ORIGINAL ARTICLE

Pattern of skin diseases in patients of chronic kidney disease

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ABSTRACT

Introduction: Dermatological manifestations are common in patients of chronic kidney disease (CKD). Skin manifestations in patients of CKD range from nearly universal xerosis and pruritus to uncommon conditions like hyperpigmentation of exposed parts, purpuric skin changes, acquired perforating dermatosis etc. Patients with CKD are often burdened by skin lesions, these findings can prompt early diagnosis of CKD and its management.

Aim and Objective: To determine the pattern of skin diseases in patients of chronic kidney disease.

Materials and Methods: This is an observational study conducted at Dayanand Medical College and Hospital, Ludhiana on patients of CKD with or without hemodialysis. A total of 100 patients of CKD (from stage 3 to 5) for atleast 1 year with skin manifestations was included in the study. Detailed cutaneous examination was done and dermatological manifestations were evaluated and compared in dialysis and non dialysis group.

Results: Out of 100 patients, 90% were in CKD stage 5 and 82% of them were on hemodialysis with slight male preponderance (51%) and mean age of 56.23 years. Diabetes mellitus was the most common cause (65%), followed by hypertension (22%). Pallor was significantly present (65%), and pruritus was the most common distressing complaint (58%) followed by xerosis (24%), half and half nails (23%), hyperpigmentation (16%), diffuse hair loss from body (14%), infections and infestations (14%), onychomycosis (12%), apthous stomatitis (9%), perforating disorders (8%), koilonychias (6%), xerostomia (2%). Less often encountered manifestations were calcinosis cutis, calciphylaxis, uremic frost. The frequency of most of the cutaneous manifestations were similar between dialysis and non dialysis patients.

Conclusions: Dermatological changes may help in early detection and treatment of CKD. Nephrogenic pruritus is the most distressing symptom, which impairs the quality of life in these patients. Recognition and management of these dermatological manifestations may vastly reduce the morbidity and improve the quality of life in these patients.

KEYWORDS: Chronic Kidney Disease(CKD), Cutaneous Manifestations

INTRODUCTION

Chronic Kidney Disease (CKD) encompasses a spectrum of different pathophysiologic processes associated with abnormal kidney function with a progressive decline in glomerular filtration rate. It is more prevalent in the elderly population. Though, in younger patients CKD is associated with progressive loss of kidney function overtime, 30% of patients over 65 years of age do not have progressive disease.[1]

The Kidney Disease Outcomes Quality Initiative (KDOQI) of the National Kidney Foundation (NKF) established a definition and classification of CKD.[2]

It defines CKD as either kidney damage or a decreased glomerular filtration rate (GFR) of less than 60 mL/min/1.73 m^2 for 3 or more months. The KDOQI classification of the stages of CKD

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is as follows:[2]

- Stage 1: Kidney damage with normal or increased GFR (>90 mL/min/1.73 m^2)
- Stage 2: Mild reduction in GFR (60-89 mL/min/1.73 m^2)
- Stage 3: Moderate reduction in GFR (30-59 mL/min/1.73 m^2)
- Stage 4: Severe reduction in GFR (15-29 mL/min/1.73 m^2)
- Stage 5: Kidney failure (GFR < 15 mL/min/1.73 m^2 or on dialysis)

Whatever the underlying etiology, once the loss of nephrons and reduction of functional renal mass reaches a critical point, the remaining nephrons undergo a process of irreversible sclerosis that leads to a progressive decline in GFR. Cutaneous disorders have a prevalence of 50 to 100% in patients of CKD.[3]

The skin, being the most visible and accessible organ of the body, may function as an important diagnostic window to the diseases affecting the internal organs including the renal system.[4]

Dermatological manifestations of chronic renal disease are of two types-

- Specific cutaneous manifestations of chronic renal failure(CRF)
- Non specific cutaneous manifestations due to treatment (drugs and dialysis).

SPECIFIC CUTANEOUS MANIFESTATIONS OF CRF

Pruritus, xerosis, pigmentary disorders including pallor, yellow discoloration and hyperpigmentation, uremic frost, perforating disorders, calcinosis cutis & calciphylaxis, purpura, gynaecomastia, vascular disorders, poor wound healing and restless leg syndrome.[5]

Cutaneous alterations in the skin of patients with chronic renal failure are frequently found, but are variable.

