Journal of Pakistan Association of Dermatologists. 2020; **30(3)**: 490-496.

Original Article

Cutaneous manifestations in patients with chronic kidney disease on hemodialysis

Shashikant Malkud, Veeresh Dyavannanavar*, Sirisha Varala

Department of Dermatology, Mahavir Institute of Medical Sciences, Vikarabad, Telangana, India.
* Department of Dermatology, Gadag Institute of Medical Sciences, Mallasamudra, Gadag Karnataka, India.
** Department of Dermatology, Osmania Medical College, Hyderabad, Telangana, India.

Abstract

Background Cutaneous manifestations are common among patients with chronic kidney disease (CKD).

Objective To assess the prevalence of various cutaneous manifestations in CKD patients on hemodialysis.

Materials and Methods Sixty patients with CKD of diverse etiology undergoing hemodialysis were examined for cutaneous changes.

Results Seventy five percent patients complained of skin problems. However, all patients on examination had at least one cutaneous manifestation attributed to CKD. Most common cutaneous finding was xerosis in 37 cases followed by pruritus in 35 cases, pallor in 28 cases, pigmentary changes in 14 cases, pedal edema in 12 cases, acquired perforating dermatoses in 3 cases, gynecomastia in 3 cases, purpura in 1 case, fungal infection in 23 cases, bacterial infection in 10 cases, and viral infection in 8 cases. Nail changes were noted in 42 cases, hair changes in 15 cases, and oral mucosal changes in 32 cases.

Conclusion Chronic kidney disease is associated with a complex array of cutaneous manifestations either due to disease or by hemodialysis. Early recognition of cutaneous signs can relieve suffering and decrease the morbidity.

Key words
Hemodialysis, pruritus, renal, xerosis.

Introduction

Chronic kidney disease is defined as the presence of kidney damage, manifested by abnormal albumin excretion or decreased kidney function that persists for more than three months.[1,2] The effects of CKD are complex and can lead to dysfunction of multiple organs including the skin.[3] It has been found that 50-100% patients with end stage renal disease have at least one associated cutaneous change.[4] These manifestations can be observed from the onset of the disease to the progression to the terminal stage and/ or after initiation of dialysis.[3] Recent advances in treatment of CKD have improved the quality of life and life expectancy of these patients resulting in change in frequency and types of disorders.[5] Patients on hemodialysis have a high prevalence of mucocutaneous changes because of several contributory factors including uremia, metabolic disorders, dialysis, and side effects of immunosuppressive drugs.[6]

Address for correspondence
Dr. Veeresh Dyavannanavar,
Associate professor, Department of Dermatology,
Gadag Institute of Medical Sciences, Mallasamudra,
Gadag–582103, Karnataka, India.
Ph: +91-7406238996
Email: drveeresh83@gmail.com

This study aimed to assess the prevalence of various dermatoses in patients with CKD undergoing hemodialysis.

Materials and Methods

This was a descriptive study conducted between May 2014 and May 2016. Sixty patients with CKD of diverse etiology undergoing hemodialysis were examined for cutaneous manifestations in a tertiary hospital. Informed consent was obtained from all study subjects. Patients undergoing hemodialysis following a renal failure or those who had undergone peritoneal dialysis were excluded from the study.

A detailed history including age, sex, underlying cause, duration of CKD, treatment history including dialysis, nature of onset and progression of skin lesions, past history of any skin disease and history of any associated comorbid conditions were recorded. Detailed cutaneous examination was done in all patients which includes morphology, site and distribution of skin lesions, nail changes and mucosal changes. Routine blood investigations for monitoring renal functions were recorded. Specific investigations like skin biopsy, Gram's stain, bacterial culture, potassium hydroxide mount and fungal culture were done wherever indicated.

Results

The total 60 patients were included in the study of which 34 were male and 26 were female. The age of the patients ranged from 16 to 72 years. Most of the patients were in the age group of 61-70 years **(Table 1)**.

Diabetic nephropathy was the most common cause of CKD. Other causes of CKD in the study group are mentioned in **Table 2**.

