

## Observational Study

# Skin disorders in peritoneal dialysis patients: An underdiagnosed subject

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## Abstract

**AIM:** To examine all skin changes in peritoneal dialysis (PD) patients followed up in our unit.

**METHODS:** Patients on PD program for at least three months without any known chronic skin disease were included in the study. Patients with already diagnosed skin disease, those who have systemic diseases that may cause skin lesions, patients with malignancies and those who did not give informed consent were excluded from the study. All patients were examined by the same predetermined dermatologist with all findings recorded. The demographic, clinical and laboratory data including measures of dialysis adequacy of patients were recorded also. Statistical Package for Social Sciences (SPSS) for Windows 16.0 standard version was used for statistical analysis.

**RESULTS:** Among the patients followed up in our PD unit, those without exclusion criteria who gave informed consent, 38 patients were included in the study with male/female ratio and mean age of 26/12 and 50.3 ± 13.7 years, respectively. The duration of CKD was 7.86 ± 4.16 years and the mean PD duration was 47.1 ± 29.6 mo. Primary kidney disease was diabetic nephropathy in 11, nephrosclerosis in six, uropathologies in four, chronic glomerulonephritis in three, chronic pyelonephritis in three, autosomal dominant polycystic kidney disease in three patients while cause was unknown in eight patients. All patients except for one patient had at least one skin lesion. Loss of lunula, onychomycosis and tinea pedis are the most frequent skin disorders recorded in the study group. Diabetic patients had tinea pedis more

frequently ( $P = 0.045$ ). No relationship of skin findings was detected with primary renal diseases, comorbidities and medications that the patients were using.

**CONCLUSION:** Skin abnormalities are common in PD patients. The most frequent skin pathologies are onychomycosis and tinea pedis which must not be overlooked.

**Key words:** Skin; Peritoneal dialysis; Onychomycosis; Tinea pedis; Xeroderma

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**Core tip:** Skin abnormalities are common in peritoneal dialysis patients. We aimed in our study to examine all skin changes in peritoneal dialysis patients followed up in our unit. Among the 38 patients included, all but one patient had at least one skin lesion. Loss of lunula, onychomycosis and tinea pedis are the most frequent skin disorders recorded in the study group. Diabetic patients had tinea pedis more frequently. No relationship of skin findings was detected with primary renal diseases, comorbidities and medications that the patients were using. Skin changes are commonly overlooked and should be sought for timely diagnosis and treatment.

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## INTRODUCTION

The chronic uremic status and the concomitant metabolic disorders may lead to a variety of structural and functional changes in the skin and its appendages. Dermatologic abnormalities are common in chronic kidney disease (CKD) and almost all patients have at least one of the cutaneous involvements<sup>[1]</sup>. These abnormalities range from the frequently seen xerosis and pruritus to the more rare disorders like hyperpigmentation, purpuric skin changes, acquired perforating dermatosis, and nail abnormalities<sup>[1-3]</sup>. Some of these disorders are described specifically in end stage renal disease (ESRD) like acquired perforating dermatosis, bullous dermatoses, metastatic calcification, and nephrogenic systemic fibrosis, while the others are nonspecific findings that may be associated with various entities. These include pruritus, color changes, xerosis, and half-and-half nails<sup>[4]</sup>. Symptoms associated with skin disorders can lead to varying degrees of discomfort, anxiety, depression, sleeping disorders and can affect the quality of life leading to distorted mental and physical health<sup>[5]</sup>.

The skin changes observed in hemodialysis (HD)

patients have been studied previously<sup>[2,6,7]</sup>. But, data about peritoneal dialysis (PD) patients regarding skin changes is lacking in the literature except for a few studies subjecting only skin color changes and xerosis<sup>[8-10]</sup> and another study reported in 1992<sup>[1]</sup>.

We aimed in our study to examine all skin changes in PD patients followed up in our PD unit.

