

Frequency and pattern of muco-cutaneous manifestations in patients with chronic kidney disease on hemodialysis

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Abstract

Introduction: Dermatological changes are frequently seen in patients with chronic kidney disease (CKD). Aim of this study was to evaluate the frequency and pattern of hair, nail and cutaneous problems and number of patients with cutaneous manifestations and complications at the site of A-V fistula among CKD patients.

Material and Methods: It was a cross-sectional, observational study conducted in dermatology and nephrology departments at government medical college Kota, Rajasthan between June 2017 and December 2017. Patients with CKD were examined for the diagnosis of dermatological manifestations. An experienced dermatologist confirmed the diagnosis and histopathological examination was performed for doubtful cases. Disease characteristics like primary disease causing CKD, duration of CKD, stage of CKD, personal/family history of structural kidney defects, and duration of hemodialysis were recorded.

Results: A total of 100 patients were included in the study. One or more muco-cutaneous manifestations were seen in 94(94%) patients. Xerosis was the most common skin manifestation observed in 70(70%) patients. The most common nail manifestation was leukonychia, seen in 22(22%) patients. The most common mucosal manifestations were ulcerative mucositis, observed in 22(22%) patients. The most frequently observed hair manifestation dry and lustreless hairs seen in 26(26%). Local cutaneous changes at the site of A-V fistula were observed in 57(57%) patients.

Conclusion: In the present study, muco-cutaneous manifestations were common in CKD with E-GFR <15 ml/min. Among cutaneous manifestations, xerosis was the most common cutaneous finding and leukonychia was the most common nail manifestation.

Keywords: Chronic kidney disease, Muco-cutaneous manifestation, E-GFR (estimated glomerular filtration rate), Hemodialysis, Xerosis.

Introduction

Chronic kidney disease (CKD) is a disease defined as the presence of kidney damage (characterized by albuminuria) or decreased level of kidney function lasting more than three months, irrespective of diagnosis.¹ The prevalence of CKD is approximately 1000 per million in Indo-Asian population.²

According to Singh *et al.*,³ the prevalence of CKD stage 3 and above in semi-urban India is 4.2%; while another study by Singh *et al.*⁴ in urban population reports it to be 6%.⁴ A study by Verma *et al.*⁵ stated that the prevalence of CKD stage 1-3 in mixed population is 13%.

A wide variety of muco-cutaneous disorders are seen in patients with CKD. An early identification of these manifestations could aid in the diagnosis of early CKD stages. As reported in literature, 50-100% of the patients have at least one identifiable dermatological disease and 41% have one specific manifestation related to the underlying renal pathology.

Our study aimed to evaluate the epidemiology of patients with CKD in relation to age, sex, and predisposing factors; the prevalence and pattern of various muco-cutaneous patients in patients of CKD on hemodialysis; and the association of local cutaneous complication at the site of cannula insertion into the arteriovenous (A-V) fistula.

Material and Methods

This was a cross-sectional, observational study that was conducted in patients who attended the outpatient and inpatient department of our institution. 100 consecutive patients with CKD lasting for at least 3 months were studied for six months between July 2017- December 2017. The study was conducted in accordance with the International Conference of Harmonization-Good Clinical Practice (ICH-GCP) guidelines. All patients provided informed written consent.

Patients included were 18 years of age or older who had a diagnosis of CKD for at least 3 months. Patients who were on peritoneal dialysis, had renal transplantation, or had acute renal failure were excluded from the study. Other exclusion criteria included patients with known immunosuppression including those with HIV positive status, solid organ transplant, malignancy, and genetic immunodeficiency disorders.

Assessment and procedures

The diagnosis and staging of CKD was based on clinical examination by an experienced nephrologist. In case of doubt, the diagnosis was further confirmed by relevant laboratory and radiological investigations and renal biopsy. Several dermatological manifestations were observed by the investigator and confirmed by an experienced dermatologist under adequate natural light. The muco-cutaneous manifestations were recorded in a predesigned Performa and

photographic documentation was done at the same sitting. Specific investigations such as Gram stain, Tzanck smear, KOH mount, and skin biopsies were performed wherever indicated.

The demographic and other clinical characteristics of the patients were documented properly. Various non-infective and infective manifestations involving skin, nails, hair and oral mucosa were documented separately. Grading of xerosis was done using modified Morton scale (0=no xerosis, 1=rough skin without scaling, 2=rough skin with scaling). Grading of pruritus was performed using numerical rating scale (0-3=mild pruritus, 4-7=moderate pruritus, 7-9=severe pruritus, 9-10= very severe pruritus). Severity of CKD was done as recommended by Kidney disease outcome quality initiative (K-DOQI) practice guidelines.

