

Original Research Article

Cutaneous manifestations in chronic renal failure patients on hemodialysis and medical management

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ABSTRACT

Background: Over the past few decades, the developments in the field of Nephrology have improved the life expectancy of patients with chronic kidney disease (CKD). This situation provides more time for the dermatological conditions to manifest. The objective of the present study was to evaluate the different clinical patterns of cutaneous manifestations in chronic kidney disease and also to compare the cutaneous manifestations in CKD patients on dialysis and medical management.

Methods: 120 consecutive cases of chronic kidney disease were included in the study. This included inpatients and outpatients, patients on medical management as well as those undergoing hemodialysis. A detailed history was taken and complete dermatological examination was performed. Digital photographs of skin lesions were taken. Relevant investigations like complete blood counts, blood urea, serum creatinine, serum electrolytes were performed routinely. Special investigations like KOH mount for fungus, Tzanck smear and skin biopsies were performed when clinically indicated.

Results: The number of cutaneous manifestations present in each patient is compared based on severity and duration of CKD. 82.8% of patients with severe CKD had more than one dermatoses compared to 60% of patients with mild CKD. So, multiple cutaneous manifestations could be found in the same patient, as the severity of CKD increases. Xerosis and hyperpigmentation were more prevalent in patients undergoing dialysis than those on medical management alone.

Conclusions: In patients with CKD xerosis, pruritus, pigmentation, nail changes and cutaneous infections were the predominant cutaneous manifestations. The prevalence of xerosis and hyperpigmentation were higher in patients with longer duration of disease and increased as the severity of CKD increased. The prevalence of pruritus was independent of the duration and severity of CKD.

Keywords: Chronic kidney disease, Cutaneous manifestations, Dermatoses

INTRODUCTION

The skin and the kidney constitute two major organ systems of the human body, which partner many important functions and in turn share a number of diseases. The skin is an external reflection of many renal pathologies and hence serves as an indispensable tool for the clinician. Over the past few decades, the improvement in the field of Nephrology has drastically improved the life expectancy of patients with chronic kidney disease, which resulted in dramatic increase in the number of

patients with chronic kidney disease (CKD). This scenario provides more time for the dermatological conditions to manifest. Studies show that 50-100% of patients with end stage renal disease are affected by at least one dermatological disorder.^{1,5}

CKD encompasses a spectrum of different pathophysiological processes associated with abnormal kidney function, and progressive decline in glomerular filtration rate (GFR).² Chronic renal failure means the process of continuing significant irreversible reduction in

nephron number, and typically corresponds to CKD stages 3-5, alternatively it can be defined as the irreversible, substantial loss of renal function causing ill health usually referred to as uremia.³

The true prevalence of chronic renal failure is unknown because many patients are asymptomatic or its presence has not been recognized. The prevalence of end-stage renal disease will vary from country to country and will depend upon the incidence of particular disease and the availability and capacity of dialysis and transplant programs. There is a remarkable difference in incidence of CKD according to age, gender and race. The incidence is particularly high in low and middle income countries. In community based studies in India, the CKD prevalence has been reported between 0.16% and 0.79%.^{3,4}

The dermatologic disorders in chronic kidney disease can be attributed to the etiology, the disease per se or the treatment and have significant effects on the patient's quality of life. Hence, it is important from the perspective of a dermatologist to be aware of the various cutaneous manifestations resulting from CKD and its treatment for effective management of these problems.

The objective of the present study was to evaluate the different clinical patterns of cutaneous manifestations in chronic kidney disease, to compare the cutaneous manifestations of CKD patients with mild, moderate, severe disease, also to compare the cutaneous manifestations in CKD patients on dialysis and medical management and to study the pattern of cutaneous dermatoses in relation to the duration of CKD.

METHODS

Study design

The study was a prospective observational study.

Study setting

This study was conducted at SRM Medical College Hospital and Research Centre, which is a super specialty, tertiary care centre from March 2012 to August 2013. This study was approved by the ethical committee of the hospital.

