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Original Research Article

Chronic kidney disease and its reflections on skin: a study from North-East India

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ABSTRACT

Background: Chronic kidney disease is associated with a variety of cutaneous manifestations as a result of underlying etiology as well as the various treatment modalities.
Methods: A hospital based cross sectional study was carried out for two year among 100 diagnosed cases of chronic kidney disease admitted in the Department of General Medicine, Regional Institute of Medical Sciences, Manipur, India having at least one mucocutaneous manifestation. Complete clinical and dermatogical evaluation and relevant investigations were done in all patients.
Results: There were 57% male and 43% female patients. The maximum number of study subjects belonged to the age range of 41 to 60 years. Diabetes mellitus was the commonest (39%) cause of chronic kidney disease in this study, followed by hypertension (32%), chronic interstitial nephritis and chronic glomerulonephritis (9%) each, other diseases (7%) and obstructive uropathy (4%). Sixty three percent of the patients were managed under conservative therapy and rest (37%) was on dialysis. Xerosis (72%) was the most common cutaneous manifestation followed by pallor (64%), pruritis (56%), hyperpigmentation (51%), yellowish hue (21%), dermatitis (10%) and others (24%). Infectious skin manifestations were present in 43% of study population, among which fungal, bacterial, viral disease constituted 19%, 17% and 7% respectively. Mucosal changes, hair changes and nail changes were reported in 77%, 68%, 119% cases respectively.
Conclusions: Early recognition and management of the dermatological manifestations vastly reduce the morbidity and improve the quality of life in chronic kidney disease patients.

Keywords: Chronic kidney disease, Cutaneous manifestation, Dialysis

INTRODUCTION

Chronic kidney disease (CKD) is an irreversible deterioration in renal function classically developing over years and is defined as kidney damage or glomerular filtration rate <60 ml/min/1.73 m^2 for 3 months or more irrespective of the cause.[1] Most patients with severe CKD progress to end stage renal disease (ESRD) with significant morbidity and mortality. It is a worldwide problem and accounts for approximately 8,50,000 deaths every year and 15 million disability adjusted lives; ESRD is the 12th cause of death and 17th cause of disability globally.[2] Cutaneous manifestations are common in all stages of CKD particularly towards ESRD with a

prevalence of 50–100%.[3,4] With the advent of hemodialysis as a therapeutic modality for ESRD, some skin manifestations such as uremic frost and erythema papulatum uremicum have become rare, however, many other abnormalities of skin and appendages have emerged. Skin manifestations specific to dialysis patients include acquired perforating dermatosis, calcific uremic arteriolopathy (calciphylaxis), bullous lesions, and nephrogenic fibrosing dermopathy. On the other hand, pruritus, xerosis, nail disorders, hair disorders, pigmentary changes, purpura, mucosal changes, pallor, and uremic frost, though not specific to hemodialysis, are more frequent. These manifestations may also vary across regions, with individual dietary habits, socioeconomic and nutritional status, and racial differences.[6] Because there are no data on the pattern of mucocutaneous manifestations in CKD patients from this part of the country, this study was carried out. The objective of the study was to determine the prevalence of cutaneous manifestations in CKD patients and to assess the correlation between mucocutaneous changes in relation to etiology of CKD patients.

METHODS

A hospital based cross sectional study was carried out at the Regional Institute of Medical Sciences, Imphal, Manipur in the Department of Dermatology in collaboration with the Department of General Medicine among 100 CKD patients admitted in the Department of Medicine from September 2009 to August 2011. Ethics committee approval from the institute was obtained. All enrolled patients participated after providing informed written consent. Details of medical history, clinical and mucocutaneous findings, and investigations were recorded in a predesigned proforma. Patients of both sexes having CKD with serum creatinine >1.5 mg/dl were included in the study. Patients of systemic lupus erythematosus, patients on immunosuppressive drugs and pregnant patients were excluded from this study. Potassium hydroxide mounts, skin biopsy, Gram's and Giemsa staining, and bacterial or fungal cultures were performed in selected cases, when indicated. Fine needle aspiration cytology was done in one patient with calcinosis cutis for confirming the diagnosis. Xerosis was classified into mild (dryness not justifying medical attention), moderate (dryness with roughness) and severe (dryness with roughness and scaling). A subjective evaluation method was used for grading pruritus based on the presence (present or absent) and intensity (mild for occasional itching, moderate for paroxysmal itching when retiring or awaken and severe for recurrent itching that disturbs during sleep and daily activities).

