

## Original Research Article

# A clinico-epidemiological study of cutaneous changes in chronic kidney disease

Chirag Maheshwari<sup>1</sup>, Ajay Kumar<sup>2\*</sup>, Sanjeev Gupta<sup>1</sup>

<sup>1</sup>Department of Dermatology, MMIMSR, Mullana, Ambala, India

<sup>2</sup>Department of Dermatology, Dr D Y Patil Medical College, Pune, India

**Received:** 18 September 2016

**Accepted:** 14 October 2016

### \*Correspondence:

Dr. Ajay Kumar,

E-mail: [ajajkmathur@gmail.com](mailto:ajajkmathur@gmail.com)

**Copyright:** © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

## ABSTRACT

**Background:** Chronic kidney disease (CKD) has emerged as a major public health problem in South Asia. This is attributable to the increase in prevalence of co-morbidities particularly hypertension and diabetes mellitus. Cutaneous manifestations are observed throughout the course of the disease and serve as markers of the disease and its progression. Early diagnosis and treatment is critical in halting the progression of the disease. The objective was to study the prevalence of co-morbidities as well as cutaneous changes in patients with CKD from a rural or semi-urban background in a tertiary care hospital.

**Methods:** A total of 50 patients with CKD aged 18 years or above detected and managed at a tertiary care teaching hospital in North India were included in the study.

**Results:** The age of the patients ranged from 18 to 78 years. 35 patients (70%) had a rural background while 15 patients (30%) had a semi-urban background. 37 patients (74%) had co-morbidities including hypertension, diabetes mellitus or both. 17 patients (34%) were on conservative management while 33 patients (66%) were undergoing haemodialysis. Skin changes included nephrogenic pruritus in 30 patients (60%), xerosis in 25 patients (50%), cutaneous infections and infestations in 25 patients (50%), pallor in 22 patients (44%), acquired perforating disorders in 6 patients (12%), purpura in 5 patients (10%), hyperpigmentation in 4 patients (8%) and yellow skin in 1 patient (2%). Hair changes were observed in 20 patients (40%), nail changes in 24 patients (48%) and mucosal changes in 20 patients (40%). None of the patients were found to have bullous dermatoses, calcific uraemic arteriopathy or nephrogenic systemic fibrosis. 4 patients (8%) included in the study initially reported to dermatology OPD with a specific dermatosis and were detected to have CKD.

**Conclusions:** The prevalence of co-morbidities including hypertension and diabetes associated with CKD may be lower in rural and semi-urban populations. Nephrogenic pruritus is the most distressing change which impairs the quality of life in these patients. Cutaneous changes may help in early detection and treatment of CKD.

**Keywords:** Chronic kidney disease, Co-morbidities, Cutaneous markers

## INTRODUCTION

Changing lifestyles with economic resurgence of the Indian economy have led to an increase in the prevalence of non-communicable diseases particularly hypertension and type 2 diabetes.<sup>1</sup> Consequently there has been a significant increase in the prevalence of CKD. Cutaneous

changes are generally observed after the development of CKD but may be the presenting feature. CKD is associated with a wide range of dermatological manifestations. Studies on the prevalence of cutaneous changes in CKD in India have largely been urban population based studies.<sup>2-4</sup> The present study is a rural and semi-urban population based study.

**METHODS**

An observational cross-sectional study was carried out to evaluate the prevalence of various dermatological disorders in patients of CKD. Staging of CKD was carried out as per Kidney Disease Outcomes Quality Initiative (K/DOQI) guidelines.<sup>5</sup> Creatinine clearance was calculated using the Cockcroft-Gault equation. All patients of CKD in stages 1 to 5 on conservative treatment or on haemodialysis were included in the study. Patients who had undergone renal transplant were not included. The study was approved by the institutional ethics committee and written informed consent was obtained from all patients. A total of 50 patients were included in the study. Sequential sampling was carried out till the sample size was met.

