

A Study of Mucocutaneous Manifestations in Patients with Chronic Kidney Disease

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Abstract

Background: Chronic renal failure is associated with diverse mucocutaneous manifestations as a result of underlying etiology as well as due to various treatment modalities which can significantly impair the quality of life.

Aim: To study the clinicodemographic profile of Chronic Kidney Disease (CKD) patients and to compare the cutaneous manifestations in CKD both on dialysis and pre-dialysis group.

Methods: This study was carried out in the Department of Dermatology, Venereology and Leprology, Medicine and Dialysis unit at Shree Krishna Hospital, Karamsad, Anand. One hundred and twenty patients with CKD were examined for mucocutaneous changes over a period of one year. The descriptive statistics was used to describe the quantitative data and the qualitative data was presented using frequency and analyzed using Chi Square test.

Result: All one hundred and twenty patients had at least one mucocutaneous condition due to CRF. The most prevalent finding was xerosis (34 Pre-dialysis+ 31 Dialysis) 65(54.2%), followed by pruritus (33 Pre-dialysis+ 24 Dialysis) 57(47%), pallor (6 Pre-dialysis+21Dialysis) 27(22.5%) and cutaneous pigmentation (10 Pre-dialysis+14 Dialysis) 24(20%). Other cutaneous manifestations included fungal 10(8.3%), viral 9(7.5%) and bacterial 7(5.8%) infections, purpura 9(7.5%), perforating disorder 6(5%), uremic frost 1 (0.83%). The nail changes included onychomycosis 5(4.2%), koilonychia 4(3.3%), half and half nail 2(1.7%), subungual hyperkeratosis 2(1.7%) and onycholysis 2(1.7%). Hair changes included brittle and lusterless hair 21(17.5%), sparse scalp hair 10(8.3%) and sparse body hair 8(6.7%). Oral changes included xerostomia 15(12.2%), ulcerative stomatitis 4(3.3%) and angular cheilitis 4(3.3%).

Conclusion: The most common mucocutaneous manifestations in the patients under our study were xerosis and pruritus, irrespective of hemodialysis status. Early recognition and treatment can reduce morbidity and improve these patients' quality of life. In all such patients, lifelong follow up is needed.

Keywords: chronic renal failure; mucocutaneous manifestations; chronic kidney disease

Introduction

Chronic kidney disease (CKD) is a worldwide public health problem. Adverse outcomes of CKD include loss of kidney function, sometimes leading to kidney failure, cardiovascular disease and mucocutaneous manifestations. These can be prevented or delayed by early diagnosis and treatment. Unfortunately, CKD is under-diagnosed and under-treated [1]. Indeed, it has been recently estimated that the age-adjusted incidence rate

of End stage renal disease (ESRD) in India is 229 per million population [2], and >100,000 new patients enter renal replacement programs annually [3]. Mucocutaneous manifestations usually reflect the internal condition. CKD is an irreversible deterioration in renal function classically developing over months or years through five stages and is defined as kidney damage or glomerular filtration rate <60 ml/min/1.73 m² for 3 months or more irrespective of the cause [4]. Cutaneous manifestations are common in all stages of CKD particularly towards

ESRD with a prevalence of 50–100% [5, 6]. Prolonged life expectancy as a result of prompt treatment with hemodialysis enables newer cutaneous manifestations to appear [7]. Some of the skin changes like pruritus, xerosis, hyperpigmentation, nail disorders, hair disorders, calciphylaxis, purpura and acquired perforating dermatosis are said to be present regardless of hemodialysis but some skin manifestations such as uremic frost and erythema papulatum uremicum have become rare due to hemodialysis. At the same time many other abnormalities of skin and appendages have emerged due to hemodialysis, like calcific uremic arteriopathy, bullous lesions, and nephrogenic fibrosing dermopathy. Xerostomia, macroglossia, and ulcerative stomatitis are the commonly seen mucosal findings. Hair can be sparse and lustreless in CKD patients. Half and half nails, koilonychia, onycholysis, absent lunulae, and onychomycosis are common nail manifestations [8].