## MATERIALS AND METHODS

Patients who gave informed consent among those who were on PD program for at least three months and followed up in our PD unit were included in the study. Patients were using either conventional glucose based solutions or biocompatible solutions as well as icodextrin. Patients with already diagnosed skin disease, those who have systemic diseases that may cause skin lesions, patients with malignancies and those who did not give informed consent were excluded from the study. All patients were examined once by the same predetermined dermatologist with all findings recorded. Baseline data including age, gender, concomitant diseases, duration of CKD and PD therapy, and the medications used by each patient were recorded. Concurrent medications and dose of monthly erythropoietin were also documented. Laboratory investigations in the form of complete blood counts, blood glucose, urea, creatinin, uric acid, aspartate transaminase, alanine transaminase, alkaline phosphatase, gamma glutamyl transferase, total protein, albumin, bilirubin, electrolytes, calcium, phosphorus, parathyroid hormone, ferritin, transferrin saturation, vitamin B12, folic acid, total cholesterol, Low-density lipoprotein cholesterol, and triglyceride levels at the time of physical examination and hepatitis panel collected from the most recent data in the patients' files were recorded. Among PD related parameters, weekly Kt/V urea, peritoneal Kt/V urea, residual renal glomerular filtration rate (GFR) and the transport type of the patients were obtained.

### Statistical analysis

Statistical Package for Social Sciences (SPSS) for Windows 16.0 standard version was used for statistical analysis. Numerical parameters were expressed as mean  $\pm$  SD. Intergroup comparisons of nonnumeric parameters were done by  $\chi^2$  test were used.  $P$  values less than 0.05 were accepted as statistically significant.

## RESULTS

Among the 52 patients followed up in our PD unit, three patients were already on treatment for a symptomatic skin disorder (one for psoriasis, two for xerosis cutis), one patient had breast cancer and 10 patients rejected to be examined by the dermatologist. The remaining 38 patients were included in the study. Female/male ratio and the mean age were 26/12 and  $50.3 \pm 13.7$  years, respectively. The duration of CKD was  $94.3 \pm 49.9$  mo and the mean PD duration was  $47.1 \pm 29.6$  mo. The PD modality was continuous ambulatory peritoneal dialysis

**Table 1** Biochemical and hematological laboratory data of the patients

Parameter	Mean $\pm$ SD	Parameter	Mean $\pm$ SD
Hemoglobin (g/dL)	10.9 $\pm$ 1.3	Phosphorus (mg/dL)	4.7 $\pm$ 1.0
Hematocrit (%)	32 $\pm$ 3	Parathyroid hormone (pg/mL)	600 $\pm$ 502
Ferritin (ng/dL)	288 $\pm$ 294	Alkaline phosphatase (U/L)	180 $\pm$ 342
Transferrin saturation (%)	25 $\pm$ 10	Alanine transaminase (U/L)	12.8 $\pm$ 5.4
Total protein (g/dL)	6.9 $\pm$ 0.5	Aspartate transaminase (U/L)	16.2 $\pm$ 6.6
Albumin (g/dL)	3.5 $\pm$ 0.3	Total bilirubin (mg/dL)	0.5 $\pm$ 0.4
Uric acid (mg/dL)	5.6 $\pm$ 1.0	Direct bilirubin (mg/dL)	0.1 $\pm$ 0.02
Calcium (mg/dL)	8.9 $\pm$ 0.6	Gamma glutamyl transferase (U/L)	24.8 $\pm$ 22.4

**Table 2** The medications used by the patients

Drug	n (%)	Drug	n (%)
Calcium-containing phosphorus binders	27 (71)	Alpha blockers	6 (16)
Diuretics	25 (66)	Acetylsalicylic acid	6 (16)
Active vitamin D	21 (55)	RAS blockers	5 (13)
Erythropoiesis stimulating agents	20 (53)	Cinacalcet	5 (13)
Calcium channel blockers	18 (47)	Allopurinol	3 (7)
Beta blockers	13 (34)	Fibrates	1 (2.6)
Statins	14 (37)	Sevalemer	1 (2.6)
Essential amino acid	10 (26)		

RAS: Renin-angiotensin-aldosterone system.