**RESULTS**

The age of the patients ranged from 18 to 78 years the highest frequency being in the 40 to 49 years age group. There was a male preponderance, 38 patients (76%) being male and 12 (24%) female. 35 patients (70%) had a rural background while 15 patients (30%) had a semi-urban background as presented in Table 1. Co-morbidities were associated in 74% of patients and included hypertension in 22 patients, diabetes mellitus in 7 patients and both hypertension and diabetes mellitus in 8 patients as given in Table 2. While 17 patients (34%) were being managed conservatively 33 patients (66%) were undergoing haemodialysis as given in Table 3. Skin changes were observed in 94% of patients the commonest being nephrogenic pruritus as seen in Table 4. Hair changes including dry lusterless hair were observed in 40% of patients as in Table 5, nail changes including Lindsay’s nails in 48% of patients and mucosal changes including xerostomia in 40% of patients as given in Table 6 and 7.

A diagnosis of CKD was made in 4 patients (8%) when they presented in dermatology OPD with a specific dermatosis and were then referred to the nephrology unit for evaluation.

**Table 1: Sample characteristics.**

Age in years	Number of patients		Residence		Total
	Male	Female	Rural	Semi urban	
10 – 19	1	0	1	0	1
20 – 29	2	1	3	0	3
30 – 39	7	0	5	2	7
40 – 49	10	5	14	1	15
50 – 59	9	1	3	7	10
60 – 69	7	3	7	3	10
70 – 79	2	2	2	2	4
<b>Total</b>	<b>38</b>	<b>12</b>	<b>35</b>	<b>15</b>	<b>50</b>

**Table 2: Co-morbidities.**

Co-morbidity	Number of patients	Percentage
<b>Hypertension</b>	22	44
<b>Diabetes mellitus</b>	7	14
<b>Both</b>	8	16
<b>Neither</b>	13	26
<b>Total</b>	<b>50</b>	<b>100</b>

**Table 3: Treatment modalities.**

Modality	Number of patients	Percentage
<b>Conservative</b>	17	34
<b>Haemodialysis</b>	33	66
<b>Total</b>	<b>50</b>	<b>100</b>

**Table 4: Prevalence of skin changes.**

Cutaneous change	Number of patients	Percentage
<b>Pruritus</b>	30	60
<b>Xerosis</b>	25	50
<b>Infections &amp; infestations</b>	25	50
<b>Pallor</b>	22	44
<b>Perforating disorders</b>	6	12
<b>Purpura</b>	5	10
<b>Hyperpigmentation</b>	4	8
<b>Yellow skin</b>	1	2
<b>No change</b>	3	6

**Table 5: Prevalence of hair changes.**

Hair change	Number of patients	Percentage
<b>Sparse hair</b>	15	30
<b>Dry lusterless hair</b>	6	12
<b>No change</b>	30	60

**Table 6: Prevalence of nail changes.**

Nail change	Number of patients	Percentage
<b>Lindsay’s nails</b>	6	12
<b>Koilonychia</b>	5	10
<b>Onychomycosis</b>	4	8
<b>Beau’s lines</b>	3	6
<b>Subungual hyperkeratosis</b>	3	6
<b>Burnished nails</b>	3	6
<b>No change</b>	26	52

**Table 7: Prevalence of mucosal changes.**

Mucosal change	Number of patients	Percentage
<b>Xerostomia</b>	11	22
<b>Stomatitis</b>	4	8
<b>Oral thrush</b>	3	6
<b>Angular cheilitis</b>	2	4
<b>No change</b>	30	60

## DISCUSSION

The burden of CKD in South Asia is not known due to lack of registration and reporting of cases.<sup>6</sup> In an epidemiological study in Delhi and its surrounding areas the burden of CKD was found to be 13.3% as compared to a study near Shimoga, Karnataka in which the burden of CKD was found to be 16.54 % by the Cockcroft Gault (CG) equation.<sup>1,7</sup> Data from these CKD epidemiological studies however is unreliable due to the absence of equations validated for the South Asian population.<sup>1</sup>

In developing countries CKD primarily affects the young and the middle aged with limited access to renal replacement and hence the burden of the disease is considerable higher.<sup>6</sup> In the present study the age of the patients ranged between 18 and 78 years the highest prevalence being in the 40 to 49 years age group.

Prevalence studies on the cutaneous changes associated with CKD have been carried in various regions of India.<sup>2-4</sup> Most of these have been urban population based studies. We have carried out a rural and semi-urban population based prevalence study on cutaneous changes in CKD in patients mainly from the Saharanpur district of Uttar Pradesh in North India. In our study 70% of patients had a rural background while 30% had a semi-urban background. While 34% of patients were being managed conservatively, 66% of patients were receiving haemodialysis.