Table 1 Age and sex distribution of study subjects

Age in years	*No. of patients*	*Male*	*Female*
1-10	0	0	0
11-20	1	1	0
21-30	3	2	1
31-40	4	2	2
41-50	15	6	9
51-60	13	9	4
61-70	17	10	7
71-80	7	4	3
Total	60	34	26

Table 2 Etiology of chronic kidney disease in the study subjects

Sr#	*Etiology chronic kidney disease*	*No. of patients*
1	Diabetic nephropathy	28 (46.6%)
2	Chronic tubulointerstitial nephritis	10 (16.6%)
3	Chronic glomerulonephritis	9 (15%)
4	Nephrotic syndrome	4 (6.6%)
5	Hypertensive nephrosclerosis	3 (5%)
6	IgA nephropathy	2 (3.3%)
7	Lupus nephritis	2 (3.3%)
8	Autosomal dominant polycystic kidney disease	1 (1.6%)
9	Ischemic renal failure	1 (1.6%)

Various cutaneous changes, nail changes, hair changes and mucosal changes in the study subjects are shown in **Table 3**.

Discussion

About 50-100% of the patients with CKD presents with at least one skin lesion. These clinical manifestations can precede or follow the initiation of dialysis. Sometimes this may be the first clinical sign of kidney disease.[3] Various specific and nonspecific cutaneous and mucosal changes are associated with renal disease. Specific manifestations include acquired perforating dermatoses, bullous dermatoses, metastatic calcification, and nephrogenic systemic fibrosis. Nonspecific manifestations include xerosis, pruritus, pallor, pigmentary changes etc.[5]

Total 60 patients with CKD on hemodialysis were included in the study. Forty five patients

Table 3 Various cutaneous manifestations in the study group

Clinical mani-festations		*No. of patients*
Skin changes	Xerosis	37
	Pruritus	35
	Pallor	28
	Pigmentary changes	14
	Acquired perforating dermatosis	3
	Gynecomastia	3
	Purpura and ecchymosis	1
	Bacterial infection	10
	Fungal infection	23
	Viral infection	8
Nail changes	Koilonychia	14
	Half and half nail	8
	Nail dystrophy	6
	Onycholysis	6
	Subungual hyperkeratosis	6
	Beau's lines	5
	Leukonychia	3
	Pitting	2
	Clubbing	2
	Splinter hemorrhage	2
Oral mucosal changes	Glossitis	10
	Chelitis	7
	Pigmentation of oral mucosa	8
	Xerostomia	6
	Macroglossia	1
Hair changes	Dry lusterless hair	10
	Sparse body hair	4
	Diffuse alopecia	3

(75%) had some skin problem. However, all patients on clinical examination had at least one cutaneous manifestation attributable to CKD. Most of the patients were in the age group of 61-70 years. Male patients outnumbered female patients with male to female ratio of 1.3:1. This finding is in concordance with Udayakumar *et al.*[7] and Thomas *et al.*[5] study.

Diabetic nephropathy was the most common cause (46.9%) of CKD in our study followed by chronic tubulointerstitial nephritis (16.6%) and chronic glomerulonephritis (15%). Thomas *et al.* in his study noted diabetic nephropathy was the most common cause (42.2%).[5]