Non modifiable risk factors for the progression of CKD are genetic, age, family history, gender, ethnicity. Modifiable risk factors are diabetes,

hypertension, anemia, smoking, inflammation, obesity, nephrotoxic drugs, systemic conditions, persistent activity of underlying disease, persistent proteinuria, hyperlipidemia, hyperphosphatemia, cardiovascular disease. Other factors include elevated angiotensin II, hyperaldosteronism, increased endothelin, decreased nitric oxide

Specific mucocutaneous manifestations of CKD include acquired perforating dermatosis, calcific uremic arteriopathy (calciphylaxis), bullous lesions and nephrogenic fibrosing dermopathy. Nonspecific manifestations include pruritus, xerosis, nail disorders, hair disorders, pigmentary changes, purpura, mucosal changes, pallor, and uremic frost etc. Based on Etiology these can be divided into: 1) Associated with ESRD, 2) Due to Uremia, 3) associated with dialysis, 4) Due to renal transplant

According to site of involvement they can be divided as follows:

Skin	Nail	Hair	Mucosa
Xerosis	Half and half nail	Sparse scalp hair	Xerostomia
Pallor	Koilonychia	Sparse body hair	Ulcerative stomatitis
Pruritus	Onychomycosis	Brittle lusterless hair	Angular cheilitis
Cutaneous pigmentation	Subungual hyperkeratosis		Uremic breath
Fungal infection	Onycholysis		Teeth markings
Bacterial infection	Mee's line		
Viral infection	Beau's line		
Purpura	Splinter hemorrhage		
Perforating disorder			
Uremic frost			

The cutaneous, mucosal, nail and hair changes in CRF patients are impacted by climatic conditions of the locale, race, socioeconomic conditions of patients, accuracy of diagnosis and the light of environment in which cutaneous examination have been done [9]. The present clinicodemographic study is aimed to reflect the frequency of different dermatologic changes including those of skin, mucous membrane, hair and nails in patients of CRF in both pre-dialysis and dialysis group.

Methods

A cross sectional study was carried out in the Department of Dermatology, Venereology and Leprology, Medicine and Dialysis unit at Shree Krishna Hospital, Karamsad, Anand after approval from ethical committee at a tertiary care hospital over a period of 1 year. Patients with Chronic Kidney Disease (CKD) attending the Nephrology OPD, Dermatology Department (OPD), Medicine Department (OPD and IPD), and Dialysis Unit of Shree Krishna Hospital were recruited after taking their written consent. A detailed history was taken, and a thorough general, physical, local and systemic, cutaneous examination was carried out. If not done previously, investigations like Histogram with DC,

Random blood sugar, Blood urea, Serum Creatinine, Serum electrolytes, serum calcium, phosphorus, thyroid, parathyroid hormone level, renal biopsy were done. Skin biopsy, KOH wet mount, tzank smear of the skin were done when clinically indicated. Photographs were taken after taking patient's consent and ensuring them that confidentiality will be maintained at all levels.

Result

Total 120 patients with chronic kidney disease (CKD) were included in the study. Sixty-eight (56.7%) patients were in pre-dialysis group and fifty-two (43.4%) were in dialysis group. The age of the patients ranged from 11 years to 73 years, with the mean age of 53.14 years. 51-60 years was the most commonly affected age group in pre-dialysis group. More than 60 years was the most commonly affected age group in dialysis group. According to education wise distribution maximum patients were graduate 53(44.2%) while 12(10%) patients were illiterate and 12(10%) were post graduate. Occupation wise, highest number of cases was found to have office jobs with 30(25%) cases.

Cutaneous manifestation	Pre-dialysis		Dialysis		Total	P value
	Male	Female	Male	Female		
Xerosis	14	20	16	15	65(54.2%)	0.573
Pallor	3	3	7	14	27(22.5%)	0.805
Pruritus	19	14	11	13	57(47.5%)	0.962
Cutaneous pigmentation	4	6	6	8	24(20%)	0.162
Fungal infection	3	3	3	1	10(8.3%)	0.847
Bacterial infection	3	1	1	2	7(5.8%)	
Viral infection	3	1	2	3	9(7.5%)	
Purpura	1	2	3	3	9(7.5%)	0.622
Perforating disorder	1	1	3	1	6(5%)	0.681
Uremic frost	0	0	1	0	1(0.83%)	0.941
Others	1	2	7	5	15(12.5%)	

Xerosis was the most common cutaneous abnormality in sixty-five (54.2%) cases, while pruritus was present in fifty-seven (47.5%) cases and pallor was present in twenty-seven (22.5 %) cases.