The increase in the burden of CKD in the Indian population has been attributed to the increase in the prevalence of co-morbidities such as hypertension and diabetes.<sup>1,7</sup> In a study by Deshmukh et al 91.42% of patients had co-morbidities including hypertension in 37.15% of patients, diabetes in 14.28% of patients and both diabetes and hypertension in 37.15% of patients.<sup>2</sup> In our study 74% of patients had co-morbidities that included hypertension in 44% of patients, diabetes in 7% of patients and both diabetes and hypertension in 8% of patients. The lower prevalence of co-morbidities in our study may be attributed to the rural and semi-urban background of the patients.

### *Nephrogenic pruritus*

Nephrogenic pruritus is perhaps the most distressing cutaneous manifestation of CKD. In our study pruritus

was the most common symptom and it was observed in 30 patients (60%). It was associated with excoriations, pigmentation, lichenification, prurigo nodularis or acquired perforating dermatosis in some patients. The prevalence of nephrogenic pruritus has ranged from 26.7 to 65.17% in various studies.<sup>2,4,8,9</sup> The factors implicated in the pathogenesis of nephrogenic pruritus include integumentary changes related to xerosis, chemical neurotransmitters including enkephalins, pentapeptide and serotonin, microinflammation with elevated Th 1 lymphocytes, divalent ions such as calcium and phosphorus, parathyroid hormone, opioid peptides and mast cell proliferation with elevated histamine.<sup>4,10-13</sup> Nephrogenic pruritus is refractory to treatment but may respond to emollients, topical calcineurin inhibitors, UVB phototherapy, gabapentin, the opioid antagonist naltrexone and parathyroidectomy. Renal replacement is the only definitive treatment of nephrogenic pruritus.

### *Xerosis*

Xerosis characterized by dry skin with scaling and a 'cracked porcelain appearance' is a commonly observed cutaneous change in patients of CKD particularly those on dialysis.<sup>10</sup> Xerosis was observed in 25 patients (50%) in our study. It has been attributed to increased transepidermal water loss (TEWL) and a functional abnormality of eccrine sweat glands.<sup>10</sup> The prevalence of xerosis has ranged from 52.8 to 80% in various studies.<sup>2,4,8,9</sup>

In the present study 25 patients (50%) had infections and infestations. Out of these patients 15 had fungal infections, 7 had furunculosis, 2 had carbuncles and 1 had scabies. The increased prevalence of infections and infestations in CKD may be attributed to impaired cellular immunity with decreased T-lymphocyte count.<sup>3,4</sup> The prevalence of infections and infestations has ranged from 17.14 to 40% in various studies.<sup>2-4</sup>

### *Pallor*

Pallor due to anaemia was observed in 22 patients (44%) in our study. Anaemia is attributable mainly to reduced erythropoietin production in CKD.<sup>2</sup> The prevalence of pallor has ranged from 45.45 to 68.57% in various studies.<sup>2-4,8</sup>

### *Acquired perforating dermatoses*

Acquired perforating dermatoses are characterized by dome shaped papules or nodules with central keratin plugs distributed mainly over the extensor aspects of extremities and trunk. In the present study perforating dermatoses were observed in 6 patients (12%). In some of the patients the dermatosis was associated with pruritus and exhibited the Koebner isomorphic response with development of new lesions at the site of trauma due to scratching as seen in Figure 1.

Perforating dermatoses represent a disturbance in the dermal-epidermal interface and exhibit the phenomenon of transepidermal elimination (TEE) of material that is extruded from the dermis through the epidermis. The prevalence of acquired perforating dermatoses in several studies ranged from 17.14 to 21%.<sup>2,3</sup>

### **Purpuric lesions**

Purpuric lesions were observed in 5 patients (10%) in our study. These lesions have been attributed to increased vascular fragility and abnormal platelet function in CKD. The use of heparin during dialysis also contributes to the defect in haemostasis.<sup>3</sup> Purpuric lesions in CKD have been reported in various studies.<sup>3,4</sup>