Participants

120 consecutive cases of chronic kidney disease were included in the study. This included inpatients and outpatients, patients on medical management as well as those undergoing hemodialysis.

Exclusion criteria

Patients with acute renal failure and patients who had undergone renal transplantation.

Data was collected as per proforma after obtaining informed consent from the patients. A detailed history was taken and complete dermatological examination was performed. Digital photographs of skin lesions were taken.

Relevant investigations like complete blood counts, blood urea, serum creatinine, serum electrolytes were performed routinely. Special investigations like KOH mount for fungus, Tzanck smear and skin biopsies were performed when clinically indicated.

The severity of CKD was graded based on serum creatinine values as:

- Mild = serum creatinine 1.6 to 3.9 mg/dl
- Moderate = serum creatinine 4.0 to 6.9 mg/dl
- Severe = serum creatinine >7mg/dl.

Statistical analysis

All data collected using a proforma were entered in Microsoft Excel 2007 sheet and a master chart was prepared. The data was analysed using Statistical package for social studies (SPSS) software version 17.0. Chi square test was used to evaluate correlations between variables. A p value of <0.05 was considered significant.

RESULTS

The study population comprised of 120 patients with 77 (64.17%) males and 33 (35.83%) females. The age of the patients ranged from 16-90 years with a mean of 53.29 years and 95.8% of the patients were aged above 30 years as given in Table 1.

Table 1: Demographic characteristics of study population.

Age groups	No. of patients	%	Male	%	Female	%
10-20	1	0.83	1	0.83	0	0
21-30	4	3.33	2	1.67	2	1.67
31-40	16	13.33	11	9.17	5	4.17
41-50	27	22.5	13	10.83	14	11.67
51-60	39	32.5	28	23.33	11	9.17
>61	33	27.5	22	18.33	11	9.17
Total	120	100	77	64.17	43	35.83

The duration of CKD in the study group at the time of presentation is depicted below in Table 2. The duration of CKD ranged from 3 months to 120 months. The average duration of CKD at the time of presentation was 38.9 months.

Table 2: Distribution of patients according to duration of CKD.

Duration of CKD (months)	No. of patients	%
1-12	25	20.83
13-24	26	21.67
25-36	25	20.83
36-48	16	13.33
48-60	14	11.67
>60	14	11.67

The severity of CKD is presented in Table 3. Severe CKD was present in 51.67% of the patients, with 42 males and 20 females, accounting for 35% and 16.6% of patients in the study. Moderate CKD was seen in 25% of total patients comprising of 19 males (15.8%) and 11 females (9.2%). Mild CKD was found in 28 patients (23.33%), with 16 males (13.3%) and 12 females (9.7%).

Out of 120 patients, 32 received medical treatment and 88 were on dialysis. Majority of the patients (n=23) undergoing medical treatment had mild CKD accounting for 19.17% of the study patients. Majority of the patients (61) undergoing dialysis had severe CKD (50.8%), comprising of 41 males (34.17%) and 20 females (16.67%) respectively as presented in Table 4.

In this study the duration of dialysis ranged between 3 months to 8 years, with maximum number of patients (27) between 1-12 months forming 30.68% of patients on dialysis, comprising of 17 males (19.32%) and 10 females (11.36%). 90% of patients were on dialysis for 1-48 months duration.

A summary of the cutaneous manifestations observed in the study are tabulated below in Table 5. At least one skin manifestation was observed in 96.7% of the study group. Xerosis and pruritus were the most common manifestations observed in 60% and 46.7% of the cases respectively. The other important manifestations observed were pigmentary changes (37.5%), pallor (17.5%), nail changes (21.7%), hair changes (15%), cutaneous infections (17.5%), perforating disorders (7.5%) and mucosal changes (7.5%). AV fistula dermatitis as an iatrogenic manifestation was observed in 1.67% of the cases. Other nonspecific manifestations were observed in 21.67% of patients. Pallor was observed in 21(17.5%) patients, comprising of 10% males and 7.5% females. Perforating disorders were observed in 4.17% of males and 3.3% females in a total of 7.5% of patients.

