion with the most prevalent disorder being hyperpigmentation.

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.[4] 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. Dermatologic conditions such as uremic frost, erythema papulatam uremicum, uremic roseola, and uremic erysipeloid now seldom occur. Various specific and non-specific skin abnormalities are observed in patients with ESRD. Non-specific disorders include pigmentary disorders, pruritus, xerosis, acquired ichthyosis, and half-and-half nail. Specific disorders include acquired perforating dermatosis, calciphylaxis, bullous dermatoses, and fibrosing dermopathy of uremia.[5] With an almost 50-100% prevalence in dialysis populations, skin disorders are frequently the subject of patients' complaints.[6] Skin diseases have a considerable negative effect on a patient's quality of life. They can induce serious discomfort, anxiety, depression and sleeping disorders and have an overall negative effect on mental and physical health. Although the majority of dermatological disorders in 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 dramatically alter their course and even save a patient's life. Hence the present study was carried out with objective to study the dermatologic manifestations among patients with chronic kidney disease on maintenance hemodialysis at Manik Hospital, Aurangabad and also to evaluate the prevalence Xerosis and other dermatologic problems in this population.

METHODS

Study area

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

Study period

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

Sample size

Seventy seven consecutive chronic kidney disease patients receiving maintenance hemodialysis for more than 3 months at Manik hospital, Aurangabad were studied.

Inclusion criteria

Chronic kidney disease patients undergoing maintenance hemodialysis for more than 3 months included in the study.

Exclusion criteria

Exclusion criteria were patients undergoing hemodialysis following a renal transplant failure; patients who had undergone peritoneal dialysis; patients with a history of pruritus or dermatologic disease antedating renal failure; patients with systemic diseases such as malignancy, cholestatic liver disease, and those with psychiatric disorders or non-compliance to hemodialysis treatment.

Sample collection

Hundred (100) patients on maintenance hemodialysis selected for study. Twenty three excluded (15–not in regular follow up, 5–hemodialysis following a renal transplant failure, 3–following peritoneal dialysis) and remaining 77 patients included for study.

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. 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.

Grading of xerosis (as follows): 0: Absent; 1: Mild (only on legs); 2: Moderate (all of the extremities) and 3: Severe (generalized).

Data analysis

Descriptive baseline characteristics were summarized as percentages, mean and standard deviations (SDs). For the analysis of the parametric variables we used the t-test. The χ^2 test was used to compare data between the itching and nonitching groups. ANOVA was applied for comparison of data among more than 2 groups and $p<0.05$ was considered statistically significant.

RESULTS

The present study comprises 77 patients of chronic kidney disease on maintenance hemodialysis during the period of January 2015 to December 2015. 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±15.22 years (range 21–85 years). Age group between 51 to 60 years had highest representation.

As shown in Figure 1 that Diabetic Nephropathy (DNP) emerged as commonest etiology of CKD (35), followed by chronic interstitial nephritis (CIN)–30% and chronic glomerulonephritis (CGN)–26%. Other diseases like autosomal dominant polycystic kidney disease (ADPKD), renovascular disease (RVD) and hypertension (HTN) as a cause of ESRD were seen only in 9% cases.

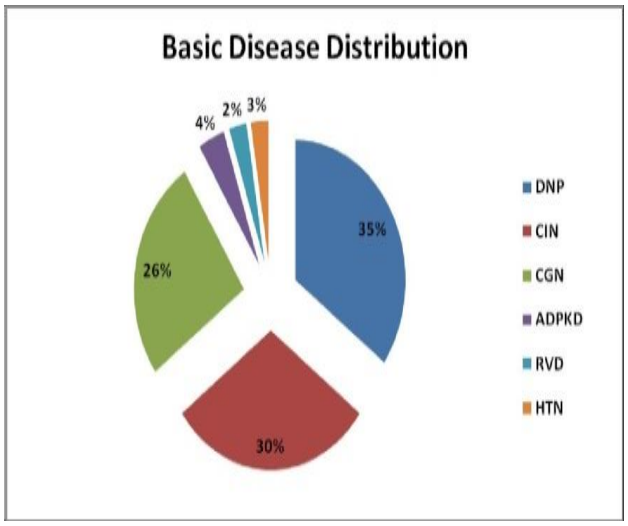

Figure 1: Distribution of basic diseases.

Table 1: Prevalance of skin manifestations in various etiologies of CKD.