(CAPD) in 31 patients and automated peritoneal dialysis (APD) in seven patients. Diabetes mellitus was the most common cause of ESRD ( $n = 11$ , 28.9%). Other causes of ESRD were hypertensive nephrosclerosis ( $n = 6$ , 15.7%), urological disorders ( $n = 4$ , 10.5%), chronic glomerulonephritis ( $n = 3$ , 7.8%), chronic pyelonephritis ( $n = 3$ , 7.8%), autosomal dominant polycystic kidney disease ( $n = 3$ , 7.8%); while the etiology was not known in the remaining eight patients (21%). Hypertension ( $n = 24$ , 63.1%), diabetes mellitus ( $n = 13$ , 34.2%), hyperlipidemia ( $n = 11$ , 28.9%), hypothyroidism ( $n = 8$ , 21%), ischemic heart disease ( $n = 7$ , 18.4%), malignancies ( $n = 3$ , 7.8%), cerebrovascular disease ( $n = 1$ , 2.6%) were recorded as comorbidities.

The biochemical and hematological laboratory data of the patients are presented in Table 1. The mean Kt/V urea and weekly creatinine clearance values were  $2.46 \pm 0.67$  and  $78 \pm 33$  L/wk per  $1.73 \text{ m}^2$ , respectively. The medications that the patients were using are presented in Table 2.

All patients except for one patient had at least one skin lesion. The skin disorders recorded in patients are presented in Table 3. Loss of lunula, onychomycosis and tinea pedis are the most frequent skin disorders recorded in the study group.

Diabetic and nondiabetic patients were similar regarding skin findings except for tinea pedis which was more common in diabetic patients ( $n = 8$ , 61% vs  $n = 7$ , 28%;  $P = 0.045$ ). Patients using erythropoiesis stimulating agents have lower rate of xeroderma cutis compared to those not using them ( $n = 11$ , 55% vs  $n = 3$ , 17%;  $P = 0.014$ ) as well as lower rate of onychomycosis ( $n = 5$ , 25% vs  $n = 11$ , 61%;  $P = 0.024$ ). Loss of lunula was more rare in patients on statin treatment ( $n = 1$ , 7% vs  $n = 16$ , 67%;  $P < 0.001$ ).

Patients using diuretics had higher rate of tinea pedis ( $n = 13$ , 52% vs  $n = 2$ , 15%;  $P = 0.028$ ). No relationship of skin findings was detected with primary renal diseases, comorbidities and medications that the patients were using.

## DISCUSSION

Skin abnormalities are common in patients with ESRD. Previous studies were mostly about the skin findings in patients on HD treatment. On the other hand, studies about dermatological abnormalities in PD patients are limited to a few studies in which only hyperpigmentation and xerosis were searched for, and an old study in which PD patients were regarded as a separate group<sup>[1,8-10]</sup>.

It was reported in the study by Picó *et al.*<sup>[1]</sup> that patients on different dialytic treatments have different skin abnormalities. The pathologies underlying skin changes in uremic patients are accumulation of uremic toxins, metabolic abnormalities and dryness of the skin<sup>[11-13]</sup>. Besides, there are findings supporting the role of the type of dialysis on the profile of skin changes<sup>[2,14]</sup>. It has been reported that signs and symptoms related to skin increase after starting HD treatment<sup>[2]</sup>. There may also be role of the apparatus used during dialysis and chemical irritation due to dialysis solutions besides dialysis adequacy. In fact, allergic skin reactions have been reported in 10% of patients using icodextrin<sup>[15]</sup>.

We evaluated in our study the prevalence of skin abnormalities in patients on PD treatment and its relationship with primary renal disorder, comorbidities and the medications.

The most frequent skin finding in our study population was loss of lunula which was observed in 44.7% of our patients. No data was found in the literature about loss

**Table 3** The skin findings of the patients

Lesion	n (%)	Lesion	n (%)
Loss of lunula	17 (44.7)	Koilonychia	1 (2.6)
Onychomycosis	16 (42.1)	Pigmented purpuric dermatosis	1 (2.6)
Tinea pedis	15 (39.5)	Neurodermitis	1 (2.6)
Xeroderma cutis	14 (36.8)	Prurigo nodularis	1 (2.6)
Hyperpigmentation	11 (28.9)	Splinter hemorrhage	1 (2.6)
Nevus	6 (15.8)	Subungual hyperkeratosis	1 (2.6)
Acne	4 (10.5)	Verruca vulgaris	1 (2.6)
Uremic pruritus	3 (8.1)	Vitiligo	1 (2.6)
Contact dermatitis	2 (5.3)	Half and half nail	1 (2.6)
Folliculitis	2 (5.3)	Acne rosacea	1 (2.6)
Chronic eczema	1 (2.6)		