Statistical analysis

The statistical analysis was carried out using Statistical Package for Social Sciences (SPSS Inc., Chicago, IL, version 23.0 for windows). All qualitative data were presented as frequency, percentage and proportions. All quantitative variables were estimated by using the measures of central location (mean, median) and the measures of dispersion (variance). Correlation between nominal data was sought using Spearman rank correlation coefficient (rho coefficient). P-value of <0.05 was considered significant.

Results

A total of 100 patients of CKD on hemodialysis were included in our study. Overall, the mean (SD) age of patients was 44.7(15.66) years (range 18-88); 58.5% were men. The overall distribution of patients by age, sex, disease characteristics, duration of CKD, and severity of CKD using e-GFR are presented in Figures 1a-1d. The most common etiology causing CKD was hypertension (41.5%), which was followed by diabetes mellitus (21%). The mean (SD) duration of CKD was 23(22.91) months. Majority of patients had severe CKD as indexed by e-GFR < 15 ml/min/1.73m².

Dermatological manifestations

In our study, at least one dermatological (skin, mucosa, nails, hair) manifestation was found in all patients. Skin manifestation was found in 94(94%) cases. Xerosis was the most common skin manifestation seen in 70(70%) patients. The most common location was a limited distribution to extremities, especially on extensor aspect. According to the modified Morton grading scale, grade 1 xerosis was found in 40(40%) patients, while grade 2 xerosis was found in 30(30%) patients. Grades of xerosis were negatively correlated with e-GFR.

Pruritus was observed in 35(35%) patients. According to body surface area (BSA) I involvement, it occupied <30% of BSA in 18 %, 30-60 % BSA in 8% and >60 % BSA in 9% patients. The most common localization of pruritus was a bilaterally symmetrical distribution over back. In terms of severity, it was of mild grade in 30%,

moderate grade in 30%, severe grade in 35%; while in 5% of patients it was of severe grade in patients suffering from pruritus, interfering with sleep, daily chores and other activities of daily living. In terms of diurnal variation 70% patients reported a nocturnal increase in severity of pruritus, while patients with severe to very severe grades of pruritus reported continuous itching throughout day and night. Among specific manifestations, pseudo-porphyrria and acquired perforating dermatoses were seen in 8 patients (8%) each. (Table 1 and 2)

Table 1: Non- infectious

	Number of cases	Total frequency (%)
manifestations of CKD patients Manifestation		
eXerosis	70	70
Pruritus	35	35
Pallor	23	23
Hyperpigmentation	34	34
Purpura	10	10
Pseudoporphyria	8	8
Acquired perforating dermatosis	8	8
Drug rash	1	1
Yellow pigmentation	7	7
Gynecomastia	5	5
PPKD	2	2
Finger papules	1	1
Necrobiosis lipoidica	1	1
Eczema	2	2
Exfoliative dermatitis	1	1
Melasma	1	1
Senile comedons	2	2
Seborrheic keratosis	3	3
IGH	2	2

Nail manifestations

Nail manifestations were seen in 72 (72%) patients. The commoner nail manifestation were Leukonychia in 22(22%) patients and Lindsay nails in 21 patients (21%). (Table 3)

Oral mucosal manifestations Oral mucosa changes were observed in 68 (68%) patients. The commoner were ulcerative mucositis observed in 22 (22%) patients and bald/depapillated tongue 20 (20%). (Table 4)

Hair manifestations

Hair manifestations were seen in 42(42%) patients with the most common being dry and lustreless hairs seen in 26(26%) patients. (Table 5)

Changes at the site of A-V fistula

Changes at the site of A-V fistula were seen in 57 (57%) patients. Dyspigmentation due to repeated puncture marks occurred in 24 (24%) patients and aneurysmal venous dilatation were seen in 11(11%) patients.

Discussion

Our study demonstrated that cutaneous examination of patients with CKD led to the identification of at least one dermatologic condition in all patients. This may be expected, because most patients with CKD have an underlying disease process with cutaneous manifestations, along with uremia and conditions associated with renal replacement therapy or renal transplantation. Mucocutaneous manifestations are common in CKD and range from commonly observed disorders xerosis, hyperpigmentation, pruritus, Lindsay nails, ulcerative mucositis, diffuse hair loss to uncommon ones like calciphylaxis, nephrogenic systemic fibrosis, acquired perforating disorder, and pseudo-porphyrria. Different studies have documented variable prevalence of mucocutaneous manifestations as shown in table 5. In our study, we found that at least one muco-cutaneous manifestation (skin, mucosa, hair, nails) manifestation was observed in all patients. This is comparable to other studies that have documented at least one dermatological manifestation in all patients (100%). (6,7) The cutaneous, mucosal, nail and hair changes in CKD patients may be dependent on the climatic conditions of patients, accuracy of diagnosis, and light in which cutaneous examination was carried out.