Out of 65 patients with xerosis, thirty-one (25.8%) cases had Dry skin, while twenty (16.7%) had smooth skin and fourteen (11.7%) had dry skin with scaling. 34 cases were of pre-dialysis group and 31 were of dialysis group. From all the patients ,total 26(21.7%) patients had infections, fungal in 10(8.3%), bacterial in 7(5.8%), and viral in 9(7.5%). In our study, out of 65 patients with xerosis, thirty one(25.8%) cases had dry skin, while twenty(16.7%) had smooth skin and fourteen(11.7%) had dryskin with scaling, according to modified morton's scale for xerosis. Out of 120, 16 cases had pigmentation over photo exposed areas and 8 had over non-photo exposed areas, 10 were pre-dialysis patients and 14 were of dialysis group. Among 120, 10 having sparse scalp hair, 8 having sparse body hair, 21 having brittle lusterless hair, 16 were pre-dialysis patients and 23 were dialysis patients. In our study, we did not find any patients with Mees lines, Beau's lines or splinter hemorrhages in neither dialysis nor pre-dialysis group.

Discussion

Among 120 CKD patients in our study, 66 were males and 54 were females. 68 were of pre dialysis and 52 were of dialysis group. In the dialysis group the most commonly affected age group was more than 60 years with twenty (38.5%) cases followed by fifteen (28.9%) cases in 51-60 years age group. In pre dialysis group, the most commonly affected age group was 51-60 years with twenty one (30.8%) cases followed by nineteen (28%) cases who were more than 60 years. In our study, age ranged between 11 and 73 where as in Rashpa et al [10], 21 was the youngest and 85 was the oldest age.

In our study, all 120 patients had at least one dermatological manifestation, 92.5% had at least one skin manifestation. Along with skin, nail, hair and mucosal manifestations were seen in 12.5%, 32.5% and 19.2% respectively. In Chanda et al [11], out of 100 patients, 95% had at least one skin manifestation and nail, hair, and mucosal manifestations were seen in 46%, 16%, and 10% respectively. In Pico et al [9] and Bencini et al [12] prevalence of mucocutaneous disorders with kidney disease was seen in 100% and 79% respectively. Nunley [6] reported that 50-100% of patients with ESRD had at least one cutaneous lesion. Udayakumar et al [8] has studied cutaneous disorders in hemodialysis group and changes were present in 82% cases.

Xerosis was the most common dermatological manifestation in our study, which was comparable to other studies with an overall prevalence in 65 (54.2%) cases, out of which 34 cases were of pre dialysis and 31 cases of dialysis group [10, 11, 13]. When compared, there was no statistical significance in our study where as in chanda et al [11], dialysis group had statistically significant higher prevalence ($P = 0.014$) compared to pre-dialysis patients. Prevalence of xerosis in CKD patients in different studies was reported to be variable (59-93%) [12].

Gilchrest et al. [14] observed xerosis in 69% of pre dialysis and 70% hemodialysis patients. These figures were reported to be 62% and 91% respectively by Yopisowitchet al. [15] Thomas et al^[16] had 66.7% cases of pruritus of variable intensity in CKD which was comparable to Anderson et al^[17]. It may or may not improve from hemodialysis and occurs in 15-49% during predialysis and in 19-90% hemodialysis patients [6, 7, 18, 19].

In our study, pruritus was present in 57 (47.5%) cases. Pruritus was found in 33(48.5%) patients of pre dialysis group, 24(46.2%) patients of dialysis group and there was no significant difference. In chanda et al [11], pruritus was found in 38% patients out of which dialysis group (63.16%) had higher prevalence compared to the pre-dialysis group (36.84%). The

reported prevalence of pruritis in the predialysis period ranges from 22% to as high as 85% [14].

Cutaneous pigmentation was present in 24 (20%) cases in our study, 10(15.15%) in pre dialysis group and 14(30%) in dialysis group .Sixteen (66.67%) cases had pigmentation over photo exposed areas and 8(33.33%) cases over non photo exposed areas. In Rashpa et al [10], pigmentation in photo-exposed skin was observed in 47 (38.5%) cases out of which 48% of the hemodialysis and 52% were of pre dialysis group. The prevalence of pigmentation is reported to be in 22-54% patients which correlates to the duration of dialysis [5, 7, 20]. In chanda et al [11] pigmentation was found in 32 patients, out of which dialysis group (65.63%) had higher prevalence compared to pre-dialysis group (36.84%).