Pruritus, increasing with deteriorating renal function, is a very frequent complaint.[6] The aetiology is unclear, but it tends to become more severe with loss of renal function.[7] Pruritus can be accompanied by dryness of the skin but no correlation exists between the two: 48% of patients with chronic renal insufficiency indicate pruritus, but xerosis cutis can be demonstrated in 60%.[8] Xerosis cutis increases the susceptibility to infections and this is aggravated by delayed wound healing of the skin.[9]

Alterations in the cutaneous pigmentation, in particular macular hyperpigmentation of the palms and soles, and diffuse hyperpigmentation of the mucosal membranes, can be seen relatively early during progression of the disease.[10]

Premature ageing of the skin occurs mainly as a result of actinic elastosis.

Lindsay's half and half nails, which are typically seen in patients on dialysis can also be present. They are characterized by proximal white discoloration and distal red/brownish color.

The frequently reported intraoral findings in CRF patients are xerostomia, macroglossia, and ulcerative stomatitis.[5] Hairs are sparse and lustreless.[10]

NON SPECIFIC CUTANEOUS MANIFESTATIONS DUE TO TREATMENT

Patients with CKD on hemodialysis (HD) experience many dermatological symptoms during treatment. Since these symptoms are only detected in advanced cases of the disease, they are not valuable in the diagnosis of kidney failure.[11]

Complete and precise examination of skin, hair, nails, and mucosal membranes may reveal a

wide variety of manifestations including hyperpigmentation, xerosis, ichthyosis, pruritus, onychomycosis, onycholysis, splinter hemorrhages, subungual hyperkeratosis, brittle hair, sparse body and scalp hair.[3,5]

The prevalence of skin disorders in dialysis population is nearly 100% and are responsible for considerable distress to the patients.[12]

Early diagnosis and treatment of the underlying cause and/or institution of secondary preventive measures is imperative in patients with CKD. This may slow, or possibly halt the progression of the disease. The medical care of patients with CKD should focus on preventing the progression of CKD, treating the pathologic manifestations of CKD and timely planning for long-term renal replacement therapy, including dialysis and transplantation.

MATERIALS AND METHODS

This observational study which was conducted for a period of 1 year from 1st January 2017 to 31st December 2017 in Department of Dermatology, Venereology & Leprosy and Nephrology at Dayanand Medical College and Hospital, Ludhiana on patients of chronic kidney disease (stage 3 to stage 5). The study included both admitted patients in department of nephrology and those attending nephrology OPD and dermatology OPD.

METHOD OF COLLECTION OF DATA

Inclusion criteria

- Patients diagnosed to have Chronic Kidney Disease, who presented with cutaneous lesions and symptoms.
- Patients on haemodialysis and peritoneal dialysis at dialysis unit of nephrology department who presented with cutaneous lesions and symptoms.

Exclusion criteria

- Patients on oral steroids
- Patients with underlying systemic lupus erythematous
- Patients with active malignancy
- Patients who underwent renal transplantation.
- Stage 1 and stage 2 of CKD

A detailed history was taken with particular reference to the duration, initial site of appearance of lesion, extension of lesions and symptoms, duration of renal disease and duration of symptoms, duration of skin ailment, duration of dialysis, onset of changes with relation to renal disease and dialysis. History of underlying systemic conditions like diabetes mellitus, hypertension, tuberculosis, connective tissue disorder etc was obtained. Clinical photographs were taken at the same sitting. The skin, hair, nails and mucosa was examined in detail for:

1. Specific lesions of chronic kidney disease
2. Presence of cutaneous infection
3. Associated skin lesions

All the patients were thoroughly investigated with routine haematological and biochemical investigations. Wherever required radiographs and ultrasonography was done. All these patients were managed with drugs and dialysis according to severity of CKD. The severity of chronic kidney disease was graded into stage 1-5 based on GFR (CKD-EPI equation). Staging of CKD was done according to the Kidney Disease Outcomes Quality Initiative (KDOQI) clinical practice guidelines as follows:

Stage 1 –GFR > 90 ml/min

Stage 2 – GFR 60-90ml/min

Stage 3 - GFR 30-59 ml/min
Stage 4 –GFR 15-29 ml/min
Stage 5 –GFR <15 ml/min

The data obtained was tabulated, statistically analysed with frequency and percentages, and compared with other similar studies.

