Original Research Article

DOI: https://dx.doi.org/10.18203/issn.2455-4529.IntJResDermatol20205601

Muco-cutaneous manifestations of chronic kidney disease with or without hemodialysis

Titiksha Hans¹, Devendra Kumar², Soumya Agarwal^{1*}, Aliza Shoeb Zaidi¹, Swosti Mohanty¹, Aditi Wadhwa¹

¹Department of Dermatology, ²Department of Medicine, Era's Lucknow Medical College, Lucknow, U. P., India

Received: 07 November 2020 Revised: 14 December 2020 Accepted: 15 December 2020

*Correspondence: Dr. Soumya Agarwal,

E-mail: scorpsoumya@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: Mucocutaneous manifestations significantly impair the quality of life of patients with chronic kidney disease (CKD) but are usually understudied. Our objective was to study the patterns and prevalence of mucocutaneous and nail involvement in CKD patients and to compare those in patients with or without haemodialysis.

Methods: Ninety patients aged 18-80 years having CKD (M: F=1.64:1) since mean duration of 4.43 ± 9.9 months were studied in an observational cross-sectional study. Sixty-two (68.9%) patients were on hemodialysis since 42.64 ± 63.14 months. Detailed history and examination, and relevant investigations like KOH mount, skin biopsy, gram stain and culture were done when required. Data was analyzed using SPSS version 21 software. Relevant tests were applied, p<0.05 was considered statistically significant.

Results: Xerosis in 43 (47.7%), pruritus in 26 (28.9%), ichthyosis in 11 (12.2%), and skin pallor in 7 (7.8%) patients were major dermatoses. Xerosis was more commonly found in patients on haemodialysis (37.8%) as compared to those without dialysis (9.9%) (p-0.046). Bullous lesions, perforating folliculitis and foot ulcers occurred in 1 (1.1%) patient each. Common nail abnormalities were longitudinal ridging (21.1%), leukonychia (13.3%), Lindsay's half-and-half nails (4.4%) and dystrophic nails (4.4%). Mucosal manifestations were coated tongue (2.2%%), angular cheilitis (2.2%), and pigmented tongue (1.1%).

Conclusions: Xerosis, pruritus, ichthyosis skin pallor, longitudinal ridging, leukonychia, coated tongue, and angular cheilitis were the common mucocutaneous manifestations in our study. Early recognition and management of these dermatoses plays a crucial role in a holistic patient treatment, reduce disease morbidity and improve their quality of lives.

Keywords: Chronic kidney disease, Haemodialysis, End stage renal disease, Cutaneous manifestations

INTRODUCTION

Chronic kidney disease (CKD) is defined as an irreversible deterioration in renal function classically developing over years and is defined as kidney damage or glomerular filtration rate $<60~\text{ml/min/1.73}~\text{m}^2$ for 3 months or more irrespective of the cause. It typically progresses through five stages, and culminates in end-

stage renal disease (ESRD) in most of the patients. The prevalence of CKD continues to rise, owing to an increase in the number of patients with diabetes and hypertension and an elderly population. The estimated age-adjusted incidence rate of ESRD is 229 per million population, whereas more than 100,000 new patients enter renal replacement programs annually in India.² Mucocutaneous manifestations of renal failure are

predominantly related to chronicity of the disease and have a high prevalence among dialysis patients. Approximately 96% patients of CKD present with at least one mucocutaneous manifestation.³

The patients present with an array of cutaneous manifestations including xerosis, pruritis, pigmentation, bullous lesions, perforating disorders, nephrogenic systemic fibrosis, nail changes etc. The various factors responsible for the skin changes are uraemia, metabolic disorders, dialysis and side effect of immunosuppressive drugs.4 Cutaneous involvement increases the morbidity of patients and affects their quality of life quite adversely. There is a paucity of data on the mucocutaneous involvement and changes in nails and hair of patients with CKD especially from this part of the world. Therefore, we conducted an observational study on patients of CKD to identify and compare the cutaneous manifestations including changes in mucous membranes, and nails between patients on haemodialysis and those who are not on haemodialysis.