### **Hyperpigmentation**

Diffuse hyperpigmentation in sun exposed areas was observed in 4 patients (8%) in the present study. This is attributable to an increase in beta melanocyte stimulating hormone (beta MSH) due a failure to remove it by renal excretion or dialysis.<sup>2</sup> This results in an increase in the production of melanin in the basal layer of the epidermis.<sup>10</sup> The prevalence of hyperpigmentation has ranged from 10.1 to 43% in various studies.<sup>3,4,8</sup>

### **Yellowish skin**

Yellowish colour of the skin was observed in only one patient (2%) in our study. The yellowish tinge in the skin occurs due to the deposition of retained liposoluble pigments such as lipochromes and carotenoids in the dermis.<sup>10</sup> The prevalence of yellow skin has ranged from 10 to 17.7% in some studies.<sup>3,4</sup> The low prevalence of yellow skin in our study may be attributable to masking of yellow colour by the dark Indian complexion.<sup>3</sup>

### **Hair changes**

The hair changes that were observed in 20 patients (40%) included sparse scalp hair in 15 patients and dry lusterless hair in 6 patients. Dry lusterless hair is attributable to decreased sebum secretion.<sup>2</sup> The prevalence of hair changes may vary from 25.7 to 38% in different studies.<sup>2,8</sup>

### **Nail changes**

Nail changes were observed in 24 patients (48%) in our study and included half and half nails in 6 patients, koilonychia in 5 patients, onychomycosis in 4 patients, Beau's lines in 3 patients, subungual hyperkeratosis in 3 patients and burnished nails in 3 patients. Lindsay's nails or half and half nails as shown in Figure 2 are characterized by a white proximal band attributable to chronic anaemia and a distal brown portion due to melanin deposition resulting from increased beta MSH levels.<sup>10</sup> Pruritus is often accompanied by burnished or shiny nails as a result of friction due to scratching.<sup>13</sup> The

prevalence of nail changes in CKD may vary from 29.3 to 60% in different studies.<sup>2,8</sup>

### **Mucosal changes**

Mucosal changes in the oral mucosa were observed in 40% of patients in the present study and included xerostomia in 11 patients, stomatitis in 4 patients, oral candidiasis in 3 patients and angular stomatitis in 2 patients. The prevalence of xerostomia varied from 5.05 to 31% in various studies.<sup>3,4,8</sup> Stomatitis may be associated with predialysis urea levels above 150 mg per 100 ml. The prevalence of stomatitis has ranged from 29 to 43.4% in some studies.<sup>2,8</sup> Oral candidiasis was observed in 2 patients (4%) in our study. Uraemic foetor is an ammoniacal odour attributable to the breakdown of urea in saliva to ammonia. Though uraemic foetor has been reported in 8 to 16.7% patients in some studies<sup>[6, 8]</sup> we did not observe any patient with uraemic fetor in our study. The specific dermatoses of CKD that were not observed in the present study include bullous dermatoses, calcific uraemic arteriopathy and nephrogenic systemic fibrosis.

### **Bullous lesions**

Bullous lesions on the dorsa of hands and feet and sometimes on the face are common in patients of CKD on haemodialysis. These bullous lesions may either represent a sporadic form of porphyria cutanea tarda with raised uroporphyrin levels or pseudoporphyria triggered by drugs such as tetracycline or frusemide with normal uroporphyrin levels.<sup>10,11</sup> Bullous lesions were not observed in any patient in our study possibly because of the small sample size.

### **Calcific uraemic arteriopathy**

Calcific uraemic arteriopathy or calciphylaxis is a progressive cutaneous necrosis due to calcification of small and medium vessels in patients of CKD with secondary hyperparathyroidism. It is a life threatening condition that may present with an ascending acral gangrene or as a necrotic calcifying panniculitis.<sup>10,11</sup> We did not observe any case of calcific uraemic arteriopathy in our study.

### **Nephrogenic systemic fibrosis**

Nephrogenic systemic fibrosis is a disabling scleromyxoedema like condition characterized by indurated plaques mainly over the lower trunk and lower limbs with a peau d orange appearance attributable to the use of gadolinium based radiocontrast media in patients of CKD.<sup>10,11</sup> We did not observe any case of nephrogenic systemic fibrosis in our study.

Cutaneous changes may help in the early detection of CKD. An early diagnosis of CKD was made in 4 patients (8%) included in our study when they presented in

dermatology OPD with specific dermatoses including half and half nails and perforating dermatoses and were then referred to the nephrology unit for evaluation.



