

# Comparative study of cutaneous manifestations in patients with chronic kidney disease, patients on haemodialysis, and renal transplant recipients

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## Abstract

**Introduction.** A wide variety of skin diseases occur in patients with chronic renal failure (CRF). These diseases are either related to the underlying chronic kidney disease (CKD) or to its treatment modalities like hemodialysis (HD) and renal transplant (RT). The studies comparing cutaneous manifestations in CKD, CKD with HD and RT recipients (RTR's) have been limited.

**Material and methods.** 106 patients with CKD, 101 patients with CKD and who are undergoing HD and 80 RTR's having at least one dermatological complaint formed the study groups. Detailed cutaneous examination was done for all patients and dermatological manifestations were compared among various study groups.

**Results.** The most prevalent finding in CKD patients was xerosis (69%) followed by pruritus (67%) and pigmentation disorders (11%). Other cutaneous manifestations included acquired perforating diseases (APD) (7.5%); fungal (9.4%), viral (7%) and bacterial (2%) infections and nail changes (11%). The manifestations found in CKD patients on HD were xerosis (65%) followed by pruritus (62%), pigmentation disorders (20%), APD (6%); fungal (9.9%), viral (4%) and bacterial (5%) infections and nail changes (19%). In RTR's, however, infections (47%) were the most prevalent finding. Others were xerosis (20%), pruritus (9%), pigmentation disorders (5%), APD (1%), nail changes (5%) and lesions of aesthetic interest (14%). Manifestations like pruritus, xerosis, hyperpigmentation and infections differed significantly when compared amongst three groups.

**Conclusions.** Cutaneous manifestations are common and different in CKD, HD and RTR group of patients. While xerosis and pruritus were common in CKD and HD group, infections were most prevalent in RTRs.

## Key words

hemodialysis, Renal transplant, CKD, cutaneous manifestations

## INTRODUCTION

CKD (chronic kidney disease) is associated with a constellation of cutaneous manifestations. Cutaneous disorders can precede or follow the initiation of HD (haemodialysis) treatment, and there are more chances to develop newer skin changes during the course of HD, which may affect the quality of life. Moreover, chronic use of immunosuppressants after renal transplantation with its various side effects, opportunistic infections and increased risk of malignancies, potentially affect the skin. There are few comparative studies of cutaneous manifestations in the CKD and HD group [1] and studies on the same in RTRs (renal transplant recipients). [2–6] This study was conducted to compare the frequency and type of dermatological manifestations in patients with CKD and patients undergoing HD and RTR's.

## MATERIALS AND METHOD

In accordance with internal guidelines of the institute, approval by the Institutional Review Board of the hospital, and after taking informed consent from each patient, a

descriptive study was performed on all the patients with CKD and patients on HD and RTRs who had at least one cutaneous disorder from May 2008 – May 2010. The patients were divided in 3 groups:

Group A – all age groups and gender irrespective of the cause and duration of CKD, and not on HD. CKD was defined as either kidney damage or a decreased kidney glomerular filtration rate (GFR) of less than 60 mL/min/1.73 m<sup>2</sup> for 3 or more months [7].

Group B – all age groups and gender irrespective of duration of HD.

Group C – all age groups and gender irrespective of duration of RT. Patients on chronic ambulatory peritoneal dialysis and not willing to participate in the study were excluded.

Complete dermatologic history was obtained and a thorough skin examination carried out. Clinical photographs were taken for the record. Specific investigations, e.g. skin biopsy and histopathological examination were performed wherever necessary. Required laboratory studies, such as KOH mount, grams stain, fungal culture, culture and sensitivity for bacterial infections, were performed after written informed consent from the patient. In addition to dermatological examination, a standardized questionnaire was administered to all patients to obtain a detailed personal history, including information on age, gender, occupation, cause of renal failure, duration of chronic kidney disease,

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haemodialysis, duration of skin change and onset of changes in relation to the duration of chronic kidney disease, and improvement if noted following haemodialysis, date of renal transplant, and current immunosuppressive drug regimen. Information of past medical history of all patients recorded in their medical documents about hypertension and diabetes mellitus was taken into consideration.

CKD patients were separated into 5 groups according to CKD stage KDOQI (kidney dialysis outcome quality initiatives)(2002). Similarly, HD patients and RTRs were also separated into 5 groups according to the duration of HD and post renal transplant respectively.

