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A comparative study of cutaneous manifestations in chronic kidney disease patients with those under dialysis and post-renal transplant patients

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Abstract
Background: Dermatologic abnormalities are very common in Chronic kidney disease (CKD) patients and significantly impacts quality of life. They range from nearly universal xerosis and pruritus to uncommon conditions like acquired perforating dermatoses and nephrogenic systemic fibrosis.
Cutaneous manifestations may vary among CKD patients with those on dialysis or received renal-transplantation. Early recognition of these conditions can significantly reduce the morbidity and mortality of these patients.
Objective: To study the skin manifestations in CKD patients and how it differs from those undergoing dialysis or post-renal transplant patients. To find out how skin features vary with the duration of CKD and duration of dialysis.
Methods: Institution based descriptive study was conducted in 45 patients with ESRD (patients with irreversible decline in kidney function) of diverse etiology who attended the nephrology or dermatology department. A detailed clinical history was taken and history of any comorbid condition were recorded. A detailed physical and dermatological examination was done in all cases. Dermatological manifestations observed were documented.
Results: Total 45 patients (24 male and 21 females) included in this study. All patients present with at least 1 form of skin alteration. The manifestations are different in CKD pts. compared to those on dialysis or post-transplant group & hence need a different approach towards management. Due to prolonged use of immunosuppressant in kidney transplant recipients, opportunistic infections are very common.
Conclusion: World is facing an escalate in the incidence of chronic kidney disease (CKD). Dermatologic abnormalities are very common in CKD patients and significantly impacts quality of life. They range from nearly universal xerosis and pruritus to uncommon conditions like acquired perforating dermatoses and nephrogenic systemic fibrosis. Cutaneous manifestations may vary among CKD patients with those on dialysis or received renal-transplantation. Duration of dialysis or time since transplant also affect the cutaneous abnormalities in CKD patients. Early recognition of these conditions can significantly reduce the morbidity and mortality of these patients.

Keywords: Chronic kidney disease, cutaneous features, dialysis, renal transplant, pruritus, xerosis

Introduction
There are a variety of dermatological diseases that are more commonly seen in patients with chronic kidney disease (CKD) and dialysis or renal transplants than the general population. Chronic kidney disease (CKD) is defined as kidney damage or glomerular filtration rate <60 ml/min/1.73 m2 for 3 months or more irrespective of the cause leading to an irreversible deterioration in renal function classically developing over years [1]. CKD is a worldwide problem and accounts for approximately 850,000 deaths every year and 15 million disability adjusted lives; ESRD is the 12th cause of death and 17th cause of disability globally [2]. Skin manifestations are common in all stages of CKD particularly towards ESRD with a prevalence of 50-100% [3, 4]. Patients with chronic kidney disease (CKD) commonly exhibit cutaneous manifestations associated with impaired renal function. With the advent of hemodialysis as a therapeutic modality for ESRD, some skin manifestations such as uremic frost and erythema papulatum uremicum have become rare. Skin manifestations specific to dialysis patients include acquired perforating dermatosis, calcific uremic arteriolopathy (calciphylaxis), bullous lesions, and nephrogenic fibrosing dermopathy. On the other hand,

pruritus, xerosis, nail disorders, hair disorders, pigmentary changes, purpura, mucosal changes, pallor, and uremic frost, though not specific to hemodialysis, are more frequent. However, it may be difficult to implicate either CKD or hemodialysis alone for any particular cutaneous manifestation as many of them are associated with both [5]. These manifestations may also vary across regions, with individual dietary habits, socioeconomic and nutritional status, and racial differences [6]. These skin manifestations are different in post-renal transplant patients. In renal transplant, the use of immunosuppressive drugs, indispensable to avoid organ rejection, implies an increased risk of several infectious and neoplastic diseases [7].
Cutaneous infections have a very high incidence in patients submitted to renal transplant and are diagnosed in 55-97% of these individuals [8].

Materials and Methods

Total 45 patients (24 male and 21 females) included in this study and they were divided in 3 groups, each consisting of 15 patients:

- Group 1-CKD patients.
- Group 2-CKD patients who received or on dialysis.
- Group 3-CKD patients who received kidney transplant.

Informed consent was taken followed by history & clinical examination. Clinical picture of lesion was taken and skin biopsy for histopathology was done in clinically confusing cases. KOH mounts, Gram's and Giemsa staining, and bacterial or fungal cultures were performed when needed. Data were analyzed statistically using SPSS software (version 20).
All patients visiting surgery department with CKD, CKD patients who received on dialysis & CKD patients who received kidney transplant Pt. willing to give informed consent for participation & photograph were included in this study. Patient of acute kidney disease and transplant failure patients on dialysis or those not willing to give consent were excluded.