RESULTS

The present study was conducted to study the various dermatological manifestations associated with CKD. A total of 100 patients of CKD were evaluated and detailed dermatological history & examination was carried out. The results and observations are as follows:

- Males constituted 51% of patients, while females constituted 49% of patients.
- The majority of patients were in 60-69 years age group (36%). Mean age was 56.23 years.
- Out of 100 patients, 57 (57%) had duration of CKD between 1-3 years and 39 (39%) had duration less than 1 year.
- Diabetes mellitus was most common etiological factor of CKD, seen in 65% of patients followed by hypertension in 22% of patients.
- 82% of patients were undergoing haemodialysis.
- The mean values of haemoglobin, blood urea, serum creatinine in our study were: 8.51 gm% (S.D=1.650 gm %), 144.45 mg/dl (S.D=64.85 mg/dl), 6.37 mg/dl (S.D=2.394 mg/dl) respectively
- Among the various dermatological manifestations, pruritus was the most common complaint in 58 % of patients followed by xerosis in 24%.
- Pallor was observed in 65% of patients and acquired perforating disorders in 8% of patients.
- Hyperpigmentation and ecchymosis were observed in 16% & 11% of patients respectively.
- Among the cutaneous infections and infestations like carbuncle, folliculitis, herpes simplex, herpes zoster, hepatitis C, fungal infections, scabies accounted for 14% of skin changes in patients.
- Nail changes were present in 68% of patients. The most common nail findings were half and half nails in 23% followed by onychomycosis in 12% of patients.
- Hair changes were seen in 24% of patients. Diffuse hair loss from the body was the most common finding present in 14% of patients.
- Pallor was the most common oral mucosal finding in 27% of patients.
- Rarely encountered conditions like uremic frost and calciphylaxis were also seen in 1% of patients each.
- Miscellaneous cutaneous findings like maculopapular rash, endogenous eczemas, acne corporis, icthyosis, vitiligo vulgaris, leucocytoclastic vasculitis, lichen simplex chronicus, photocontact dermatitis, calcinosis cutis, squamous cell carcinoma *in situ*, granuloma annulare, necrobiosis lipoidica, urticaria were also observed.

DISCUSSION

Dermatological manifestations of chronic kid-

ney disease generally appear subsequent to the development of the disease, but may be the presenting sign and in some cases they may even precede the primary disease manifestations. Chronic Kidney disease is associated with wide array of dermatological manifestations. These dermatological manifestations cause considerable distress to the patient and impair the quality of life. Alleviation of these symptoms go a long way in improving the quality of life of the patients.

One hundred patients of different age group and sex diagnosed as chronic kidney disease were enrolled in the present study and the results obtained were evaluated and compared.

The age of the patients ranged from 17-86 years with the mean age of 56.23 years. Maximum number of patients were in 60-69 years age group (36%), followed by 50-59 years age group (28%).

The mean age in our study was 56.23 years as compared to the studies by Sultan MM *et al*[13] (49.5), Thomas EA *et al*[14] (50.5), Eman *et al*[15] (50.2). Singh *et al*[16] and Udayakumar *et al*[5] reported mean age of 40.5 and 43 years respectively.

In the present study, 51 patients were male while 49 were female. The male and female had almost similar preponderance (M:F= 1.04:1) while the result of the study group by Thomas EA *et al*[14] had a male preponderance (M:F= 3.71:1).

The mean values of haemoglobin, blood urea, serum creatinine in our study were 8.51gm% (S.D=1.650 gm%), 144.45 mg/dl (S.D=64.85 mg/dl), 6.37 mg/dl (S.D= 2.394 mg/dl) respectively.

The duration of chronic kidney disease varied from few weeks to several years, the highest frequency being in 1-3 year group. The majority of CKD patients were of stage 5 (90%) followed by stage 4 (10%) and none of the patient was in stage 3.