Skin manifestation	DM	CIN	CGN	ADPKD	Others	Total
	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)
Xerosis	25 (37.31)	18 (26.86)	17 (25.37)	03 (4.48)	04 (5.97)	67 (87.01)
Pruritus	18 (40.91)	12 (27.27)	09 (20.45)	02 (4.54)	03 (6.82)	44 (57.14)
Pallor	06 (31.58)	07 (36.84)	06 (31.58)	00	00	19 (24.67)
Pigmentation	06 (42.86)	02 (14.28)	04 (28.57)	01 (7.14)	01 (7.14)	14 (18.18)
Yellowish Tinge	04 (50.0)	02 (25.0)	01 (12.50)	00	01 (12.50)	08 (10.39)
Purpura	03 (50.0)	01 (16.67)	01 (16.67)	00	01 (16.67)	06 (7.79)
Perforating dermatosis	08 (88.89)	01 (11.11)	00	00	00	09 (11.69)
Gynecomastia	01 (50.0)	01 (50.0)	00	00	00	02 (2.59)
Bacterial infection	08 (61.54)	02 (15.38)	02 (15.38)	00	01 (7.69)	13 (16.88)
Fungal infection	10 (47.62)	06 (28.57)	04 (19.05)	00	01 (4.76)	21 (27.27)
Viral infection	04 (44.44)	02 (22.22)	01 (11.11)	01 (11.11)	01 (11.11)	09 (11.69)
Dermatitis	04 (44.44)	02 (22.22)	02 (22.22)	00	01 (11.11)	09 (11.69)
Bullous dermatosis	00	00	01 (100)	00	00	01 (1.29)
Vasculitis	02 (100)	00	00	00	00	02 (2.59)
None	00	02 (50.0)	02 (50.0)	00	00	04 (5.19)

It was seen from Table 1 that seventy three (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.

It was observed from Table 2 that all the skin manifestations were common in diabetic CKD patients. Cutaneus infections were noted in 81.48% diabetic patients, difference between diabetic and nondiabetic group was significant. Perforating dermatosis was noted in 30% of diabetic CKD patients which was significant as compared to non-diabetic disease. Nail changes (51.85%) and oral changes (74.07%) were common in diabetic group with difference statistically significant. Cryoglobulinemic vasculitis was noted in 2 diabetic patients with HCV infection.

It was seen from Table 3 that mild xerosis was noted in 55.84% patients, 24.67% patients were moderate and whereas severe xerosis was noted in 6.49% patients.

As shown in Table 4 that mild xerosis was more common, observed in 44/67 (65.67%) cases. Pruritus was present in 40% patients with no xerosis. Pruritus was present in 40/67 (58.82%) patients with some degree of xerosis. All 5 patients with severe xerosis had pruritus. Severity of xerosis correlated with presence of uremic pruritus ($p<0.05$).

Table 2: Skin manifestations: diabetic vs. nondiabetic CKD.

Skin manifestation	Diabitic CKD (N=27)	Nondiabetic CKD (N=50)	P value
	No. (%)	No. (%)	
Xerosis	25 (92.59)	42 (84)	0.3902
Pruritus	18 (66.66)	26 (52)	0.2146
Pallor	06 (22.22)	07 (14)	0.3581
Pigmentation	06 (22.22)	08 (16)	0.4994
Perforating dermatosis	08 (29.62)	01 (02)	0.0003
Cutaneous infections	22 (81.48)	21 (42)	0.0020
Nail changes	14 (51.85)	13 (26)	0.0233
Oral changes	20 (74.07)	22 (44)	0.0114
Hair changes	05 (18.51)	06 (12)	0.4354
Vasculitis	02 (7.40)	00	0.2052

Table 3: Prevalance of varying grades of xerosis.

Xerosis Grading	No. of patients	Percentage (%)
Absent	10	12.99
Mild	43	55.84
Moderate	19	24.67
Sever	05	6.49
Total	77	100

Table 4: Association between xerosis and pruritus.

Xerosis	Pruritus	No pruritus	P value
	No. (%)	No. (%)	
Absent	04 (9.09)	06 (18.18)	0.4127
Mild	19 (43.18)	24 (72.72)	0.0043
Moderate	16 (36.36)	03 (9.09)	0.0060
Severe	05 (11.36)	00 (0.00)	0.0452
Total	44 (100)	33 (100)	

Table 5: Change in xerosis over 6 months follow up.