Aims and Objectives

To study the cutaneous abnormalities in 3 groups of CKD patients.
To see the difference in skin manifestations among the 3 groups (if any).
To study the effect of duration of hemodialysis or time since renal-transplant, on the dermatological disorders occurring in CKD patients.

Results and Analysis

Total 45 patients were included in this study out of which 24 were males and 21 females. Most of them were aged between 40 to 60 years; the youngest patient was aged 14 years and the oldest, 76 years. 45 patients were divided in 3 groups-1. CKD patients 2. CKD patients on dialysis 3. CKD patients post renal transplant. Each group consisted of 15 patients. All patients examined in this study showed at least one cutaneous manifestation, although only 85% complained of some skin problem [Figure 1]. Xerosis and pruritus were the most common skin manifestation in CKD patients however its incidence was lower in post-kidney transplant patients. Least common skin finding in our study was squamous cell carcinoma [Figure 2]. In CKD patients post-transplant most common skin manifestations were fungal infections and straie most likely due to systemic steroids and immune suppressive therapy given in these patients. This difference in Xerosis and Pruritus between 3 groups was statistically significant with P-value 0.027 & 0.012 respectively. Difference in fungal infection in 3 groups was not statistically significant but for bacterial (p-value 0.046) and viral infections (p-value 0.03) it was significant.