Xerosis and pruritus were assessed based on the scoring system by EEMCO [8] (European Group on Efficacy Measurement of Cosmetics and Other Topical Products) and VAS [9] (Visual analogue score), respectively. All definitions and clinical criteria for diagnosis, e.g. pigmentary alterations, acquired perforating dermatosis (acquired perforating dermatosis, was diagnosed based on clinical presentation of itchy, keratotic papulonodular lesions, a background of chronic kidney disease, and characteristic histopathological features of transepithelial elimination on skin biopsy), infections[10], nail changes [11], bullous dermatoses, nephrogenic fibrosing dermatopathy, calciphylaxis [12], and lesions of aesthetic importance (LAI), such as acneiform eruptions, striae, moon faces, hypertrichosis and telangiectasia, which consisted of all the drug-related manifestations [13], were applied according to the literature available and as mentioned in the standard textbook of dermatology. The prevalence rates of different dermatologic manifestations in CKD patients, patients on HD and RTRs, were calculated using the statistical package SPSS for Windows version 14.0.

**Statistical analysis.** All the data was entered on a Microsoft Excel spread sheet. Statistical analysis was performed by using statistical package SPSS for Windows version 14.0. Continuous data was described as arithmetic mean and standard deviation, and categorical data as actual numbers and percentages. Tests with two-sided *P* values were performed. A *p* value less than 0.05 was considered as statistically significant.

## RESULTS

The study population consisted of 287 patients, of whom 106 were CKD patients, 101 were patients on HD and 80 were RTRs. The mean age groups in years, distribution of gender and prevalence of hypertension (HTN) and diabetes mellitus (DM) in group A (CKD), group B (HD) and group C (RTRs) patients is shown in Table 1. There was a diversity of primary diagnoses in these groups, including parenchymatous kidney diseases and obstructive uropathies.

Common and miscellaneous dermatological diseases like eczemas, parasitic infections and telogen effluvium, and complaints in all 3 groups are shown in Table 2 and Table 3, respectively. Lesions of aesthetic importance (LAI) were seen in 14% of renal transplant patients. Correlation of xerosis and pruritus score with CKD and HD stages and duration of renal transplant revealed that majority of patients had mild xerosis (Fig. 3) and mild pruritus in the 3 groups, respectively. Fungal infections noted in the 3 groups were: pityriasis versicolor,

**Table 1.** Distribution of mean age, sex, hypertension (HTN), diabetes mellitus(DM) in the three groups

Groups	Mean age (years)	Sex (number)		HTN (%)	DM (%)
		Males	Females		
CKD	54.08	68	38	79	53
HD	52.16	71	30	98	47
RTR	34.36	64	16	82	35

**Table 2.** Distribution of common skin conditions among three groups

Groups (%)	CKD	HD	RTR
Xerosis	69	65	20
Pruritus	67	62	9
Pigmentary abnormalities	11	20	5
APD	7.5	6	1
Fungal Infections	9.4	9.9	30
Viral Infections	7	4	16
Bacterial Infections	2	5	6
Nail abnormalities	11	19	5
Lesions of aesthetic importance(LAI)	-	-	14

**Table 3.** Distribution of miscellaneous skin conditions among three groups

Groups (No.)	CKD	HD	RTR
Eczema	14	6	6
Stasis	4	0	0
Psoriasis	2	1	0
Ecchymosis	3	1	0
Parasitic Infections	1	0	2
Acne	1	4	0
Hair changes	0	1	2
Total	25	13	10

**Table 4.** Comparison of parameters between three groups by application of t-test

t-test	Pruritus	Xerosis	Hyperpigmentation	Infections
CKD versus HD	3.00**	1.71	1.69	0.21
CKD versus RTR	7.68***	7.08**	1.52	4.85***
HD versus RTR	6.30***	6.10***	2.97**	4.98***

\*\*\* p value <0.001; \*\* p value <0.01; \* p value <0.05

onychomycosis (Fig. 3), candidiasis, dermatophytoses and pityriasis folliculitis of which dermatophytoses followed by pityriasis versicolor were commonest. Viral infections observed in the 3 groups were: herpes simplex, herpes zoster (Fig. 2), viral warts, varicella and molluscum contagiosum, of which herpes zoster infection followed by herpes simplex infection were the most common. Bacterial infections observed in the 3 groups were: folliculitis, sycosis barbae, furunculosis, cellulites and ecthyma, of which folliculitis was the commonest followed by furuncles. No cases of malignancies were observed in the presented study in all 3 groups.



**Figure 1.** Xerosis



**Figure 2.** Herpes zoster



**Figure 3.** Onychomycosis



**Figure 4.** Facial melanosis

Different manifestations were compared between the 3 groups. Significant difference ( $p$  value  $<0.05$ ) was noted between CKD and RTRs groups for the presence of pruritus, xerosis and infections. The presence of pruritus,

xerosis, infections and hyperpigmentation (Fig. 4) differed significantly between HD and RTR groups. There was a significant difference ( $p$  value  $<0.05$ ) in the prevalence of pruritus between CKD and HD groups (Tab. 4).