METHODS

We conducted an observational cross-sectional study on 95 patients of CKD attending the medicine OPD or admitted in medicine IPD of Era's Lucknow Medical College and Hospital, Lucknow from February 2019 to 2020. We included all patients of chronic kidney disease stage 3, 4 and 5 with or without haemodialysis. The exclusion criteria were patients with acute renal failure, patients with human immunodeficiency virus (HIV), renal transplant recipients, hepatobiliary, pancreatic or thyroid disorders, cutaneous or systemic malignancies/infections, patients on immunosuppressive drugs, iv) pre-existing chronic dermatosis (e.g., lichen planus, psoriasis), those who do not give a written informed consent. Out of 95 patients, 3 patients suffered from other significant illnesses (two had hypothyroidism, and one had psoriasis) and 2 patients had acute renal failure. Hence, a total of 90 patients completed the study. After getting a written informed consent from the patient, the staging of CKD was done by using National kidney foundation criteria by measuring e GFR (Table 1). **Patients** were examined mucocutaneous for manifestations as well as nail changes using magnifying hand lens, and relevant investigations like KOH mount, skin biopsy, gram stain and culture were done when required to make a final diagnosis. Ethical clearance was obtained from the Institutional Ethical Committee.

Data was analyzed using SPSS (statistical package for the social sciences) version 21 software (Company: IBM Corporation, Armonk, New York, USA). The results were summarized in the form of mean ±SD for quantitative values and percentages for qualitative values. Chi square, student t-test, ANOVA and other appropriate tests were applied for comparison, and p<0.05 was considered to be statistically significant.

Table 1: Staging of CKD (national kidney foundation criteria).

Staging of CKD	Definition
Stage 1	Normal estimated glomerular filtration rate (e GFR) ≥90 ml/min per 1.73 m ² and persistent albuminuria
Stage 2	e GFR between 60 and 89 ml/min per 1.73 m ²
Stage 3	e GFR between 30 and 59 ml/min per 1.73 m ²
Stage 4	e GFR between 15 and 29 ml/min per 1.73 m ²
Stage 5	e GFR between <15 ml/min per1.73 m ² or end-stage renal disease

CKD - Chronic kidney disease; e GFR- estimated calculated creatinine clearance (e Ccr) is used as a correlate od GFR and calculated as: eCcr = (140 age) X (weight in kilograms) X (0.85 if female)/72 *serum creatinine in mg/dl.

RESULTS

Out of a total of 90 patients of CKD, 62 (68.9%) patients were on hemodialysis, and the rest 28 (31.1%) were not receiving hemodialysis. The age of the patients ranged from 18 to 80 years, and the mean age of patients with and without dialysis was 47.1±16.38 years and 52.89±13.93 years respectively. There were 56 (62.2%) males and 34 (37.8%) females in our study (M: F=1.64:1) (Table 2).

Table 2: Demographic profile of patients.

Profile of patients	Patients on haemodialysis	Patients not on haemodialysis	P value
Mean age (years)	47.1±16.38	52.89±13.93	0.108
Sex			
Males n (%)	39 (43.3%)	17 (18.9%)	0.83
Females n (%)	23 (25.5%)	11 (12.2%)	
Mean GFR (ml/min per 1.73 m²)	10.75±10.96	17.18±9.21	0.008
Mean duration of disease			

The mean duration of disease was 4.43±9.9 months. The most common etiology of CKD was hypertension (65.5%) and diabetes mellitus (44.4%), followed by idiopathic (15.5%), chronic glomerulonephritis (5.5%), polycystic kidney disease (4.4%) and gouty nephropathy in 2.2% patients in that order. The mean GFR of patients on hemodialysis was significantly lower than those

without hemodialysis $(10.75\pm10.96 \text{ vs } 17.18\pm9.21 \text{ respectively})$ (p-0.008). A total of 64 (71.1%) patients suffered from ESRD (e GFR \leq 15 ml/min per1.73 m²), and 53 (58.9%) of them were receiving haemodialysis. This was significantly higher when compared to the remaining 26 (28.9%) patients belonging to stages 1 to 4 of CKD, out of which only 9 (10%) were on haemodialysis (p<0.001). The mean duration of hemodialysis was 42.64 ± 63.14 months.