A comparison of cutaneous manifestations based on severity of CKD is summarised in Table 6. Comparison of cutaneous manifestations between patients on dialysis and medical treatment is shown in Table 7.

Out of 72 patients with xerosis, 85.71% of the patients had CKD of 49-60 months duration, followed by patients with CKD of duration >60 months (78.57%) and 25-36 months (76%). Comparatively lower number of patients had xerosis, when duration of CKD is <24 months.

Out of 72 patients with xerosis, 47 patients had severe disease, 16 patients had moderate disease and 9 had mild form of disease. Xerosis was present in 75.81%, 53.33% and 32.14% in severe, moderate and mild forms of disease respectively as shown in Figure 1.

Out of 46.67% of patients with pruritus, 53.85% of patients had CKD for 13-24 months duration, followed by 37-48 months (50%), 1-12 months (48%), 25-36 months (44%), >60 months (42.86%) and 49-60 months (35.7%) as tabulated in Table 9.

Table 3: Severity of CKD.

Severity	Total No.	%	Male	%	Female	%
Mild	28	23.33	16	13.33	12	10.00
Moderate	30	25.00	19	15.83	11	9.17
Severe	62	51.67	42	35.00	20	16.67
Total	120	100.00	77	64.16	43	35.84

Table 4: Type of treatment.

Treatment	Severity	No. of patients	%
Medical	Mild	23	19.17
	Moderate	8	6.67
	Severe	1	0.83
Dialysis	Mild	5	4.17
	Moderate	22	18.33
	Severe	61	50.83
Total		120	100

Table 5: Cutaneous manifestations in CKD.

Manifestation	Total patients	%	Male	%	Female	%
Xerosis	72	60.00	46	38.33	26	21.67
Pruritus	56	46.67	34	28.33	22	18.33
Hyperpigmentation	45	37.50	25	20.83	20	16.67
Pallor	21	17.50	12	10.00	9	7.50
Perforating Dermatoses	9	7.50	5	4.17	4	3.33
Nail Changes	26	21.67	19	15.83	7	5.83
Hair Changes	18	15.00	11	9.17	7	5.83
Mucosal	9	7.50	5	4.17	4	3.33
Infection	21	17.50	15	12.50	6	5.00
AV Fistula Dermatitis	2	1.67	2	1.67	0	0
Others	26	21.67	18	15.00	8	6.67

Table 6: Cutaneous manifestations based on severity of CKD.

Manifestation	Total patients	%	Mild CKD (28)	%	Moderate CKD (30)	%	Severe CKD (62)	%	Chi-Square *	P-Value
Xerosis	72	60.00	9	32.14	16	53.33	47	75.81	15.926	<0.001
Pruritus	56	46.67	18	64.29	10	33.33	28	45.16	1.706	0.191
Hyperpigmentation	45	37.50	7	25.00	8	26.67	30	48.39	5.531	0.019
Pallor	21	17.50	2	7.14	3	10.00	16	25.81	5.538	0.019
Perforating dermatoses	9	7.50	2	7.14	2	6.67	5	8.06	0.036	0.849
Nail changes	26	21.67	7	25.00	9	30.00	10	16.13	1.386	0.239
Hair changes	18	15.00	8	28.57	5	16.67	5	8.06	6.350	0.012
Mucosal	9	7.50	4	14.29	1	3.33	4	6.45	1.157	0.282
Infection	21	17.50	4	14.29	5	16.67	12	19.35	0.359	0.549