Statistical analysis

Done by SPSS software, version 16.0 for Windows. P value was calculated using Chi-square test and value of <0.05 was taken as statistically significant.

Ethical approval for the study was obtained from the institutional ethical committee.

RESULTS

The study sample consists of 100 patients with 57 male and 43 female patients having CKD admitted in the Department of General Medicine. In our study a slight male preponderance was found (male:female=1.3:1). Maximum number of patients (53%) was in the 41-60 years age group with youngest patient aged 20 years and oldest 83 years. Mean age was 52.73±14.46 years. The age and sex distribution of the patients are shown in Table 1. The mean duration of CKD was 19.85±11.24 months.

Table 1: Distribution of CKD by gender and age groups.

Parameters		No. of cases	%
Sex	Male	57	57
	Female	43	43
Total		100	100
Age (in years)	20-40	18	18
	41-60	53	53
	>61	29	29
Total		100	100

Table 2: Distribution of patients with respect to treatment.

Type of treatment	No. of patients	%
Conservative treatment	63	63
Hemodialysis	26	26
CAPD	11	11
Total	100	100

Majority of the patients (63%) in our study was treated conservatively followed by hemodialysis (26%) and continuous ambulatory peritoneal dialysis (11%) (Table 2). Commonest etiology of CKD was diabetes mellitus (39%) followed by hypertension (32%), chronic interstitial nephritis (9%), chronic glomerulonephritis (9%), obstructive uropathy (4%) and others (7%) (Table 3).

Table 3: Distribution of patients with respect to etiology of CKD.

Etiology	No. of patients	%
Chronic interstitial nephritis	9	9
Diabetes mellitus	39	39
Hypertenstion	32	32
Chronic glomerulonephritis	9	9
Obstructive uropathy	4	4
Others	7	7
Total	100	100

Table 4: Distribution of skin changes in relation to etiology of CKD.

Characteri-stics	Chronic interstitial nephritis (n=9)	Diabetes mellitus (n=39)	Hypertension (n=32)	Chronic glomerulo-nephritis (n=9)	Obstru-ctive uropathy (n=4)	Other	Total	P value
Yellowish hue	2	8	8	1	1	1	21	0.956
Pallor	7	22	24	5	3	3	64	0.387
Pigmentation	4	23	13	5	2	4	51	0.745
Total	13	53	45	9	6	8	136	
Xerosis								
Mild	5	28	10	6	1	6	56	0.033*
Moderate	0	6	4	0	0	0	10	
Severe	1	1	3	1	0	0	6	
Total	6	35	17	7	1	6	72	
Pruritus								
Mild	3	16	12	4	3	1	39	0.550
Moderate	0	7	5	0	0	0	12	
Severe	1	2	1	1	0	0	5	
Total	4	25	18	5	3	1	56	
Dermatitis								
Chronic eczema	0	2	0	0	0	0	2	0.997
Lichen simplex chronicus	0	1	2	0	0	0	3	
Photodermatitis	0	0	1	0	0	0	1	
Planter eczema	0	0	1	0	0	0	1	
Stasis eczema	0	1	0	0	0	0	1	
Seborrheic dermatitis	0	1	1	0	0	0	2	
Total	0	5	5	0	0	0	10	
Skin changes caused by infections in relation to CKD								
Candida	0	6	1	0	0	0	7	0.211
Pityriasis versicolor	0	2	0	2	0	1	5	0.099
Dermatophyte								
Tinea corporis	1	1	2	0	0	0	4	0.875
Tinea cruris	0	1	0	1	0	0	2	
Tinea faciei	0	1	0	0	0	0	1	
Bacterial								
Erysipelaas	0	0	1	0	0	0	1	0.619
Folliculitis	1	6	1	0	0	1	9	
Foot ulcer	0	3	0	0	0	0	3	
Furuncle	0	2	0	1	0	1	4	
Viral								
Herpes simplex	0	0	0	0	0	1	1	0.594
Herpes zoster	0	0	1	0	0	0	1	
Verruca plana	0	1	1	0	0	0	2	
Verruca vulgaris	0	2	1	0	0	0	3	
Other disorders								
Acanthosis nigricans	0	1	0	0	0	0	1	0.838
Bullae	0	0	1	0	0	0	1	
Delayed wound healing	0	0	0	1	0	0	1	
Keratosis pilaris	0	0	1	0	0	0	1	