**Figure 1: Papules with central keratotic plugs on the back of a patient of CKD with acquired perforating dermatosis exhibiting the isomorphic response.**



**Figure 2: Half and half nails or Lindsay's nails with a proximal white band and a pigmented distal portion in a patient with CKD.**

## CONCLUSION

CKD predominantly affects the young and middle aged population the highest number of patients being in the 40 to 49 years age group. The lower prevalence of co-morbidities including diabetes and hypertension in our study may be attributable to the rural and semi-urban background of the patients. The cutaneous manifestations of CKD are diverse. The commonest dermatological changes are nephrogenic pruritus, xerosis, pallor and acquired perforating disorders. Specific dermatological manifestations such as half and nails and perforating dermatoses are cutaneous markers of CKD that help in the early diagnosis of the disease. Uncommon life

threatening and disabling manifestations such as calcific uraemic arteriopathy and nephrogenic systemic fibrosis were not observed in our study. The alleviation of nephrogenic pruritus improves the quality of life in patients with CKD.

*Funding: No funding sources*

*Conflict of interest: None declared*

*Ethical approval: The study was approved by the institutional ethics committee*

## REFERENCES

1. Singh NP, Ingle GK, Saini VK, Jami A, Beniwal P, Lal M, et al. Prevalence of low glomerular filtration rate, proteinuria and associated risk factors in North India using Cockcroft-Gault and Modification of Diet in Renal Disease equation: an observational, cross-sectional study. *BMC Nephrol.* 2009;10:4.
2. Deshmukh SP, Sharma YK, Dash K, Chaudhari NC, Deo KS. Clinicoepidemiological study of skin manifestations in patients of chronic renal failure on hemodialysis. *Indian Dermatol Online J.* 2013(1):18-21.
3. Udayakumar P, Balasubramanian S, Ramalingam KS, Lakshmi C, Srinivas CR, Mathew AC. Cutaneous manifestations in patients with chronic renal failure on hemodialysis. *Indian J Dermatol Venereol Leprol.* 2006;72(2):119-25.
4. Thomas EA, Pawar B, Thomas A. A prospective study of cutaneous abnormalities in patients with chronic kidney disease. *Indian J Nephrol.* 2012;22(2):116-20.
5. National Kidney Foundation. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification and stratification. *Am J Kidney Dis.* 2002;39:1-266.
6. Abraham G, Varughese S, Thandavan T, Iyengar A, Fernando E, Naqvi SAJ, et al. Chronic kidney disease hot spots in developing countries in South Asia. *Clin Kidney J.* 2016;9(1):135-41.
7. Anupama YJ, Uma G. Prevalence of chronic kidney disease among adults in a rural community in South India: Results from the kidney disease screening (KIDS) project. *Indian J Nephrol.* 2014;24(4):214-21.
8. Masmoudi A, Hajjaji Darouiche M, Ben Salah H, Ben Hmida M, Turki H. Cutaneous abnormalities in patients with end stage renal failure on chronic hemodialysis. A study of 458 patients. *J Dermatol Case Rep.* 2014;8(4):86-94.
9. Falodun O, Ogunbiyi A, Salako B, George AK. Skin changes in patients with chronic renal failure. *Saudi J Kidney Dis Transpl.* 2011;22(2):268-72.
10. Abdelbaqi-Salhab M, Shalhub S, Morgan MB. A current review of the cutaneous manifestations of renal disease. *J Cutan Pathol.* 2003;30(9):527-38.
11. Kuypers DR. Skin problems in chronic kidney disease. *Nat Clin Pract Nephrol.* 2009;5(3):157-70.

12. Pisoni RL, Wikstrom B, Elder SJ, Akizawa T, Asano Y, Keen ML, et al. Pruritus in haemodialysis patients: International results from the Dialysis Outcomes and Practice Patterns Study (DOPPS). *Nephrol Dial Transplant.* 2006;21(12):3495-505.
13. Yonova D. Pruritus in certain internal diseases. *Hippokratia.* 2007;11(2):67-71.

**Cite this article as:** Maheshwari C, Kumar A, Gupta S. A clinico-epidemiological study of cutaneous changes in chronic kidney disease. *Int J Res Dermatol* 2016;2:103-8.