Diabetes mellitus was the most common etiological factor of CKD in this study, present in 65% of patients. 22% of patients had both hypertension whereas only 9% had both hypertension and diabetes mellitus. 6% of patients had chronic glomerulonephritis, 5% had obstruction as cause of CKD. Udaya kumar *et al* also reported similar results with diabetes in 38% and hypertension in 12% of patients.[5] Whereas, Sultan M M *et al* reported hypertension & diabetes mellitus in 60% & 14% patients respectively.[13]

The majority (82%) of CKD patients were on dialysis in our study.

Out of 100 patients screened, among the skin changes, pruritus was the most common finding and was observed in 58 (58%) patients. This is in accordance with other studies conducted by Mirza R *et al*[17] (64.66%), Sultan M M *et al*[13] (55%) Kolla PK *et al*[18] (53%) & Eman *et al*[15] (52%). Pruritus is the most characteristic & annoying cutaneous manifestation in the patients of CKD. It is not observed in acute renal failure. Pruritus may or may not improve with dialysis but may resolve after kidney transplantation.[19]

It is directly proportional to the degree of renal insufficiency.[20] Several hypothesis have been proposed for the genesis of pruritus. Etiological factors include xerosis, secondary hyperparathyroidism, increased serum levels of calcium and phosphate, increased serum levels of histamine, hyper vitaminosis A, proliferation of non specific enolase positive sensory nerves in the skin.[21]

Xerosis was found in 24 (24%) patients in our study whereas in studies by Kolla PK *et al*,[18] Sultan MM *et al*[13] and Falodun O *et al*,[22] xerosis was to the tune of 52%, 54% and 60% respectively. The presence of xerosis is attributable to the reduction in the size of eccrine sweat glands along with high dose diuretic therapies given to these patients,[23] elevated plasma Vit.A,[24] elevated retinol binding protein,[25] alkalinity of skin[26] and protein energy malnutrition.[20]

Pallor is reported to be hallmark of chronic renal failure and is primarily due to inadequate erythropoietin production by the failing kidneys. The other contributory factors may be iron deficiency anaemia and megaloblastic anaemia along with decreased survival of erythrocytes.[27] Pallor was seen in 65 (65%) patients in our study which is significantly higher than the results of Sultan MM *et al*[13] (45%), Thomas EA *et al*[14] (45.45%) & Attia *et al* (42.2%).[28]

Acquired perforating disorders were seen in 8 (8%) patients in our study which conforms to studies by Sultan MM *et al*[13] (10%), Deshmukh *et al* (17.14%)[24] & Thomas EA *et al*[14] (17.7%). The exact pathogenesis is not known but may be attributable to the dysplasia and decay of dermal connective tissue followed by transepidermal elimination. Microvascular calcium deposition interrupts the blood flow in the dermal layer resulting in necrosis and cell death. Skin trauma associated with pruritus is an inciting agent for these lesions.[29]

Hyperpigmentation was observed in 16 (16%) patients in our study as compared to 44% in study conducted by Eman *et al*.[15] Difficulty in appreciating hyperpigmentation in dark colored individuals may be responsible for the lower incidence of pigmentary changes in our study. Diffuse hyperpigmentation in sun-exposed areas is due to increased melanin in basal layer and superficial dermis due to failure of kidneys to excrete β-MSH.[30] Yellow discoloration seen in 2% patients is due to accumulation of carotenoids and urochromes in epidermis and subcutaneous tissue.[31]

Impaired cellular immunity due to decreased T-lymphocyte count leads to increased prevelance of infections in CKD patients.[5]

In the present study, infections and infestations were seen in 14% of patients. Similar results were seen by Gunipudi SK *et al*[32] who also reported fungal, bacterial, viral infections and infestations in 13.3% of patients.

Nail changes were observed in 68% of patients in our study. The most common nail changes were half and half nails followed by onychomycosis in 23% and 12% of patients respectively. Half and half nails seen in 23% of patients is present in higher frequency in accordance with study of Singh G *et al*[16] (13.3%). Koilonychia was seen in 6% of patients which was comparable to 5% in the study by Thomas EA *et al*.[14] This may be due to associated anemia in the present study. Half and half nails are characterized by distal brownish color and proximal whitish color of the nail. The white appearance of proximal half of nail is due to nail bed edema associated with dilated capillaries while the other half of nail bed appears normal.[33] Amatya *et al*[34] in a study found white nail as the most common nail finding followed by brown and half and half nails. Pallor along with absent lunula was present in (8%) of patients in our study while Levillard DT *et al*[35] reported pallor as the most common nail change in 67% of the patients. In present study other nail changes observed in (17%) of