Continued.

Characteri-stics	Chronic interstitial nephritis (n=9)	Diabetes mellitus (n=39)	Hypertension (n=32)	Chronic glomerulo -nephritis (n=9)	Obstru-ctive uropathy (n=4)	Other	Total	P value
Seborrheic keratosis	0	3	0	0	0	0	3	
Vitiligo	0	1	0	0	0	0	0	
Scabies	0	1	0	0	0	0	1	
Ecchymosis	1	4	3	1	4	4	11	
Reactive perforating collagenosis	0	0	0	1	0	0	1	
Calcinosis cutis	0	0	0	1	0	0	1	
Icthyosis	0	0	2	0	0	0	2	
Total	1	10	7	4	1	1	24	

*: Significant.

Table 5: Distribution of mucosal, hair and nail changes in relation to etiology of CKD.

Characteristics	Chronic interstitial nephritis (n=9)	Diabetes mellitus (n=39)	Hypertension (n=32)	Chronic glomerulo - nephritis (n=9)	Obstructive uropathy (n=4)	Others	Total	P value
Mucosal changes								
Macroglossia	3	8	2	3	1	2	19	0.274
Xerostomia	1	18	7	3	0	0	29	0.030*
Ulcerative stomatitis	1	7	7	1	1	2	19	0.920
Angular cheilitis	1	4	0	0	1	0	6	0.200
Coated tongue	1	2	1	0	0	0	4	0.819
Total	7	39	17	7	3	4	77	
Hair changes								
Sparse body hair	2	6	9	2	0	2	21	0.694
Sparse scalp hair	4	8	9	0	0	0	21	0.098
Dry lustreless hair	1	13	7	3	2	0	26	0.276
Nail changes								
Half and half nail	1	10	4	0	0	0	15	0.202
Apparent leukonychia	0	6	7	3	2	0	18	0.144
Onycholysis	0	6	7	0	1	0	14	0.310
Onychomycosis	0	12	0	1	1	2	16	0.009*
Subungual hyperkeratosis	1	2	2	1	2	0	8	0.051
Loss of lunula	3	10	8	3	0	1	25	0.786
Koilonychia	3	8	10	1	1	0	23	0.450
Total	8	54	38	9	7	3	119	

*: Significant.

The overall cutaneous manifestations in CKD patients are summarized in (Table 4 and 5). There were 64% patients with pallor, 51% with hyperpigmentation and 21% with yellowish hue with highest prevalence rate of pallor in chronic interstitial nephritis (77.77%) and lowest in others category of CKD (42.86%). In case of hyperpigmentation, highest prevalence rate (58.97%) was observed in diabetes mellitus cases and lowest (40.62%) in hypertension. Yellowish hue was found to be highest prevalent in obstructive uropathy and hypertension (25%)

each and lowest in chronic glomerulonephritis (11.11%). Xerosis was the commonest skin change in our study, found in 72% of the patients (Figure 1) while pruritus was the third commonest skin change (56%).