Xerosis	No. of patients (%)
Improved	06 (12)
No change	39 (78)
Worsened	05 (10)
Total	50 (100)

It was seen from Table 5 that 50 patients with some degree of xerosis, were on maintenance hemodialysis for more than 6 months. Majority of patients (78%) had no change in xerosis over 6 months. Improvement was noted in 12% while xerosis worsened in 10% cases.

DISCUSSION

The present study population comprised 77 consecutive patients of CKD on maintenance hemodialysis at Manik Hospital, Aurangabad, India during 1 year period from January 2015 to December 2015.

Prevalance of dermatologic manifestations

In present study, dermatologic manifestations were prevalent in 94.08% patients, who had at least one skin symptom or sign. Only 4 patients (all non-diabetic) were free from skin problems. This was similar to study by Pico et al and Udayakumar P et al, who have reported 100% prevalence of skin manifestations.[3,7]

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 where men (70%) were more frequently involved than women (30%).[7] 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. A study by Narita et al observed mean age of 60.27±12.8 years and gender ratio and age distribution was similar to our study.[8]

Etiology of CKD

Diabetic Nephropathy (DNP) emerged as commonest etiology of CKD (35%), while non-diabetic diseases (CIN, CGN, and other diseases) comprised 65%. The study presented from north India, which reported diabetes (30%) as commonest etiology for CKD. Study by Udayakumar P et al reported that diabetes in 38%, followed by CIN in 25% patients.[7] Basic disease presentation in our study was similar to other studies from India.

Duration of dialysis

The mean duration of dialysis in our study was 25.64±25.74 months. Pavel et al studied patients with mean duration of dialysis of 36±28.8 months, while Narita et al studied patients on longer duration on HD (mean 123.67±90.1 months).[8,9] Shorter duration of dialysis in our study was due to inclusion of non reimbursable patients, active transplant programme and possible poor follow up.

Dermatologic manifestations

Prevalence of xerosis

Xerosis was the most common skin manifestation in our study (87.01%). Mild xerosis was noted in 64.17%,

though severe xerosis was noted only in 7.46% patients. This observation was similar to most of the studies. Szepietowski et al noted xerosis in 84.5% patients, while Yosipovitch et al noted it in 77.5% cases.[10,11] Udayakumar et al observed uremic xerosis in 79% patients on hemodialysis.[7]

Diabetes vs. non-diabetes

Xerosis was noted in 92.59% diabetic population as compared to 84% in non-diabetic group, but difference was not significant (p=0.3902). Similar prevalence was noted by Udayakumar et al (86.84% diabetic cases vs 70.76% nondiabetic cases).[7] Xerosis is a known complication of diabetes.

Xerosis and pruritus

Pruritus was present alone in 4/10 (with no xerosis) while it was associated with xerosis in 58.82% patients. All 5 patients with severe xerosis had pruritus (p=0.0452). Similar observations were made in previous studies. Morton et al observed pruritus in only 16% of the cases without xerosis, and in 29% of the cases with moderate to severe xerosis.[12] Similarly, in a large series of 189 CKD patients, pruritus was noted in 39% of the cases with no xerosis, and in 77% of the cases with moderate to severe xerosis. In a series of 130 patients, pruritus was experienced in significantly more patients with severe xerosis (34%) than in those without xerosis (21%).[7] Severity of xerosis correlated with presence of pruritus in our study which can be explained by the fact that uremic xerosis has worsening effect by reducing the threshold for itch.

Change in xerosis

Majority of patients (78%) had no change in xerosis over 6 months. Improvement was noted in 12% while xerosis worsened in 10% cases. Similar observations were made by Udayakumar et al who reported worsening of xerosis in 11.39%, improvement in 6.32% and unchanged in 82.27% patients.[7] These observations suggest no change in severity of xerosis on maintenance hemodialysis.

Pigmentary alteration

Pigmentary alteration occurs in 25-70% of the dialysis population and increase over time.[2] In this study, hyperpigmentation was noted in 18.18% cases. Pallor was noted in 24.67% and a yellowish tinge was seen in 10.38% patients. Pico et al reported that 70% of 102 dialysis patients manifested cutaneous pigmentary alteration, a yellow tinge was seen in 40% of the patients, diffuse hyperpigmentation of the sun-exposed areas was seen in 22%, and skin pallor was seen in 8% of the cases.[3] Udayakumar et al observed hyperpigmentation (43% of patients) and a yellowish tinge to the skin (10%).[7] Our study population is Asian Indians with naturally dark skin resulting in less prevalence of hyperpigmentation. Low prevalence of pallor may be due to better anemia control with erythropoietin therapy.