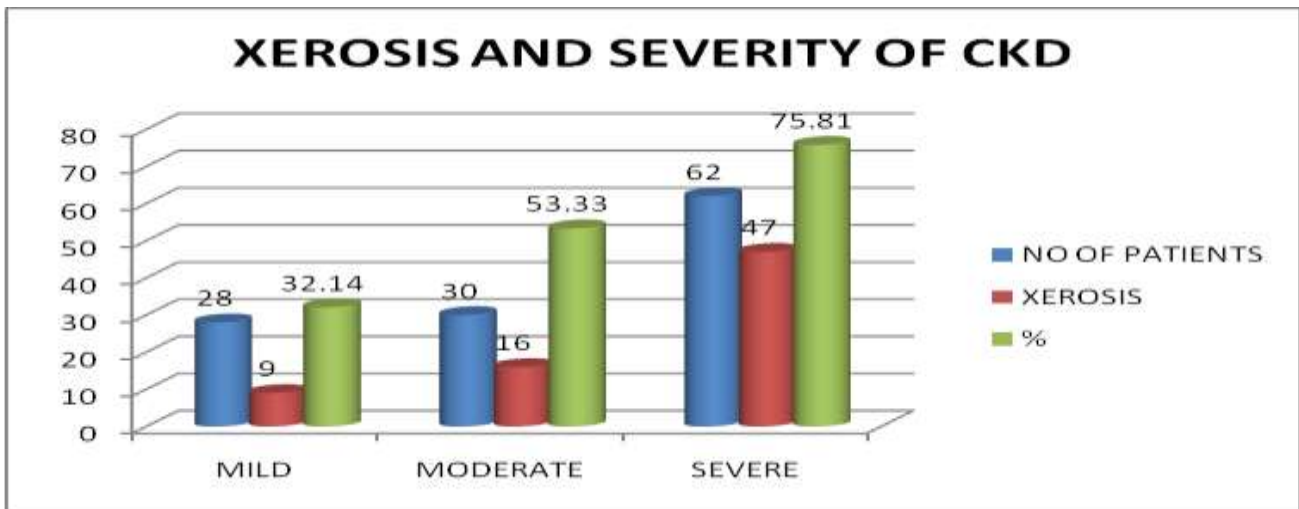
Table 7: Cutaneous manifestations based on treatment- dialysis versus medical.

Manifestation	Dialysis (88)	Medical (32)	Chi Square	P-Value
Xerosis	62 (70.5%)	10 (31.25%)	15.028	<0.001
Pruritus	39 (44.3%)	17 (53.1%)	3.568	0.059
Pigmentation	38 (43.2%)	7 (21.875%)	4.545	0.033
Perforating dermatoses	9 (10.2%)	0	5.538	0.060
Nail changes	18 (20.5%)	8 (25%)	0.286	0.593
Hair changes	9 (10.2%)	9 (28.1%)	5.896	0.015
Infections	17 (19.3%)	4 (12.5%)	0.756	0.385
Mucosal changes	7 (8%)	2 (6.2%)	0.062	0.803

Table 8: Duration of CKD and xerosis.

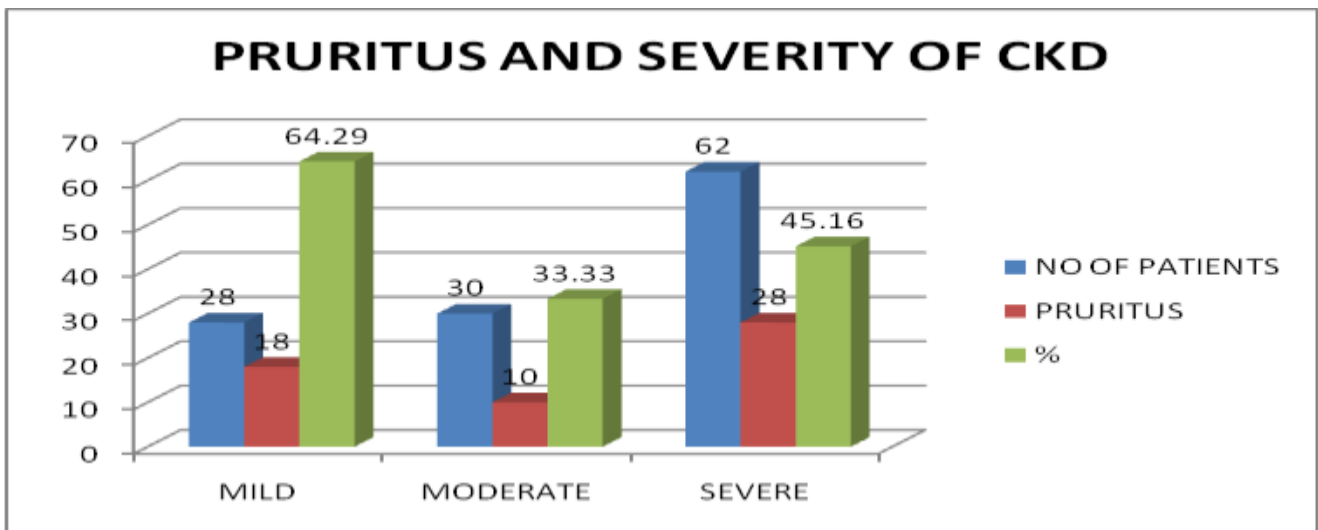
Duration of CKD in months	No of patients	Xerosis	%
1-12	25	7	28
13-24	26	13	50
25-36	25	19	76
37-48	16	10	62.5
49-60	14	12	85.71
>60	14	11	78.57