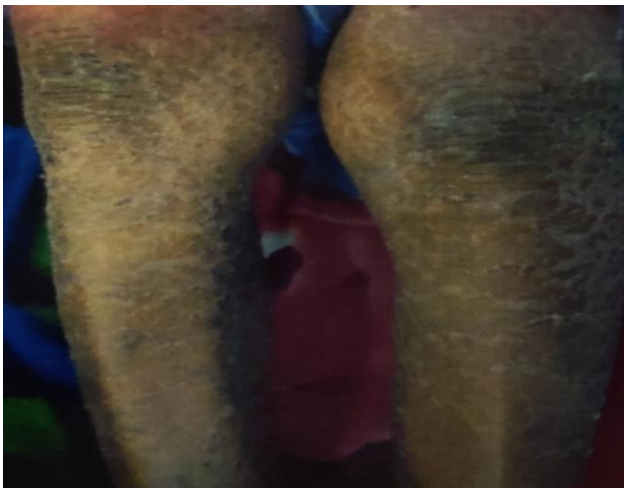

Figure 1: Severe xerosis with icthyotic scaling on the extensor of lower limbs.

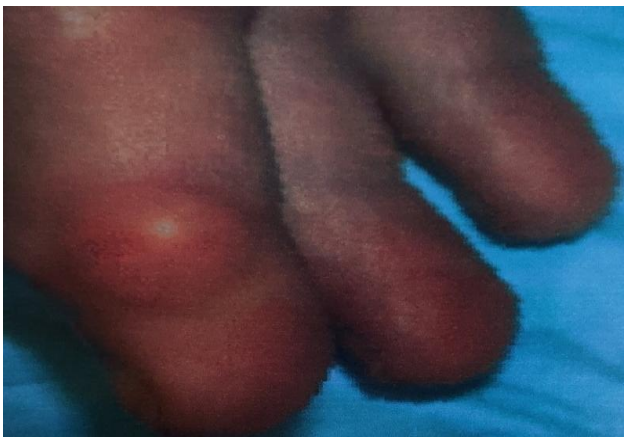

Figure 2: Calcinosis cutis in the periarticular area of the distal interphalangeal joint of middle finger.

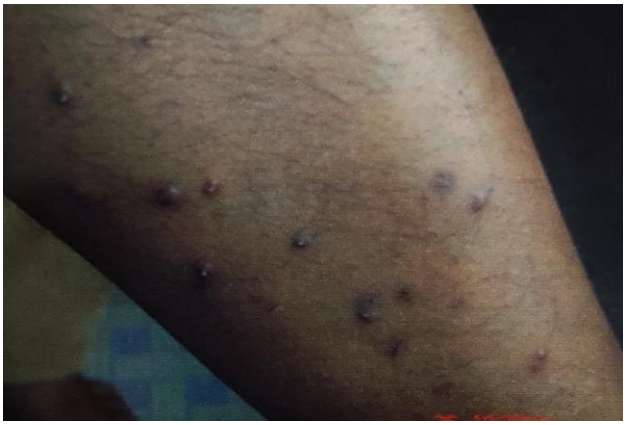

Figure 3: Reactive perforating collagenosis showing multiple discrete skin colored keratotic papules with central plugs in few.

In cases of xerosis and pruritus, the prevalence was categorized into mild, moderate and severe. The highest prevalence rate of xerosis was observed in diabetes mellitus and lowest in obstructive uropathy and the difference in prevalence rates in relation to etiologies of CKD was statistically significant (p=0.033) while pruritus showed an insignificant p–value (0.550). There were 10% cases of dermatitis in our study, with lichen simplex chronicus (3%) commonest, followed by chronic eczematous dermatitis and seborrheic dermatitis (2%) each, photodermatitis, planter eczema and stasis dermatitis (1%) each. Ecchymosis was found in 11% cases, seborrheic keratosis in 3% cases, icthyosis in 2% cases, acanthosis nigricans, bullae, calcinosis cutis (Figure 2), delayed wound healing, keratosis pilaris, reactive perforating collagenosis (Figure 3), scabies and vitiligo 1% each. Infectious skin manifestations were present in 43% of study population, among which fungal, bacterial, viral disease constituted 19%, 17%, 7% respectively.