Among cutaneous manifestations, xerosis was the most common finding, observed in 70% patients in our study. Xerosis was the most common skin manifestation seen in 70(70%) patients. The most common location was a limited distribution to extremities, especially on extensor aspect. In 15 (15%) patients, it was ichthyosiform in nature. The grades of xerosis were negatively correlated with severity of CKD as indexed by e-GFR. This was in agreement with a previous study that reported xerosis in 79% patients. This was in agreement with a previous study that reported xerosis in 79% patients; however other studies have reported xerosis in 22.8% patients.⁸⁻⁹

The higher prevalence of xerosis in the current study could be due to the poor socio-economic status of the patients leading to greater exposure to dust and detergents and poor use of emollients, in general.

Pruritus was another common manifestation observed in 35(35%) patients. The most common localization of pruritus was a bilaterally symmetrical distribution over back, followed by patchy involvement of back, forearms, and lower legs. The most common itch type was a pricking sensation over involved area in 40% patients, followed by a tingling sensation in 30% patients with 8% patients describing them as of burning quality, while remaining 22% patients were unable to give any particular quality to their itch. The provoking factors for pruritus were dry skin (xerosis) and cold dry climate. In 84.2% patients, xerosis was associated with pruritus.

Grey-brown pigmentation over photo-exposed sites was observed in 34% patients in this study. It was due to accumulation of beta-melanocytic hormone in the basal layer of superficial dermis due to its reduced excretion by the kidneys. Pico et al.⁷ reported diffuse hyperpigmentation in 70% patients, Hajheydari et al(8) in 66.3% patients,

Dyachenko et al(10) in 75.5% patients, and Udaykumar P. et al.⁶ in 43% patients. The variation in prevalence of hyperpigmentation in various studies can be explained by variation in sample size, patient profile, racial differences in hyperpigmentation, and differences in sun-exposure rates.

Acquired perforating dermatosis (APD), a disorder of trans-epidermal elimination was seen in 8% patients in our study, compared to 21% prevalence reported by Udaykumar P. et al.⁶ and 17% by Thomas EA et al.¹¹

The prevalence of pseudo-porphyrria (8%) was similar to previous studies.

Nail changes were appreciated in 72 (72%) patients, among which leukonychia was the most common seen in 22 (22%). Hajheydari et al.⁸ similarly reported it to be the most common anomaly seen in 16.8% cases. It is attributed to anemia with hypoproteinemia. The prevalence of Lindsay nail in our study is in accordance to study by Udaykumar P. et al.,⁶ who reported it in 21% patients in their study.

Hair manifestations were seen in 42 (42%) patients, in agreement with study by Hajheydari et al.⁸ in which they observed hair changes in almost 50% patients.

Oral mucosa changes were seen in 67 (67%) patients as compared to such changes observed in 21% patients in study by Udaykumar P et al.⁶ our study most common change was ulcerative mucositis seen in 21% patients. Hemodialysis was done through the creation of A-V fistula, preferably on volar aspect of non-dominant forearm. Frequent cannulation leads to multiple changes at the cannula site and increased susceptibility to infection.

Local cutaneous changes were observed in 60% patients. Dyspigmentation secondary to repeated marks at the A-V fistula was the most common finding, seen in 24 (24%) patients. Khanna D.¹² et al found it in 11% patients. Aneurysmal venous dilatation found due to repeated cannulation at the same site was seen in 12.5% patients, as compared to seen in 22.2% cases in study by Masmoudi et al.¹³

Conclusion

This study identifies complex range of cutaneous manifestations in CKD patients. Various manifestations were observed in skin, hair, nail and mucosa due to underlying metabolic abnormality or its management. The manifestations may vary due to difference in sociodemographic profile including age, sex, sun-exposure, climate, Fitzpatrick skin type, underlying cause of CKD, comorbidities in the form of medical treatment, hemodialysis, peritoneal dialysis or renal transplantation, the accuracy of clinical examination and presence of adequate light at the time of examination of the studied population. Vigilant awareness of muco-cutaneous manifestations and treatment of infections in patients with CKD is important, as prevention, early diagnosis, and management can lead to improved quality of life.

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