Chi square value: 14.780; p- value: <0.001.



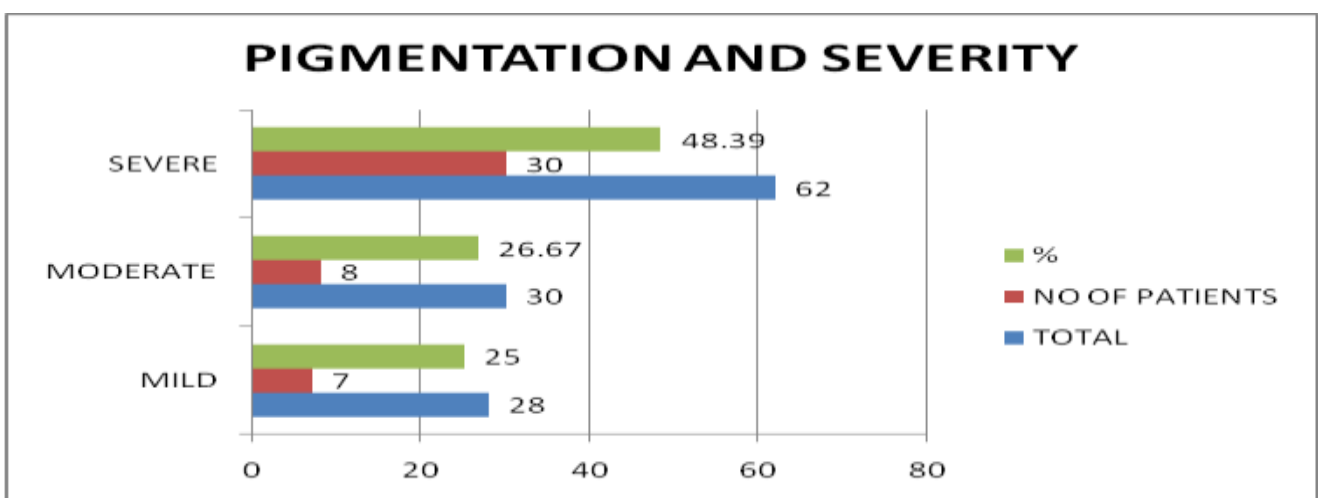
Chi square value: 15.926; p- value: <0.001.

Figure 1: Severity of CKD and xerosis.



Chi square value: 1.706; p- value: 0.191.

Figure 2: Pruritus and severity of CKD.



Chi square value: 5.531; p- value: 0.019.

Figure 3: Severity of CKD and pigmentation.

Out of 56 patients with pruritus, 18 patients had mild disease, 10 patients had moderate disease and 28 had severe form of disease. Pruritus and severity of CKD is presented in Figure 2. Pruritus was found in 64.29%, 33.33% and 45.16% in mild, moderate and severe forms of disease respectively.

Table 9: Duration of CKD and pruritus.