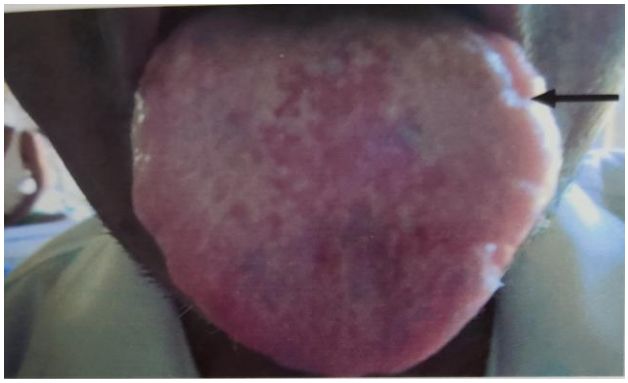

Figure 4: Macroglossia with teeth markings.

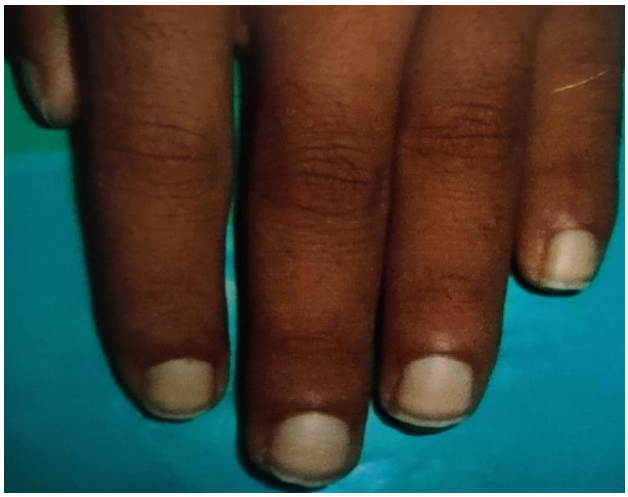

Figure 5: Apparent leuconychia with loss of lunula.

Out of 19% of fungal infection, candidal and dermatophyte infection seen in 7% each, and rest 5% was due to pityriasis versicolor. The bacterial infections reported were folliculitis (9%), furuncles (4%), foot ulcers (3%), erysipelas (1%). Viral infections included

Verruca vulgaris (3%), *Verruca plana* (2%), *Herpes simplex* and *Herpes zoster* 1% each. Mucosal changes was reported in 77% cases with commonest being xerostomia (29%), followed by macroglossia (Figure 4) and ulcerative stomatitis (19%) each, angular cheilitis (6%) and coated tongue (4%). The highest prevalence of xerostomia was found in diabetes mellitus patient (46.15%) which was statistically significant (p=0.030). Hair changes were found in 68% cases including dry lusterless hair (26%) which was the commonest, followed by sparse body hair and sparse scalp hair 21% each. Highest prevalence rate of dry lusterless hair was found in obstructive uropathy (50.00%), spare body hair in others category of CKD (28.57%) and sparse scalp hair in chronic interstitial nephritis (44.44%). A total of 119(%) of nail changes were observed in our study among which loss of lunula was the commonest (25%), followed by koilonychia (23%), apparent leuconychia (18%) (Figure 5), oncychomycosis (16%), half and half nails (15%), onycholysis (14%) and subungual hyperkeratosis (8%). Onychomycosis was found to be significantly (p=0.009) most prevalent in diabetes mellitus (30.76%).