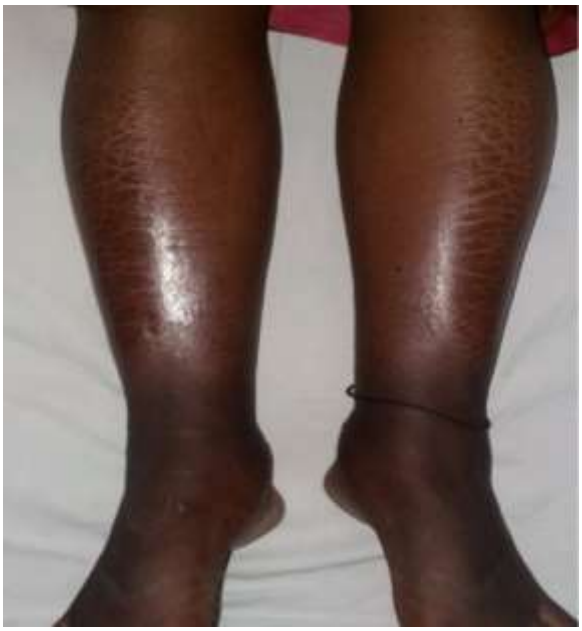

Figure 1 Patient with xerosis of skin

Xerosis

Xerosis of skin was the most common cutaneous finding noted in our study **(Figure 1)**. It has been reported to affect 50-85% of patients on maintenance dialysis.[8,9] Out of 37(61.7%) patients, generalized xerosis was seen in 27 patients and localized xerosis in 10 patients. Reduced sweat, elevated plasma vitamin A, alkalinity of skin, use of diuretics and malnutrition are the causes of xerosis in CKD patients.[10] Bencini *et al.* noted significant increased incidence of xerosis in patients with hemodialysis.[11] Incidence of xerosis in various study ranged from 66% to 86%.[5,10,12,13,14]

Pruritus

Out of 60 patients, 35(58.3%) patients were having pruritus. It was the second most common cutaneous finding observed in our patients. Most of the patients had generalized pruritus and only 8 patients had localized pruritus. Fifteen patients with xerosis had associated pruritus. Deshmuk *et*

al.[10] noted pruritus in 65.7% of patients whereas Falodun *et al.*[15] noted in 26.7% of patients. Masmoudi *et al.* noted 63% of patients with pruritus had xerosis.[4]

Pallor

Pallor of the skin is due to anemia which is a hallmark of CKD.[7] It was observed in 46.6% patients. Patient's hemoglobin level ranged from 6-11gm/ dl. Deficient erythropoietin production, dietary deficiency of iron, folic acid and vitamin B12, and hypo responsiveness to the actions of erythropoietin may contribute to anemia.[16] Hemoglobin level was less than 8gm/dl in 48% of cases as compared to 64% in Udayakumar *et al.*[10] study. This difference in finding may be due to large number of darker complexion patients in our study.

Pigmentary changes

Pigmentary changes were noticed in 14(23.3%) patients. Diffuse hyperpigmentation over sun exposed area was observed in 12(20%) patients. This finding is almost consistent with Pico *et al.* study (22%).[20] In Udayakumar *et al.* study, diffuse hyperpigmentation was noted in 43% of patients and prominent pigmentation over sun exposed areas in 26% of patients.[7] Diffuse hyperpigmentation of skin is attributed to an increase melanin in basal layer of epidermis and superficial dermis due to failure of kidney to excrete beta-melanocyte-stimulating hormone.[17]

In our study yellowish tinge to the skin was noted in 2(3.3%) patients whereas Udaykumar *et al.*[7] noted in 10% of their patients. It is due to accumulation of carotenoids and nitrogenous pigments (urochromes) in the dermis and subcutaneous tissue.[18,19] Low prevalence of this finding may be due to darker complexion of the patients in our study.

Acquired perforating dermatoses

Three patients (5%) of CKD had developed Kyrle's disease. Clinical diagnosis was confirmed by histopathology. All of them had pruritic keratotic papules with central keratin filled crater mainly on the extensor aspect of extremities and trunk. Trauma from scratching acts as a major trigger for the development of APD. All 3 patients had severe generalized pruritus which might have served as a triggering factor for APD. In our study all 3 patients with APD had type 2 diabetes mellitus. Non-insulin dependent diabetes mellitus was the most common associated finding observed by Kim *et al.*[21] Morton *et al.* also reported an increased association of diabetes in chronic renal failure patients with APD.[22] Dermal microvasculopathy related to diabetes is a predisposing factor for APD. It induces a hypoxic state in which the trauma from scratching causes dermal necrosis.[23] Acquired perforating dermatoses were reported in 17.4% cases in Deshmukh *et al.*[10] study, 21% cases in Udayakumar *et al.*[7] study and 5.2% cases in Masmoudi *et al.*[4] study.