Duration of CKD in months	No. of patients	No of patients with Pruritus	%
1-12	25	12	48.00
13-24	26	14	53.85
25-36	25	11	44.00
37-48	16	8	50.00
49-60	14	5	35.71
>60	14	6	42.86

Out of 37.5% of total patients with hyperpigmentation, 71.4% of the patients had CKD for >60 months duration. 50% of the patients had CKD between 37-48 months duration followed by 42.85% and 36% of patients between 37-48 months and 25-36 months duration respectively as in Table 10.

Table 10: Duration of CKD and pigmentation.

Duration of CKD in months	No. of patients	No. of patients pigmentation	%
1-12	25	4	16
13-24	26	7	26.92
25-36	25	9	36
37-48	16	8	50
49-60	14	6	42.85
>60	14	10	71.42

Chi square value: 12.973; p-value: <0.001.

Out of 45 patients with pigmentation, 30 patients had severe disease, 8 patients had moderate disease and 3 had mild form of disease. Pigmentation was present in 48.39%, 26.67% and 25% in severe, moderate and mild forms of disease respectively as in Figure 3.

Cutaneous infections were noted in 21 patients accounting for 17.5% of the study population. Superficial fungal infections were observed in 12 patients (10%), of whom, 4 patients had dermatophytosis and 4 patients had tinea versicolor. Viral infections were found in 3 patients (2.5%) with herpes zoster, herpes labialis and verruca vulgaris in one patient each. Bacterial infections were found in 5 patients (4.17%) with furunculosis being the commonest, found in 4 patients as given in Table 11.

Nail changes were observed in 26 patients (21.67%), commonest being half and half nails found in 12 patients

(10%). Other manifestations in decreasing frequency are onychodystrophy in 5 patients (4.17%), longitudinal melanonychia and onychomycosis in 3 patients each (2.5%), beau's lines in 2 patients (1.67%) and pitting in 1 patient (0.83%).

Hair changes were observed in 18 patients (15%) with dry, lustreless hair in 11 patients (8.3%) and diffuse alopecia in 8 patients (6.7%). Mucosal changes were observed in 9 patients. Bald tongue and fissured tongue were observed in 2 patients each, mucosal pigmentation was seen in 2 patients, oral lichen planus was seen in 1 patient. AV fistula dermatitis as an iatrogenic complication was observed in 1.7% of patients.

Table 11: Cutaneous infections.

Infection	No.	%
Fungal infections	12	10
Dermatophytosis	4	3.33
Tinea versicolor	4	3.33
Onychomycosis	2	1.67
Intertrigo	1	0.83
Oral candidiasis	1	0.83
Viral infections	3	2.50
Herpes zoster	1	0.83
Herpes labialis	1	0.83
Verruca vulgaris	1	0.83
Bacterial	5	4.17
Furunculosis	4	3.33
Cellulitis	1	0.83
Total	21	17.50

Other nonspecific findings which were observed in 26 patients are depicted below in Table 12. Pyogenic granuloma was found in one patient over an old scar of AV fistula. Gangrene of great toe was found in one patient. Biopsy of the lesion revealed cholesterol emboli in a small sized artery in dermis.

Table 12: Miscellaneous findings.

Miscellaneous	No of patients
Eczema	16
Vitiligo	2
Psoriasis	2
Lichen planus	2
Macular amyloid	1
Trophic ulcer	1
Pyogenic granuloma	1
Gangrene	1
Total	26

The number of dermatoses in each patient in relation to severity of CKD is shown in Table 13. 52 patients with severe CKD had more than one dermatoses (83.8%), compared to 21 patients with more than one dermatoses

in patients with moderate CKD(70%) and 18 patients with more than one dermatoses in patients with mild CKD (60%). However, the number of dermatoses present in the same patient does not show a higher incidence with increasing duration of CKD. The number of dermatoses in each patient in relation to duration of CKD is shown in Table 14.

Table 13: Number of dermatoses in each patient in relation to severity of CKD.