Figure 1: Xerosis of lower legs.

The most common cutaneous finding was xerosis, present in 43 (47.8%) patients, out of which 34 (37.8%) patients were on dialysis (Figure 1).



Figure 2: Acquired ichthyosis over legs.

The presence of xerosis was more common in patients on haemodialysis and the difference was statistically significant (p-0.046). Twenty-six (28.9%) patients experienced uremic pruritis out of which 20 (22.2%) patients were on dialysis. Ichthyosis was seen in 11 (12.2%) patients out of which 7 (7.8%) were on dialysis (Figure 2). Skin pallor was seen in 7 (7.8%) patients who were on dialysis. Perforating folliculitis, bullous lesions (Figure 3), and foot ulcers were present in 1 (1.1%) patient each in patients on haemodialysis (Table 3). Mucous membrane involvement was seen in 5 (5.5%) patients on haemodialysis in the form of coated tongue and angular cheilitis in 2 (2.2%) patients each (Figure 4), and pigmented tongue in 1 (1.1%) patient.

Table 3: Mucocutaneous manifestations in patients with CKD.

Manifestations	On haemodialysis (n=62) N (%)	Not on haemodialysis (n=28) N (%)	Total (n=90) N (%)	P value
Cutaneous manifestations				
Xerosis	34 (79.1)	9 (20.9)	43 (47.7)	0.046
Uremic pruritus	20 (76.1)	6 (21.4)	26 (28.9)	0.294
Ichthyosis	7 (63.6)	4 (36.4)	11 (12.2)	0.688
Skin pallor	7 (100)	0 (0)	7 (7.8)	0.066
Bullous lesions	1 (100)	0 (0)	1 (1.1)	1.0
Perforating folliculitis	1 (100)	0 (0)	1 (1.1)	0.689
Foot ulcer	1 (100)	0 (0)	1 (1.1)	0.689
Lentigo	0 (0)	1 (100)	1 (1.1)	0.311
Mucosal manifestations				
Coated tongue	2 (100)	0 (0)	2 (2.2)	1.0
Angular cheilitis	2 (100)	0 (0)	2 (2.2)	1.0
Pigmented tongue	1 (100)	0 (0)	2 (1.1)	1.0
Nail changes				
Longitudinal ridging	16 (84.2)	3 (15.8)	19 (21.1)	0.162
Leukonychia	10 (83.3)	2 (16.7)	12 (13.3)	0.328
Lindsay's half and half nail	2 (50)	2 (50)	4 (4.4)	0.162
Dystrophic nails	3 (75)	1 (25)	4 (4.4)	1.0
Onycholysis	1 (50)	1 (50)	2 (2.2)	0.528



Figure 3: Bullous lesions on foot.



Figure 4: Coated tongue.



Figure 5: Leukonychia.

Longitudinal ridging was present in nails of 19 (21.1%) patients out of which 16 (17.8%) patients were on dialysis. Twelve (13.3%) patients presented with

leukonychia out of which 10 (11.1%) patients were on dialysis (Figure 5). Lindsay's half and half nails were recorded in 4 (4.4%) patients out of which 2 (2.2%) patients were on dialysis (Figure 6). Dystrophic nails were seen in 3 (3.3%) patients with dialysis and 1 (1.1%) patient without dialysis. Onycholysis was seen in a total of 2 (2.2%) patients, one each om dialysis and without dialysis.



Figure 6: Lindsay's half and half nails.