Gynecomastia

Pituitary gland and gonadal function remain suppressed as a consequence of CKD and associated malnutrition. Following hemodialysis and resumption of an adequate diet, there will be increase excretion of gonadotrophin and estrogen hormones. This may lead to transient gynecomastia.[24] In our study gynecomastia was noted in 3(5%) patients whereas Udayakumar *et al.* noted in 1% of their patients.[7]

Purpura

Defects in primary hemostasis like increased vascular fragility, abnormal platelet function and use of heparin during dialysis are the main cause of abnormal bleeding in CKD patients.[25] In our

study purpura was noticed in 1 patient. Udayakumar *et al.* and Sanad *et al.* noticed it in 9% and 32% of their cases respectively.[7,14]

Cutaneous infection

Skin infections occur more often among patients with CKD.[26] It is due to depressed neutrophil function, impaired phagocytosis, decreased T and B lymphocyte function and reduced natural killer cell activity.[27] Deshmukh *et al.*[10] and Udayakumar *et al.*[7] reported cutaneous infection in 34.2% and 40% of cases respectively. In 32(53.3%) patients 41 cutaneous infections were noted; of which fungal infection 23, bacterial infection 10 and viral 8. High incidence of fungal infection may be due to low socio-economic status and hot humid climate in our part of country. Bencini *et al.* reported incidence of fungal infection in 67% patients with CKD undergoing hemodialysis.[11]

Nail changes

Nail changes were noted in 42(70%) patients. More than one nail change was observed in 12 patients. Masmoudi *et al.*,[4] Deshmuk *et al.*,[10] Martinez *et al.*,[28] and Al-Hamamy *et al.*[29] noted nail changes in 29.3%, 60%, 86% and 78.9% cases respectively. The most common nail finding was koilonychia (23.3%) followed by half and half nail (13.3%), nail dystrophy (10%), onycholysis (10%), and subungual hyperkeratosis (10%). Other nail changes observed were Beau's line (8.3%), leukonychia (5%), pitting (3.3%), clubbing (3.3%), and splinter hemorrhage (3.3%).

In present study half and half nail was observed in 13.3% patients. It was the most common nail change (21%) in Udayakumar *et al.* study.[7] Increased nail bed capillary density and stimulation of nail melanocytes by increased levels of plasma melanotrophic hormone are proposed etiology for band like discoloration.[29]

Temporary cessation of nail growth in the matrix due to illness results in the formation of Beau's lines.[30] It was observed in 5% cases in our study. Udayakumar *et al.* and Ozturk *et al.* noted Beau's line in 2% and 7.3% of cases respectively.[7,31]

Pitting and onycholysis were noted in 3% and 10% of cases respectively. Ozturk *et al.* noted pitting in 22% cases.[31] Sanad *et al.* reported onycholysis in 10% of cases.[14]

Hair changes

Hair changes were observed in 15(25%) patients. Deshmukh *et al.*[10] and Masmoudi *et al.*[4] reported hair changes in 25.71% and 38% patients respectively. Hair changes noted in our study were dry lusterless hair in 10(16.6%) patients, sparse body hair in 4(6.6%) patients and diffuse hair loss in 3(5%) patients. More than one hair change was observed in 2 patients. Dry and lusterless hair is due to decreased secretion of sebum.[7] In Udayakumar *et al.* study, sparse body hair was observed in 30% cases, dry lusterless hair in 16% cases and diffuse alopecia of scalp in 11% cases.[7]

Oral mucosal changes

Oral mucosal changes were noted in 32(53.3%) patients. Masmoudi *et al.* noted oral mucosal changes in 13.1% cases.[4] Glossitis was the most common finding observed (16.6%) followed by cheilitis (11.6%), pigmentation of oral mucosa (13.3%) **(Figure 2)**, xerostomia 6(10%), and macroglossia 1(1.6%). Occurrence of glossitis and cheilitis may be attributed to nutritional deficiencies like riboflavin deficiency, iron deficiency anemia and zinc deficiency.