No. of dermatoses						
Severity	1	2	3	4	5	6
Mild	8	7	4	2	4	1
Moderate	9	9	11	1	0	0
Severe	8	18	17	10	5	2

Table 14: Number of dermatoses in each patient in relation to duration of CKD.

No. of dermatoses						
Duration of CKD in months	1	2	3	4	5	6
1-12	10	6	5	4	0	0
13-24	5	9	6	2	2	1
25-36	4	7	8	2	3	0

DISCUSSION

120 cases of chronic kidney disease were examined in this study. There has been a gradual increase in the number of CKD patients referred to the Dermatology clinic for management of cutaneous problems, some of which may require prompt and aggressive treatment.

In the present study comprising of 120 patients, 64.17% were males and 35.83% were females. A male preponderance was also noted in the study by Udaykumar et al where, 70% were males and 30% were females.¹² The mean age of patients in this study was 53.29 years and 95.8% of the patients were above 30 years of age. In the study by Hajhedari et al, the mean age was 50 years which is comparable. But in other studies the patients were slightly younger.¹⁰

The average duration of CKD at the time of presentation was 38.9 months. The study population had a mix of mild, moderate and severe cases. Severe CKD was present in 51.67% of patients. While moderate CKD and mild CKD accounted for 25% and 23.33% of cases respectively.

Patients on hemodialysis accounted for 73.3% of the study population, while 26.7% patients were on medical management alone. The mean duration of dialysis in the study group was 23.1 months. Similar figures are seen in studies done by Kolla et al and Luqman et al.^{9,11}

Cutaneous manifestations in CKD patients were observed in 96.7% patients in this study, which correlates with the findings of studies of Pico et al, who reported skin findings in 100% of his patients and by Luqman et al, who reported a prevalence of 85%.^{3,11}

By far, xerosis was the most common cutaneous manifestation, documented in 60% of the patients in our study. Previous studies by Sultan et al and Kolla et al reported xerosis in 54% and 51.7% of their study population respectively, which is slightly lower than our finding.^{8,9} Xerosis was seen in 82.1% of CKD patients, when the duration of CKD was above 48 months. This was found to be statistically significant with a p value of <0.001. Xerosis was more prevalent in patients with severe CKD (75%) than those with moderate CKD (53.3%) and mild CKD (32.1%). Patients undergoing hemodialysis also showed higher prevalence, which was statistically significant when compared to those on medical management.

Pruritus is generally observed in 19-90% of CKD patients. In our study, pruritus was found in 46.7% of the patients, which is comparable to studies by Pico et al and Hajheydari et al who reported pruritus in 38.8% of patients in their study.^{2,3,10} It was also more common among CKD patients on medical management. The occurrence of pruritus was however found to be independent of duration and severity of CKD, in our study.

Hyperpigmentation in sun exposed areas is a common finding in CKD patients. Udaykumar et al and Luqman et al have reported hyperpigmentation in 43% and 44% of their patients, while in this study, it was observed in 37.5% of patients.^{12,11} Hyperpigmentation was more commonly found in patients who had longer duration of CKD and also on patients receiving hemodialysis.

Pallor, a significant finding due to anemia of CRF in the pre erythropoietin era, is seen in 50 to 70% of most of the studies. However, we observed it only in 17%.^{10,11} Frequency as low as 8% has also been reported by Pico et al.³

Perforating disorders, combining the characteristics of Kyrles disease and perforating folliculitis can be found in CRF and diabetes mellitus. In our study this finding was observed in 7.5% of the patients of the patients, while Kolla et al reported a prevalence of 6.9%.⁹ This diagnosis of perforating disorders was confirmed by skin biopsy. In our study they were exclusively seen in nine patients on hemodialysis, of whom only 3 were diabetics.

Since the barrier function of the skin is compromised in CKD patients, they are more prone for cutaneous infections. The spectrum of cutaneous fungal infections noted in our study included dermatophytosis (3.3%), pityriasis versicolor (3.3%), oral candidiasis (0.8%) and

intertrigo (0.8%). The increased prevalence of fungal infections in CKD patients is due to impaired cellular immunity due to decreased T lymphocyte count.