patients included melanonychia (3%), subungual hyperkeratosis (2%), splinter hemorrhage (2%), Mee's line (2%) and pterygium, brittle nail, beau's line, pitting, clubbing was seen in rest of patients. While, Levillard DT *et al*[35] reported Mee's lines in (16%), Beau's lines (4%), subungual hyperkeratosis (9.3%), splinter hemorrhage (4%).

The majority (76%) of patients had no hair changes. The most common hair change observed in this study was diffuse hair loss in 14% of patients. Eman *et al*[15] reported it in 48% of patients. Dry, lustureless, brittle hair, sparse scalp hair were present in 10% of patients which in accordance with the study by Udayakumar *et al*[5] who reported it in 16% of patients of CKD. The diffuse hair loss may be related to telogen effluvium associated with severity of illness, xerosis, pruritus or due to drugs such as heparin, anti-hypertensives, lipid-lowering drugs which are used in these patients.[36,37] Decreased secretion of sebum is responsible for dry and lustureless hair.[5]

Pallor was the most common oral mucosal finding seen in 27%, followed by apthous stomatitis and xerostomia in 9% and 2 % of patients respectively. Gunipudi SK *et al*[32] also reported pallor as significant mucosal finding in 28% patients. But Eman *et al*[15] reported xerostomia as significant finding in 46% of patients. It may be due to mouth breathing and dehydration.[13] Stomatitis is attributable to high blood urea levels and poor oral hygiene.[38]

Bullous dermatoses was documented in single patient (1%) on haemodialysis in our study. Khanna D *et al*[39] have reported bullous dermatoses in 2% of patients.

Uremic frost (3%) was found in the study of Udayakumar *et al*[5] while in our study it was observed in a single patient (1%).

Calciphylaxis is a life threatening complication of secondary hyperparathyroidism in CKD.[40] It was observed in single patient (1%) in our study. Sultan MM *et al* observed calciphylaxis in 2% of patients.[13] Nephrogenic fibrosing dermopathy (NFD) is another dermatosis of CKD which was not seen in our study which is characterized by progressive development of erythematous, sclerotic plaques usually pruritic on arms and legs.[5]

Various other dermatoses including maculopapular rash, endogenous eczemas, acne corporis, icthyosis, vitiligo vulgaris, leucocytoclastic vasculitis, lichen simplex chronicus, photocontact dermatitis, calcinosis cutis, squamous cell carcinoma *in situ*, granuloma annulare, necrobiosis lipoidica, urticaria accounts for (24%) were also seen in our study.

The skin, being the most visible and accessible organ of the body, functions as an important diagnostic window to the diseases affecting the internal organs including the renal system. Therefore, thorough clinical examination should be carried out to look for any dermatological markers of internal diseases for early detection and management of the disease.

CONCLUSION

The cutaneous manifestations of CKD are diverse. The commonest dermatological changes are nephrogenic pruritus, xerosis, pallor and acquired perforating dermatoses.

Specific dermatological manifestations such as half and half nails and perforating dermatoses are cutaneous markers of CKD that help in early diagnosis of the disease. Some of the

life threatening and disabling manifestations such as calcific uremic arteriolopathy was also observed while nephrogenic systemic fibrosis were not observed in our study.

The alleviation of nephrogenic pruritus improves quality of life in patients of CKD.

Skin is the mirror of internal diseases, as many systemic diseases such as CKD can be diagnosed by their dermatological manifestations. With the wider availability of haemodialysis centres, patients of CKD are surviving longer and exhibiting various dermatological manifestations. These cutaneous findings may be present before the diagnosis of CKD is made. Hence a dermatologist should undertake a detailed clinical examination and refer the patient to nephrologist to rule out CKD.

Due to constraints in the availability of dialysis and renal transplant facilities in developing countries like India, early diagnosis and management of CKD is of paramount importance. The dermatological manifestations cause significant distress to the patients and thus should be actively looked for in all CKD patients.