## DISCUSSION

In the presented study, varied types of cutaneous manifestations were observed in all 3 groups. Some of the manifestations were seen equally in all the groups, but there were others that were significantly higher in one group compared with the other. In the CKD group, xerosis, pruritus, cutaneous infections, pigmentary disorders and nail changes, in the HD group, xerosis, pruritus, pigmentary disorders, nail changes and cutaneous infections, and in the RTR group, cutaneous infections, xerosis and lesions of aesthetic interest were respectively observed in that order of frequency.

Xerosis and pruritus were the most common findings in the the CKD as well as in the HD group, which is comparable to studies by Gilchrest BA [14], Kato A et al. [15], Stahle-Backdahl et al. [16], Morton CA et al. [17], Tawade N et al. [18], Pico MR et al. (63%)[19], Ponticelli C et al. [20] and Udaya Kumar P [1]. This may be because of the similar underlying pathophysiology, i.e metabolic and hormonal derangements leading to hypervitaminosis A, hyperparathyroidism, and accumulation of middle molecules [HD group]. Both were more prevalent in the CKD stages II and III and in the initial 6 months – 1 year of initiating HD in the HD group. In the RTR group, xerosis was reported in 16 [20%] patients, which was higher than reported by Leni George et al. [3]. There was no consistent relation of the xerosis score with the post-transplant duration. Pruritus was not a significant symptom in the RTRs, which may be due to improved renal function and normalization of metabolic and hormonal derangements following renal transplant.

Pigmentary disorders like diffuse hyperpigmentation with accentuation in areas exposed to the sun were significantly higher in the HD patients, which was consistent with the study by Pico MR et al. [19] and Morton CA et al. [17] (20–22%), but not matching with the figures reported by AnneliesAvermaete et al. [21] (50%). Udayakumar et al. [1] reported hyperpigmentation in 43% with prominent hyperpigmentation in areas exposed to the sun in 26%. High numbers in HD patients compared with low frequency in CKD patients and insignificant number in RTR group may be due to poorly-dialyzable beta-MSH (Melanocyte Stimulating Hormone).

Cutaneous infections were seen in 42 [53%] of the RTRs [fungal (57%), viral (29%), and bacterial (9%)], which was higher than that reported by Wisgerhof HC et al. [22] and Leni George [3]. Pityriasis versicolor was most common in 9 (37.5%) patients followed by dermatophytosis in 5 (20%), onychomycosis in 5 (20%), candidiasis in 2 (8%) and pityriasis folliculitis in 3 (12%), similar to the previously reported studies [3, 23]. The most common viral infections were herpes zoster in 5 (38%) of the RTRs and herpes simplex in 4 (30%). Cutaneous infections were highest in the RTR group and more commonly observed in the first year of renal transplant, which can be explained by the high levels of immunosuppression caused by the medications. Cutaneous infections in the CKD and HD group were seen in almost equal percentages, but were less common when compared to the RTR group.

Nail changes were high in the HD group than the CKD group, and were the least in the RTR group. In HD patients, these changes were comparable to a study by Udaya Kumar et al. [1]. It appears that chronic kidney disease itself, not

hemodialysis specifically, may play a role in the development of these changes. The HD patients were those with end-stage renal disease, and hence showed more nail changes. In the RTR group, nail changes were probably linked to immunosuppression. Medication-related cutaneous manifestations were also observed in the RTR group and which occurred most frequently during the first 6 months after transplant due to the higher number and high doses of immunosuppressive medications.

Thus, skin disorders are common in patients with CKD, HD and RTRs, and can seriously affect the physical and mental health of patients, thereby compromising their quality of life. Some prophylactic and remedial measures at an early stage can prevent or decrease some of the adverse cutaneous effects. These include frequent application of emollients for xerosis in the early stages, thereby preventing pruritus and consequent infections. Frequent application of sunscreens, sun avoidance measures and proper clothing prevent pigmentary changes and cutaneous malignancies. Prompt early recognition and treatment of fungal, viral and bacterial infections can help in preventing serious invasive infections. Dermatologists and nephrologists should be aware of cutaneous changes in the CKD, HD and RTR group for early diagnosis and prompt treatment, thereby preventing further co-morbidities.

Taken together, this study offers hope for increasing our overall knowledge of which cutaneous manifestations are common and different in CKD, HD and RTR group of patients, and opens new avenues for further research.

Numerous factors influence the prevalence rate of the cutaneous manifestations and their diagnosis. The difference between the results obtained and the other similar studies on some specific cutaneous manifestations may be due to differences of race, socio-economic conditions, and differences of climatic conditions. The observations of this study need further similar studies in a larger prospective controlled population for a more accurate determination of the prevalence of the cutaneous manifestations in CKD, HD and RTR group of patients.

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