Other cutaneous infections noted in our study were bacterial infections in 4.2% of the patients, comprising of furunculosis (3.3%) and cellulitis (0.8%). Viral infections were found in 2.5% of the patients, with herpes zoster, herpes labialis and verruca vulgaris in 0.8% of patients each.

Luqman et al reported cutaneous infections in 11% of their patients.¹¹ Other investigators like Udaykumar et al and Pico et al reported infections in 67% and 70% of their patients respectively.^{12,3}

Nail changes were reported between 30-50% of patients with CKD. In our study, nail changes were observed in 21.67% of the patients which was lower compared to the existing literature.⁷ Half and half nails, the characteristic nail change in CKD was observed in 10% of the patients. Other nail changes observed in this study were onychodystrophy (4.17%), longitudinal melanonychia (2.5%) and Beau's lines (1.67%). Nail pitting was noted in 1 patient, who had co existing psoriasis of skin also.

Hair changes like sparse body hair, diffuse alopecia and dry lustreless hair have been reported to occur frequently in CKD. In this study, hair changes were observed in 15% of the patients and included dry lustreless hair (8.3%) and diffuse alopecia (6.7%). The cause of dry lustreless hair may be attributed to decreased secretion of sebum. Hajheydari et al, reported hair changes in 38% of the patients in their study.¹⁰ Udaykumar et al reported hair changes in 27% of their patients.¹²

Mucosal changes are common in patients with CKD and can be due to dehydration, mouth breathing, high concentration of urea and failure to breakdown to ammonia. Mucosal changes were observed in 7.5% of the patients and included mucosal pigmentation, bald tongue and fissured tongue in 1.7% of patients each. Angular cheilitis, oral candidiasis and oral lichen planus were found in 0.83% of the patients each. Udaykumar et al reported 41% prevalence of mucosal changes in their study.¹² Hajheydari et al reported mucosal changes in 24% of their patients.¹⁰

AV fistula dermatitis, as an iatrogenic complication was found in 1.7% of the patients. Other nonspecific findings were observed in 21.7% of the patients, which included eczema in 16 patients, vitiligo, psoriasis and lichen planus in 2 patients each, macular amyloid and trophic ulcer in one patient each.

One patient presented with pyogenic granuloma from an old scar of AV fistula. Another patient presented with gangrene of the great toe. Histopathological examination of skin biopsy revealed cholesterol emboli in a small artery in the dermis, which appeared as slit like spaces

that represent cholesterol crystals which previously occupied the spaces, but got dissolved by formalin fixation.

Other rare manifestations like uremic frost, bullous dermatosis, calciphylaxis, gynaecomastia and nephrogenic systemic fibrosis were not observed in this study.

The number of cutaneous manifestations present in each patient is compared based on severity and duration of CKD. 82.8% of patients with severe CKD had more than one dermatoses compared to 60% of patients with mild CKD. So, multiple cutaneous manifestations could be found in the same patient, as the severity of CKD increases. However, the number of dermatoses in the same patient did not depend on the duration of the disease.



Figure 4: Acquired reactive perforating collagenosis (ARPC), showing koebner phenomenon clinically and histology show trans epidermal elimination of altered collagen.



Figure 5: Dermatophytosis- extensive and diffusely scaly plaques.



Figure 6: Half and half nails.

CONCLUSION

In patients with chronic kidney disease, xerosis, pruritus, pigmentation, nail changes and cutaneous infections were the predominant cutaneous manifestations. The prevalence of xerosis and hyperpigmentation were higher in patients with longer duration of disease. The prevalence of xerosis and hyperpigmentation increased as the severity of CKD increased.

Xerosis and hyperpigmentation were more prevalent in patients undergoing dialysis than those on medical management alone. A statistically significant relationship could be established between xerosis and hyperpigmentation to duration, severity and the type of treatment.

The prevalence of pruritus was independent of the duration and severity of CKD. The prevalence of pruritus is more among patients who are on medical treatment alone, but the relationship was not significant.

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Conflict of interest: None declared

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

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