Pallor was observed in 22.5% of cases in our study. Six (8.8%) cases in pre dialysis and twenty one (40.4%) cases in dialysis group. There was no significant difference between dialysis and pre-dialysis groups. In chanda et al [11] and leena et al [13] pallor was the second most common manifestation observed in 57% and 82% patients respectively. Purpura was present in total 7.5% patients in our study. Three (4.54%) cases in pre dialysis group and 6(11.54%) cases in dialysis group. In Rashpa et al [10], chanda et al [11] and Thomas et al [16] purpura was present in 14.8%, 8% and 10.1% patients respectively. Udayakumaret al. [8] observed purpura in 9% patients on hemodialysis. In our study perforating disorders were present in total 6(5.5%) cases, more in dialysis group [4 cases (7.7%)] than in pre dialysis group [2 cases (3.03%)]. In Rashpa et al [10], the perforating disorders were present in 3 (2.5%) cases. Thomas et al [16] had (17.17%) patients with perforating disorders among whom, 12 patients (12.12%) were on maintenance hemodialysis. In our study, total 26(21.7%) patients had infections, fungal in 10(8.3%), bacterial in 7(5.8%), and viral in 9(7.5%). Udayakumaret al. [8] reported fungal infections in 30%, bacterial in 13%, and viral in 12% patients. JA Leena et al [13] had similar infections in 27%, 37% and 9% patients respectively.

Most common mucosal abnormality in our study was xerostomia in 15(12.2%) cases which was comparable to the 15 (12.3%) patients in rashpa et al [10]. In Chanda et al [11], mucosal changes were observed in 11 patients (dialysis 8 and pre-dialysis 3). There was no statistically significant difference in mucosal changes between dialysis and pre-dialysis groups. In our study there were 4(3.3%) cases each, of cheilitis and angular stomatitis. In Chanda et al [11] xerostomia, cheilitis, angular stomatitis and uremic breath were reported in 5%, 3%, 2%, and 1% of the patients, respectively. Onychomycosis was the most common nail finding seen in our study, in 5 (4.2%) cases, followed by koilonychia in 4(3.3%) cases which is not comparable with other studies. Most common nail finding in most of the studies is half and half nails but in our study it was present in only 2(1.7%) cases. Prevalence of half and half nail is reported to be 17-76% [21, 22]. In Thomas et al [16] Lindsay's nails (half and half nails) were the most common nail abnormality seen in this study (36.36%) and more commonly seen in hemodialysis patients. Pico et al. [14] reported that the nail changes increase with the duration of dialysis. Sparse scalp and body hair was found in 10(8.4%) and 8(6.7%) cases, and lustreless hair in 21(17.5%) cases respectively in our study where as in rashpa et al [10], 45 (35.2%), 16 (13.1%), and 15 (12.3%) were the respective values. In chanda et al [11] hair changes were observed in 16 patients (dialysis 10 and pre-dialysis 6), and difference was not statistically significant.

Conclusion

The most common mucocutaneous manifestations in the patients under our study were xerosis and pruritus, irrespective of hemodialysis status. Early recognition and treatment can reduce morbidity and improve these patients' quality of life. Patients with end stage renal failure (ESRD) may

present with an array of skin abnormalities. With the advent of hemodialysis, the life expectancy of these patients has increased, giving time for more and newer cutaneous changes to manifest. Some prophylactic and remedial measures can prevent or decrease some of the adverse changes. These include emollients for xerosis; sunscreens, sun avoidance measures and clothing for pigmentary changes and cutaneous malignancies; oral hygiene to prevent oral mucosal changes; nutritional supplementation to prevent vascular fragility, angular cheilitis and hair loss; and prompt recognition and treatment of fungal infections like onychomycosis and tinea pedis, which are increased in CRF. Lifelong follow-up is needed to reduce the morbidity from dermatoses considered CKD/hemodialysis specific that may appear over time. Short duration and the cross-sectional nature of the study are some of the limitations of this study.

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