Dermatological changes help in the early diagnosis and treatment of the disease thereby preventing progression of CKD. The management of distressing dermatological disorders significantly improves the quality of life of these patients.

Fig. 1 Distribution of etiological factors of CKD patients.
DN-Diabetic Nephropathy
HTN-Hypertension
CGN-Chronic Glomerulonephritis
PKD-Polycystic Kidney Disease
CIN-Chronic Interstitial Nephritis

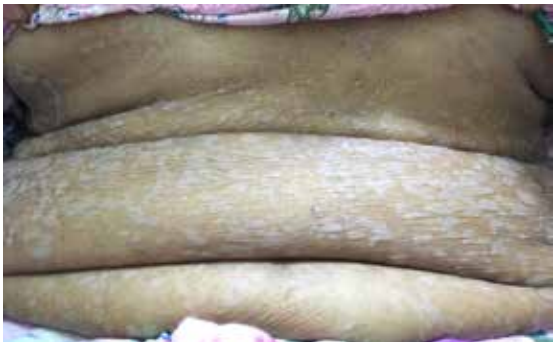

Fig. 2 A 65 year old female patient with Uremic frost.

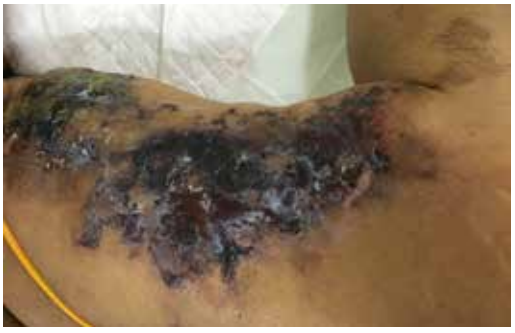

Fig. 3 A 45 year old female patient with calciphylaxisis.

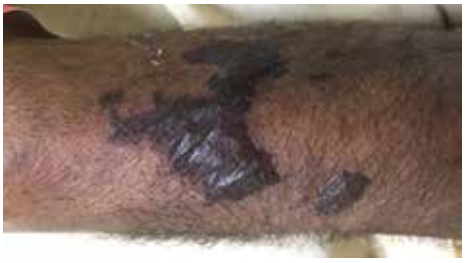

Fig. 4 A 57 year old male patient with Ecchymosis.

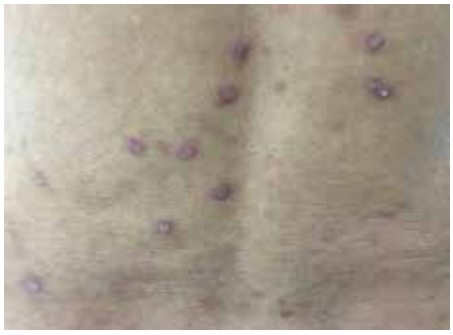

Fig. 5 A 54 year old male patient with Acquired Perforating Disorder.

Table 1 Distribution of skin changes in CKD patients

Skin Changes in CKD	No .of cases	Percentage
Pruritis	58	58.0%
Hyperpigmentation	16	16.0%
Xerosis	24	24.0%
Ecchymosis	11	11.0%
Infections And Infestations	14	14.0%
Acquired Perforating Disorder	8	8.0%
Others	24	24.0%

Table 2 Distribution of nail changes in CKD patients

NAIL CHANGES	No .of cases	Percentage
Half and Half nail	23	23.0%
Onychomycosis	12	12.0%
Koilonychia	6	6.0%
Sub-ungual hyperkeratosis	2	2.0%
Pallor	8	8.0%
Others	17	17.0%
Total	68	68.0%

Table 3 Distribution of hair changes in CKD patients

HAIR CHANGES	No .of cases	Percentage
Brittle Hair (BH)	4	4.0%
Diffuse Hair Loss (DHL)	14	14.0%
Sparse Scalp Hair (SSH)	4	4.0%
Lusterless Hair (LH)	2	2.0%
Total	24	24.0%

Table 4 Distribution of Mucosal changes in CKD patients

MUCOSAL CHANGES	No .of cases	Percentage
Pallor	27	27.0%
Apthous Stomatitis	9	9.0%
Xerostomia	2	2.0%
Other	4	4.0%
Total	42	42.0%

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