DISCUSSION

Kidney failure is among the most common systemic diseases associated with cutaneous manifestations. Out of total 100 CKD patients examined in our present study, all patients had at least one cutaneous change This is in agreement with study by Pico et al.[4] In our present study the maximum number of patients (53%), were in the 41–60 years age group with mean age 52.73±14.46 which was in accordance to study by Hajheydari et al.[6,7] There was slight preponderance of male patients (male: female=1.3: 1) comparable with other studies.[6] The most common etiology of CKD was diabetes mellitus (39%) in the present study, followed by hypertension (32%), chronic interstitial nephritis and chronic glomerulonephritis (9%) each, and the least was obstructive uropathy (4%) that was consistent with study by Girisha et al where diabetes mellitus was the most common cause (45%) of renal dysfunction followed by hypertension in 35% cases and glomerulonephritis in 4% cases.[7] Xerosis (72%) was the most common cutaneous abnormality in our present study ,as observed in various studies.[7-12] This was classified as mild 56%, moderate 10%, and severe 6%. Thirty five 87.74% of 39 diabetes mellitus patients presented with xerosis. Xerosis was predominantly seen over the extensor surfaces of the forearms and legs. Patients with generalized severe dryness had fine scaling. Skin dehydration, diuretic, reduced sebum/sweat excretion, altered skin barrier, and low emollient usage have been primarily implicated for severity of xerosis whereas marked irritancy to external factors (sun, dust, detergents) is aggravating.[5] However, prevailing dry and cold climate in this region was an additional aggravating factor in our patients. Pallor was the second most common finding 64% in our study population that was consistent with studies by Chanda et al, Girisha et al, Udaykumar et al, Deshmukh et al with 57%, 65%, 60% , 68.57% of the patients respectively having pallor.[7-9,12] Deficient erythropoietin production by the failing kidneys and dietary deficiencies of iron, folic acid, and vitamin B12 contribute to anemia.[12] Pruritis was the third commonest cutaneous abnormality found in 56% of patients in the present study. Twenty five (64.10%), of 39 diabetes mellitus patients presented with pruritis. Out of 37 patients on dialysis, pruritis improved in eight (21.62%) patients and worsened in 3 (8.10%) patients following dialysis. Kumar et al, Deshmukh et al reported pruritis in 53% and 65.71% respectively, of chronic renal failure patients on hemodialysis, whereas Ghunawat et al, Rashpa et al reported pruritus in 42%, 46.7% of the CKD patients that was consistent with our study findings.[9-12] However Girisha et al reported pruritus in only 15 % cases, which was much lower compared to our observation.[7] Recent studies have reported a decline in the incidence of pruritus possibly due to better dialysis techniques.[14] Pruritis is one of the most characterstic and annoying cutaneous symptoms of CKD although the exact etiology of pruritis is unknown. But pruritis may be due to variety of causes such as degree of renal insufficiency, secondary hyperparathyroidism, xerosis, increased serum levels of magnesium, calcium phosphate, aluminium, increased serum levels of histamine, proliferation of nonspecific enolase positive sensory nerves in the skin, hypervitaminosis A, iron deficiency anemia and slowly accumulated or deposited pruritogen (s) are the likely causes. Hyperpigmentation was seen in 51% and a yellowish hue to the skin was seen in 21% of patients in this study. Hyperpigmentation was mainly found on the sun exposed areas and it was more diffuse in dialyzed patients. One case of vitiligo was found in the present study. It was localized in the both hands. Kumar et al reported hyperpigmentation in 43% of patients and yellowish hue to the skin in 10% of patients and Rashpa RS et al reported hyperpigmentation and yellowish hue in 38.5%, 5.7% cases respectively.[9,10] Here, we see that our study the incidence of pigmentary changes were more prevalent compared to other studies. The pigmentation in patients with chronic renal failure is secondary to failure of the kidneys to excrete β melanocyte stimulating hormone, which stimulates melanin secretion in the basal layer and superficial dermis.[15] It has been attributed to the accumulation of carotenoids and nitrogenous pigments (urochromes) in the dermis or the presence of lipochromes and carotenoids in the epidermis and subcutaneous tissue.[16,17] Skin infections were seen in 43% of patients in our study comprising fungal 19%, bacterial 17%, and viral 7%, while Ghunawat et al, Deshmukh et al reported a much lower incidence of skin infection in their studies 33%, 34.39% respectively.[11,12] Increased susceptibility to infection can either be due to inflammation caused by the use of nonsterile dialysate and non-biocompatible membranes during hemodialysis or CRF per se due to diminished T and B lymphocyte function and count, and reduced natural killer cell activity.[4,8] Ecchymosis was seen in 11% of CKD patients in this present study that was compatible with other studies.[9] Defects in primary hemostasis like increased