DISCUSSION

Xerosis was the most common cutaneous manifestation seen in 43 (47.8%) of our patients, and ichthyosis was noticed in 11 (12.2%) patients. Xerosis mainly involved lower legs, thighs and forearms. Patients on haemodialysis were significantly more affected. Xerosis is a well-documented manifestation in 23-90% patients irrespective of dialysis status, and can present with a variable severity.^{3,5-7} Skin dehydration, hypervitaminosis A, diuretics, decreased excretion of sebum/sweat, altered skin barrier, have been primarily implicated for severity of xerosis while certain external factors (sun, dust, detergents) can cause irritation and aggravate the condition. 3,8,9-11 Excessive ultrafiltration, low emollient usage, and less hydration of stratum corneum might be responsible for more significant xerosis in patients on dialysis compared to those without dialysis. All patients responded well to regular emollient application.

Pruritus was mild to severe in 26 (28.9%) patients, but there was no significant difference among patients with or without hemodialysis. Pruritus of variable intensity is seen in a large proportion of patients with ESRD, it may be episodic or continuous, and generalized or localized. Hemodialysis may or may not improve uraemic pruritus and occurs in 15-49% during predialysis and in 19-90% hemodialysis patients.^{3,12-14}. The pathogenesis of pruritus in renal failure still remains unclear but xerosis and ichthyosis may aggravate pruritus.³ Other possible factors include secondary hyperparathyroidism, mast cell proliferation and degranulation, pruritogenic cytokines,

deranges in divalent ion metabolism and abnormal pattern of cutaneous innervations. ¹⁵ It is likely that pruritus results from slowly accumulated or deposited pruritogens, the nature of which is uncertain. Increased serum histamine levels may be due to allergic sensitization to various dialyzer membrane components and due to impaired renal excretion of histamine. ¹⁴ Secondary skin lesions including chronic prurigo excoriations, or acquired perforating dermatosis may also follow long standing uremic pruritus.

We documented skin pallor in 7 (7.8%) patients on haemodialysis. Anaemia occurs in 34-94.3% CKD patients mainly from decreased renal erythropoietin, poor erythrocyte survival iron, folic acid, or vitamin B12 deficiency, and blood loss during dialysis.^{7,14,16} The frequency of pallor was low in our study probably due to inability to appreciate pallor in dark-skinned individuals.

Other less common manifestations were bullous lesions, perforating folliculitis, foot ulcers and lentigo. Bullae may result from transfusion-related iron overload often affects 2-18% patients. Perforating folliculitis is significantly common among diabetic CKD patients, though the pathophysiology remains unclear. Milliarly, peripheral neuropathy may increase the risk of foot ulcer/amputation. We also found these manifestations more commonly in patients on haemodialysis.

Coated tongue in 2 (2.2%) patients, angular cheilitis in 2 (2.2%) patients, and pigmented tongue in 1 (1.1%) patient were the usual mucosal manifestations. Nutritional deficiencies, candidiasis, poor oral hygiene, smoking, consumption of alcohol or hot/spicy foods, and dehydration, are the possible pathogenetic triggers. ^{16,18}

Nail changes have been described in approximately 71.4% uraemic patients. The common nail findings in our study were longitudinal ridging (21.1%), and leukonychia (13.3%).

Longitudinal ridging are indentations or projections in the nail plate due to trauma, physiological or secondary alterations to diseases, or nail matrix tumors. Leukonychia occurs frequently due to nail pallor in patients having anaemia. The characteristic nail change in CKD is Lindsay's half and half nails, a band of discoloration over the distal nail plate arising from increased density of nail bed capillaries, with a reported prevalence of 17-76%. 14,19,20 We found Lindsay's half and half nails in 4.4% patients.

We found that most of the mucocutaneous manifestations were present more commonly in patients on haemodialysis as compared to those not on haemodialysis. It is possible that the successful use of haemodialysis in CKD and ESRD has increased the life expectancy of patients, giving time for more and newer cutaneous and mucosal conditions to manifest.

CONCLUSION

Xerosis, pruritus, ichthyosis skin pallor, longitudinal ridging, leukonychia, coated tongue, and angular cheilitis, were the most common mucocutaneous manifestations in our study irrespective of their haemodialysis status. Xerosis was seen in a higher number of patients on haemodialysis. Our study limitations include a smaller number of patients, and lack of follow up. Early recognition and management of these dermatological manifestations is vital in order to reduce the morbidity and improve the quality of life of patients.