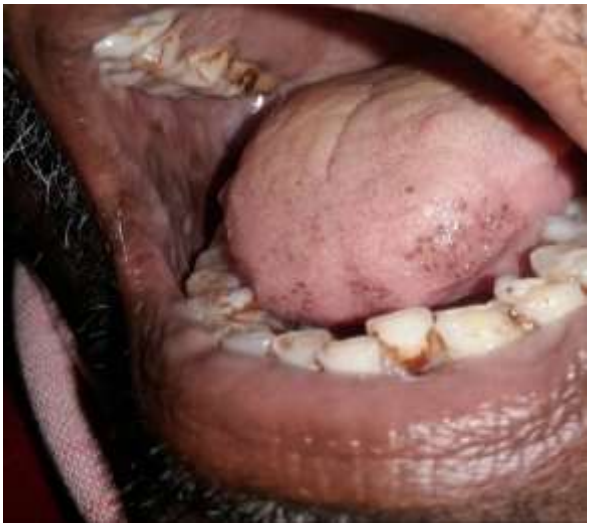

Figure 2 Patient with oral mucosal pigmentation

In 1986 Mathew *et al.* first reported teeth indentation with macroglossia in 92% patients with CKD.[32] Udayakumar *et al.* and Sanad *et al.* reported macroglossia in 35% and 43% cases respectively.[7,14] More effective treatment of CKD in recent years might have contributed to the decrease in prevalence of macroglossia among the patients compared to the past.

Xerostomia in CKD patients may be due to dehydration and mouth breathing.

We had noticed xerostomia in 6(10%) patients. Sanad *et al.*[14] and Udayakumar *et al.*[7] noticed xerostomia in 46% and 31% of cases respectively.

Patients with CKD presents with an array of cutaneous manifestations. Newer changes are being described since the advent of hemodialysis which prolongs the life expectancy. Many of the skin problems are benign and do not affect the course of CKD. However some of them may suggest the presence of serious systemic disorder in the patient. An interdisciplinary management involving dermatologists and nephrologists are essential to acquire better outcome and to improve the quality of life of patients.

Conclusion

Cutaneous manifestations are common in CKD patients. Patients presenting with these symptoms should be suspected to have derangements in their renal function and need to be evaluated.

References

1. KDOQI clinical practice guidelines and clinical practice recommendations for anemia in chronic kidney disease. *Am J Kidney Dis* 2006;**47**:S11–S145.
2. Levey AS, Eckardt KU, Tsukamoto Y, Levin A, Coresh J, Rossert J *et al.* Definition and classification of chronic kidney disease: a position statement from Kidney Disease: Improving Global Outcomes (KDIGO). *Kidney Int* 2005;**67**:2089–100.
3. Lupi O, Rezende L, Zangrando M, Sessim M, Silveira CB, Sepulcri A *et al.* Cutaneous manifestations in end-stage renal disease. *An Bras Dermatol* 2011;**86**:319-26.
4. 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**:86-94.
5. Thomas EA, Pawar B, Thomas A. A prospective study of cutaneous abnormalities in patients with chronic kidney disease. *Indian J Nephrol* 2012;**22**:116-20.
6. Hajheydari Z, Makhlough A. Cutaneous and mucosal manifestations in patients on maintenance hemodialysis: a study of 101 patients in Sari, Iran. *Iran J Kidney Dis* 2008;**2**:86-90.
7. 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**:119-25.
8. Markova A, Lester J, Wang J, Robinson-Bostom L. Diagnosis of common dermopathies in dialysis patients: A review and update. *Semin Dial* 2012;**25**:408–18.
9. Szepietowski J, Balaskas E, Taube K, Taberly A, Dupuy P. Quality of life in