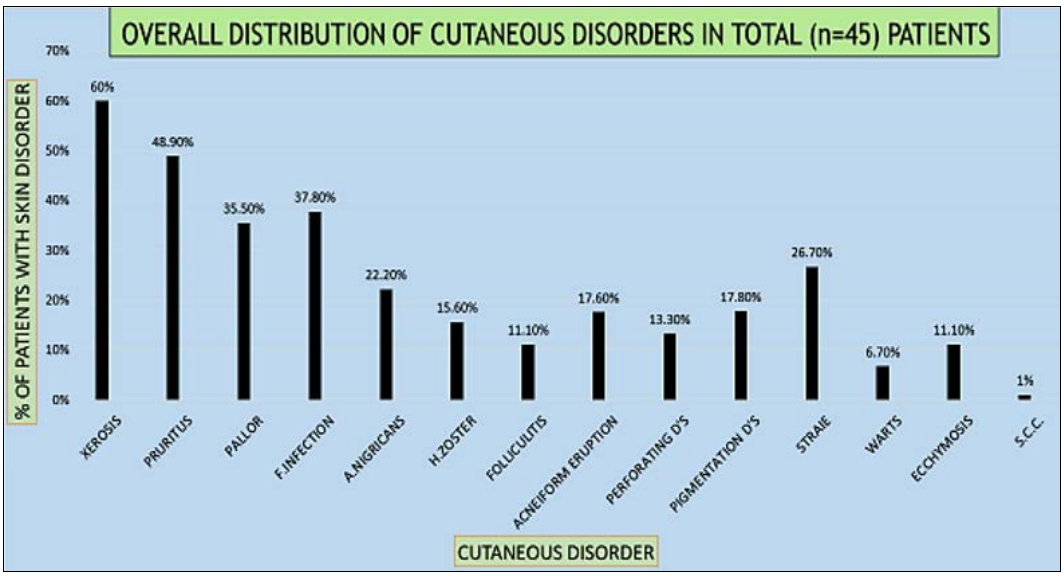

Fig 1: Overall distribution of cutaneous disorders in total (n = 45) patients

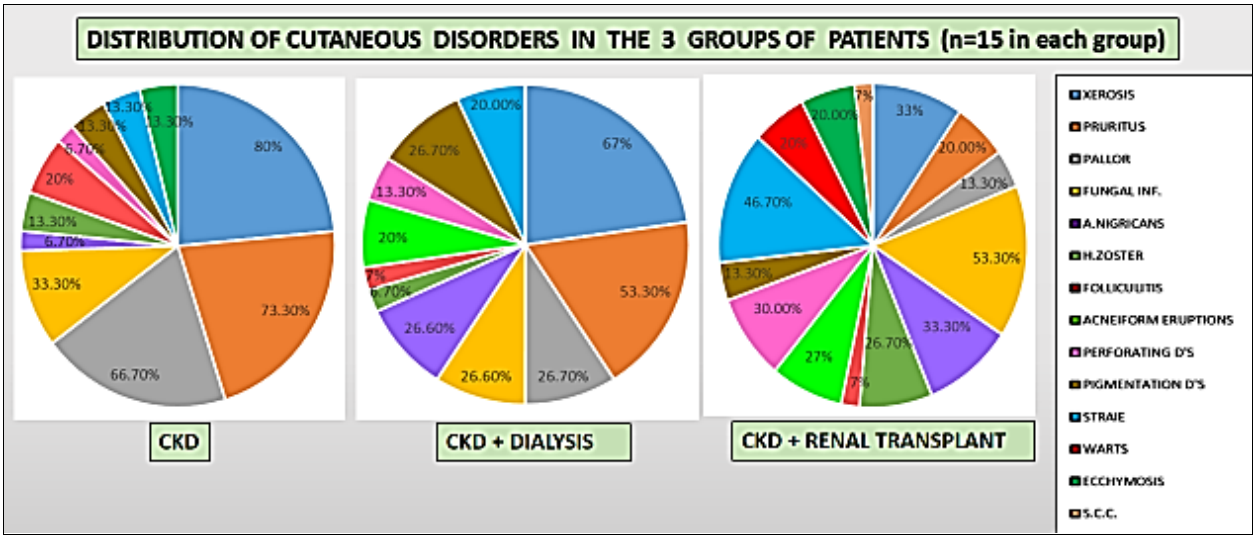

Fig 2: Distribution of cutaneous disorders in the 3 groups of patients (n = 15 in each group)

Discussion

Cases of chronic kidney disease are increasing exponentially. All patients present with at least 1 form of skin alteration, skin can act as mirror for multisystem changes in these patients. The manifestations are different in CKD pts. compared to those on dialysis or post- transplant group & hence need a different approach towards management. Xerosis was the most common skin finding in CKD and dialysis patients followed by pruritus most likely due to high dosage of diuretics, reduction in size of sweat glands, and excessive ultrafiltration in CKD patients. Xerosis predominantly affected extensor surfaces of fore-arms, legs, and thighs. Post-transplant patients show higher incidence of opportunistic infections as compared to xerosis and pruritus, most likely due to immune suppressants given to these patients. Two types of pigmentary charges were observed-hyperpigmentation (seen in 17.1% of patients) and a yellowish tinge to the skin (5%). Diffuse hyperpigmentation on sun exposed areas is attributed to an increase in melanin in the basal layer and superficial dermis due to failure of the kidneys to excrete beta-melanocyte-stimulating hormone (β-MSH). The high incidence of infections might be due to diabetes, low albumin, elevated intracellular calcium, acidosis, or repetitive vascular procedures. Among the acquired perforating disorders, only Kyrle's disease was noticed, and others like perforating folliculitis, and perforating collagenosis were not found in our study.

Nail changes commonly seen in CKD patients are onychomycosis, discolouration, onycholysis, and splinter hemorrhages. Hair changes include discoloration and dryness, possibly due to decreased sebum secretion [9, 10]. Hemodialysis patients show following oral mucosa changes xerostomia, angular cheilitis, gingivitis, and uremic breath. Possible causes include dehydration, mouth breathing, and high concentration of urea, and failure to breakdown into ammonia [11]. Incidence of acquired perforating diseases in CKD patients was claimed to be high in previous studies, E.A. Thomas *et al*. reported it to be 17.7%, this study found it be only 6.7% [12]. Infectious complications are more common in contrast to reported by previous studies. Study by E.A. Thomas showed it be only 24.2%, most common being bacterial infections 11.1%. In this study infections accounted for 66.6% cases in CKD group & fungal infection were most common (33.3%). Dialysis group showed fungal infection (26.7%) > viral infections (6.7%). However, study by P. Udaykumar *et al*. found it to be fungal infection followed by bacterial [13]. In post-transplant patients' study by H. Ghaninejad *et al*. found that most common infection was viral (65%) mainly HPV (40%) [14]. Trend noted in this study was fungal infections were most common (53.5%) followed by viral (46.7%) and bacterial infections comprised 13.3% of total infections in post-transplant patients. Among viral infections most common was herpes-zoster (26.7%) followed by warts (20%). Type of infection was affected by time since transplant. Herpes zoster and candidiasis were early onset infections. Warts, onycomycosis and versicolor occurred late. These findings are similar to the results of Sandhue *et al*., and Formicone *et al*., studies [15, 16].

Conclusion

All 45 of our CKD patients showed at least one cutaneous alteration. 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 CKD. Recognition and management of some of these dermatological manifestations vastly reduce the morbidity and improve the quality of life in CKD patients.

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