Funding: No funding sources Conflict of interest: None declared Ethical approval: The study was approved by the institutional ethics committee

REFERENCES

- 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.
- Singh AK, Farag YM, Mittal BV, Subramanian KK, Reddy SRK, Acharya VN, et al. Epidemiology and risk factors of chronic kidney disease in India -Results from the SEEK (Screening and Early Evaluation of Kidney Disease) study. BMC Nephrol. 2013;14:114.
- 3. Khanna D, Singhal A, Kalra OP. Comparison of cutaneous manifestations in chronic kidney disease with or without dialysis. Postgrad Med J. 2010;86:641-7.
- 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.
- 5. 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.
- 6. Mirza R, Wahid Z, Talat H. Dermatologic manifestations in chronic renal failure patients on hemodialysis. J Liaquat Uni Med Health Sci. 2012;11:24-8.
- 7. Shah A, Hada R, Kayastha BM. Dermatological disorders in chronic kidney disease with and without maintenance hemodialysis. JNMA J Nepal Med Assoc. 2013;52:365-71.
- 8. Salhab AM, Shalhub S, Morgan MB. A current review of the cutaneous manifestations of renal disease. J Cutan Pathol. 2003;30:527-38.
- 9. Lupi O, Rezende L, Zangrando M, Sessim M, Silveira CB, Sepulcri MA, et al. Cutaneous manifestations in end stage renal disease. An Bras Dermatol. 2011;86:319-26.

- Petkov T, Dencheva R, Tsankov N. Skin changes of patients on dialysis treatment. J Turk Acad Dermatol. 2010;4:4301.
- 11. Szepietowski JC, Reich A, Schwartz RA. Uremic xerosis. Nephrol Dial Transplant. 2004;19:2709-12.
- Pico MR, Somolinos LA, Sanchez JL, Burgos Calderon R. Cutaneous alterations in patients with chronic renal failure. Int J Dermatol. 1992;31:860-3.
- 13. Akhyani M, Ganji MR, Samadi N, Khamesan B, Daneshpazhooh M. Pruritus in hemodialysis patients. BMC Dermatol. 2005;5:7.
- 14. Udayakumar P, Balasubramanian S, Ramalingam KS, Lakshmi C, Shrinivas CR, Mathew AC. Cutaneous manifestations in patients with chronic renal failure on hemodialysis. Indian J Dermatol Venereol Leprol. 2006;72:119-25.
- 15. Szepietowski JC, Schwartz RA. Uremic pruritus: Review. Int J Dermatol. 1998;37:247-53.
- Sanad EM, Sorour NE, Saudi WM, Elmasry AM. Prevalence of cutaneous manifestations in chronic renal failure patients on regular hemodialysis: a hospital based study. Egyptian J Dermatol Venereol. 2014;34:27-35.

- 17. Kaminski M, Frescos N, Tucker S. Prevalence of risk factors for foot ulceration in patients with end-stage renal disease on haemodialysis. Intern Med J. 2012;42:120-8.
- 18. Sultan MM, Mansour HH, Wahby IM, Houdery AS. Cutaneous manifestations in Egyptian patients with chronic renal failure on regular hemodialysis. J Egypt Women Dermatol Soc. 2010;7:49-55.
- 19. 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;7:313-9.
- Rashpa RS, Mahajan VK, Kumar P, Mehta KS, Chauhan PS, Rawat R, et al. Mucocutaneous manifestations in patients with chronic kidney disease: A cross-sectional study. Indian Dermatol Online J. 2018;9:20-6.

Cite this article as: Hans T, Kumar D, Agarwal S, Zaidi AS, Mohanty S, Wadhwa A. Muco-cutaneous manifestations of chronic kidney disease with or without hemodialysis. Int J Res Dermatol 2021;7:85-90.