patients with uraemicxerosis and pruritis. *Acta Derm Venereol*. 2011;**91(3)**:313–7.
10. 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;**4**:18-21.
11. Bencini PL, Montagnino G, Citterio A, Graziani G, Crosti C, Ponticelli C. Cutaneous abnormalities in uremic patients. *Nephron* 1985;**40**:316-21.
12. Mourad B, Hegab D, Okasha K, Rizk S. Prospective study on prevalence of dermatological changes in patients under hemodialysis in hemodialysis units in Tanta University hospitals, Egypt. *Clin Cosmet Investig Dermatol* 2014;**7**:313-19.
13. Tajbakhsh R, Dehghan M, Azarhoosh R, Haghighi AN, Sadani S, Zadeh SS *et al.* Mucocutaneous manifestations and nail changes in patients with end-stage renal disease on hemodialysis. *Saudi J Kidney Dis Transpl* 2013;**24**:36-40.
14. Sanad EM, Sorour NE, Saudi WM, Elmasry AM. Prevalence of cutaneous manifestations in chronic renal failure patients on regular hemodialysis: a hospital-based study. *Egypt J Dermatol Venerol* 2014;**34**:27-35.
15. Falodun O, Ogunbiyi A, Salako B, George AK. Skin changes in patients with chronic renal failure. *Saudi J Kidney Dis Transpl* 2011;**22**:268-72.
16. Mehdi U, Toto RD. Anemia, diabetes, and chronic kidney disease. *Diabetes Care* 2009;**32**:1320-26.
17. Smith AG, Shuster S, Thody AJ, Alvarez-Ude F, Kerr DN. Role of the kidney in regulating plasma immunoreactive beta-melanocyte stimulating hormone. *Br Med J* 1976;**1**:874-6.
18. Sultan MM, Mansour HH, Wahby IM, Houdery AS. Cutaneous manifestations in egyptians patients with chronic renal failure on regular hemodialysis. *J Egypt Women Dermatol Soc* 2010;7:**49**-55.
19. Comaish JS. Ashcroft T, Kerr DN. The pigmentation of chronic renal failure. *J Am Acad Dermatol* 1975;**55**:215-17.
20. Picó MR, Lugo-Somolinos A, Sánchez JL, Burgos-Calderón R. Cutaneous alterations in patients with chronic renal failure. *Int J Dermatol* 1992;**31**:860-3.
21. Kim SW, Kim MS, Lee JH, Son SJ, Park KY, Li K *et al.* A clinicopathologic study of thirty cases of acquired perforating dermatosis in Korea. *Ann Dermatol* 2014;**26**:162-71.
22. Morton CA, Henderson IS, Jones MC, Lowe JG. Acquired perforating dermatosis in a British dialysis population. *Br J Dermatol* 1996;**135**:671-7.
23. Hong SB, Park JH, Ihm CG, Kim NI. Acquired perforating dermatosis in patients with chronic renal failure and diabetes mellitus. *J Korean Med Sci* 2004;**19**:283-8.
24. Lindsay RM, Briggs JD, Luke RG, Boyle IT, Kennedy AC. Gynecomastia in chronic renal failure. *Br Med J* 1967;**4**:779-80.
25. Remuzzi G. Bleeding in renal failure. *Lancet* 1988;**28**:1205-8.
26. Avermaete A, Altmeyer P, Bacharach-Buhles M. Skin changes in dialysis patients: a review. *Nephrol Dial Transplant* 2001;**16**:2293-6.
27. Gagnon AL, Desai T. Dermatological diseases in patients with chronic kidney disease. *J Nephropathol* 2013;**2**:104-109.
28. Martinez MA, Gregório CL, Santos VP, Bérgamo RR, Machado Filho CD. Nail disorders in patients with chronic renal failure undergoing hemodialysis. *An Bras Dermatol* 2010;85:**318**-23.
29. Al-Hamamy HR, Al-Mashhadani SA, Fadheel BM , Salman SH. Nail changes in hemodialysis patients and renal transplant recipients: a case-control study. *Am J Dermatol Venereol* 2014;**3**:30-4.
30. Singh G. Nails in systemic disease. *Indian J Dermatol Venereol Leprol* 2011;77:646-651.
31. Ozturka P, Ozyurta K, Kurutasb E, Kalenderc M, Atasevend A, Dogane E. Nail disorders in patients with chronic renal failure undergoing peritoneal dialysis. *World J Nephrol Urol* 2014;**3**:30-4.
32. Mathew MT, Rajarathnam K, Rajalaxmi PC, Jose L. The tongue sign of CRF: Further clinical and histopathological features of this new clinical sign of chronic renal failure. *J Assoc Phy Ind* 1986;**34**:52.