Perforating dermatosis

Perforating dermatosis (PD) was observed in 11.68% patients. A similar incidence of 11% has been recently reported in Britain.[12] Udayakumar et al encountered perforating dermatosis in 21% patients on maintenance dialysis. In this study, PD was noted in 29.62% diabetic CKD patients significantly higher than non-diabetic cases (p=0.0003).[7] Similar observation reported by Udayakumar et al who noted PD in 35.6% diabetic kidney disease patients.[7] Daisy et al reported diabetes in 66.66% (14/21) of PD patients.[13] Saray et al studied 22 case of acquired perforating dermatosis, of them dialysis dependent chronic renal failure (72.7%) and diabetes mellitus (50%) were the most commonly associated conditions.[14] Thus our study concurs with other studies that this peculiar skin disorder is probably linked to diabetes with dialysis dependence, though such changes are also noted in diabetics in predialysis phase.

Purpura

In present study purpura was noted in 7.79% patients. Similar finding reported by Udayakumar et al who noted purpura in 9% patients.[7] Easy bruising was also reported in a previous study. Singh et al observed these changes in 20% of CRF patients even not on dialysis.[15] Defects in primary hemostasis like increased vascular fragility, abnormal platelet function and the use of heparin during dialysis are the main causes of abnormal bleeding in these patients.[16]

Bullous dermatosis

In present study bullous dermatosis was noted in one patient over dorsum of hands and fingers, who had chronic HCV infection. Gilcherest et al reported 5 cases of self-limited bullous dermatosis restricted to light exposed areas, primarily involving the dorsa of the hands.[17] It has been reported in patients with chronic renal failure being treated with HD with a prevalence ranging from 1.2 to 18%.[18] The sporadic form of PCT occurs in approximately 5% of patients on dialysis; this form is caused by increased uroporphyrin concentrations and can be triggered by ingestion of alcohol, estrogens or iron and by chronic infections such as hepatitis B, hepatitis C or HIV.[19]

Gynecomastia

Gynecomastia was noted in 2 patients. One patient had decompensated chronic liver disease secondary to chronic HCV infection. Other patient developed gynecomastia after initiation of HD which may be due to possible 'refeeding' after the start of treatment.[20] Udayakumar et al observed gynecomastia in one patient.[7]

Cutaneous infections

Cutaneous infections were noted in 55.84% (13 bacterial, 21 fungal and 09 viral) patients. Fungal infections were noted in 27.27% patients. Udayakumar et al also reported high incidence of skin infections (67%).[7] He noted 13% bacterial, 42% fungal and 12% viral infections in his stage V CKD patients on hemodialysis. Cutaneus infections were noted in 81.48% diabetic patients. All cutaneous infections, (bacterial, fungal and viral) were mostly seen in diabetic group (p=0.0020). Udayakumar et al noted both bacterial and fungal infections to be commoner in diabetic group.[7] High incidence of skin infections in present study could be explained on the basis that these patients have impaired cell mediated immunity and have predisposing conditions of xerosis and pruritus.

CONCLUSION

Chronic kidney disease patients have prolonged life expectancy due to hemodialysis, hence they should be looked for presence of various skin manifestations which can affect the usual work and cause sleep disturbance which adds to the morbidity and mortality. Prevalence of dermatologic manifestations was 94.08% in this study population of hemodialysis. Diabetic nephropathy was the commonest etiology of CKD with majority cases were in the age group 51-60 years. Xerosis was the commonest sign (87.01%) and pruritus was the commonest symptom (57.14%). Cutaneous infections (55.84%) were quite common (55.84%) in this hemodialysis population which can be treated effectively with appropriate diagnosis. All the skin manifestations were commoner in diabetic CKD patients. Cutaneous infections, perforating dermatosis, nail chages and oral mucosal changes were significantly higher in diabetic population. Pruritus was present in 58.82% patients with xerosis. Majority of patients had no change in xerosis and pruritus over 6 months of hemodialysis therapy. Good dermatological assessment is routinely required in all dialysis patients for better quality of life and reducing/ ameliorating its impact on overall health.

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