vascular fragility, abnormal platelet function and the use of heparin during dialysis are the possible causes. Total 119 of nail changes were found in this study. Loss of lunula was the most common nail abnormality 25% in this study, which was followed by koilonychias 23%, apparent leukonychia 18%, onychomycosis 16%, half-and-half nail 5%, onycholysis 14%, subungual hyperkeratosis in 8%. Ten (25.64%) of 39 diabetic patients presented with loss of lunula. Twelve (30.76%) of onychomycosis and 10 (25.64%) of half-and-half nail were found in diabetes mellitus. Chanda et al found nail changes in 46% cases, with commonest being absent lunula (26%), similar to our study. Deshmukh et al, reported nail changes in 60% cases with Beau's line (28.57%) as commonest change.[12] Rashpa et al reported nail pallor in (35.2%) patients as the most common finding and absent lunula observed (23.8%) cases that was comparable with our study.[10] Half and half nails, a band of discoloration over the distal nail plate from increased density of nail bed capillaries, were found in 5% cases in our study whereas Chanda et al, Girisha et al, Kumar et al, Deshmukh et al, Ghunawat et al, Rashpa et al reported it in 38%, 21%, 21%, 19.04%, 30%, 16.4% cases respectively and Ghunawat et al, Girisha et al reported it to be the commonest nail change in their studies.[7-12] Thus, contrary to other published studies in our country, the findings in our study show loss of lunula as the most common type of nail change. In the present study, total 68% hair changes were observed comprising dry lusterless hair 26% that was commonest, followed by sparse body hair and sparse scalp hair 21%, each. Dry lusterless hair might be due to decreased secretion of sebum.[9] Kumar et al found sparse body hair in 30% and sparse scalp hair in 11% patients.[9] In our study with 68% mucosal changes, xerostomia 29% was the commonest manifestation, followed by ulcerative stomatitis and macroglossia 19%, each, angular cheilitis 6% and coated tongue 4%. Out of 19% of ulcerative stomatitis patients, 16% had predialysis blood urea level of >150 mg/100 ml, while other 3% had <150 mg/100 ml did not show these changes. Kumar et al reported xerostomia in 31% patients, that was similar to our finding and ulcerative stomatitis in 29% patients and macroglossia, ulcerative stomatitis, angular cheilitis and coated tongue in 35%, 29%, 12%, 11% patients respectively.[9] When we compare the findings with our present study, we see that all mucosal changes are less prevalent in our patients which may be due to effective preventive measures, differences in choice of management, socio-economic and climatic condition and race. Reactive perforating collagenosis was seen in 1 (%) patient of the present study in a 34 years old, non-diabetic, hepatitis C virus positive male patient with 9 years history of renal transplantation for CRF. He was on conservative therapy and presented with gradual onset of pruritic, dome shaped papules with central crusts; arising on the extensor limb surface. Kumar et al, Deshmukh et al reported prevalence of acquired perforating dermatosis 21%, 17.14% cases respectively.[9,12] One patient (1%) of this study subjects presented with firm papules and nodules in the periarticular regions of interphalangeal joints of fingers in hands which was clinically diagnosed as calcinosis cutis and confirmed by the fine needle aspiration cytology and Von Kossa staining. Hajheydari et al and Falodun et al found no case of calcification and acquired perforating dermatosis in their studies.[6,15] Prevalence of xerosis, pruritis, hyperpigmentation, infection, onychomycosis and xerostomia were quite high among the diabetes mellitus patients and their prevalence rate were 48.61%, 44.64%, 45.09%, 64.10%, 30.76% and 46.15% respectively.

Clinical conditions like calciphylaxis and nephrogenic fibrosing dermopathy and nephrogenic systemic fibrosis were not observed in this study. Shorter duration of treatment of our study group and the high mortality rate among the CKD patients in our part of country might be possible explanation.

CONCLUSION

All our 100 CKD patients showed at least one cutaneous alteration. Patients with CKD may present with an array of skin abnormalities. With the advent of hemodialysis, the life expectancy of these patients has increased, giving time for more and newer cutaneous changes to manifest. Our observations necessitate a joint effort between dermatologists and nephrologists for early recognition and management of these comorbidities which may significantly improve the quality of life of patients.

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