of lunula in PD patients. Ozturk *et al*<sup>[16]</sup> reported in their study related to nail changes in HD patients, that loss of lunula was present in 58% of HD patients while the rate was 8% in the control group. Renal transplant recipients were compared with healthy subjects regarding nail changes in Egypt<sup>[17]</sup>. The rates were similar in both groups (30% vs 26%), and the finding was accepted as a normal variation<sup>[17]</sup>.

Half and half nail was detected in only one patient in our study, while it was reported at an average rate of 20% in studies reaching even 76%<sup>[4,18,19]</sup>. Ozturk *et al*<sup>[16]</sup> reported that half and half nail was present in 15% of the HD patients involved in their study. Picó *et al*<sup>[11]</sup> also reported increased frequency of this abnormality in HD patients. All these findings lead to the idea that half and half nail may be related with HD specifically.

Hyperpigmentation was observed 28.9% of patients in our study. Increased melanocyte stimulating hormone levels, increased dermal melanin density, dermal accumulation of urochrome pigments and carotenoids are responsible for hyperpigmentation in patients with ESRD<sup>[14,20]</sup>. Increased length of time on dialysis and loss of residual renal functions increase the frequency of hyperpigmentation. Hyperpigmentation has been reported to be present in patients with ESRD at rates between 17% and 22%<sup>[1,2,21]</sup>. The frequency of splinter hemorrhages and echymoses was higher in relatively old studies, while their rates have decreased in recent studies<sup>[14]</sup>. Patients in our study did not have any sign of skin hemorrhage.

Xerosis cutis is one of the most frequent skin lesions in patients with ESRD. Besides decreasing the quality of life, xerosis caused delayed wound healing and propensity to skin infections<sup>[13,22]</sup>. The rate of xerosis cutis in the literature is about 50%-85% while the corresponding number in our study is 36.8%<sup>[23]</sup>. Morton *et al*<sup>[10]</sup> found higher incidence of xerosis and pruritus in PD patients compared to HD patients. They stated that this difference may be related to defects in calcium homeostasis.

We detected onychomycosis and tinea pedis in 42.1% and 39.5% of the patients, respectively in our study. The corresponding rates were 52% and 25% in the study by Picó *et al*<sup>[11]</sup> which is the single study in which skin findings of PD patients were evaluated. Moreover, the

authors stated that they were more frequent in diabetic PD patients compared to HD patients and non-diabetic counterparts respectively. Tinea pedis was more frequent in diabetic subjects in our study also ( $P = 0.045$ ). The glucose content of dialysis solutions and the resultant worsening in glucose regulation may cause a propensity for infection.

Patients using diuretics had higher rate of tinea pedis ( $P = 0.028$ ). This may be related with hypervolemia and so edema which necessitates use of diuretics. But it can be just a speculation, because clinical findings of patients were not recorded.

There was no correlation between the frequency of skin lesions and other comorbid diseases, dialysis adequacy parameters and metabolic abnormalities including hyperphosphatemia.

Patients using erythropoiesis stimulating agents have lower rate of xeroderma cutis and lower rate of onychomycosis compared to those not using them.

The other less frequent skin findings detected in our patients are presented in Table 2. It was striking that acquired perforating dermatosis, bullous dermatoses, metastatic calcification and calciphylaxis which are regarded as specific manifestations of HD patients and related to mortality in some cases, were not reported in our study group<sup>[14,24,25]</sup>. There was no control group consisting of HD in our study; but when compared with the results of studies carried out with HD patients, PD patients seem to be protected from severe skin lesions. Onychomycosis and tinea pedis comprised the majority of skin pathologies in our study<sup>[11]</sup>.

There may be several reasons for the difference between these two dialysis modalities regarding patterns of skin pathologies. The ultrafiltration process spread to 24 h protects PD patients from hemodynamic instability; and generally prevents excessive ultrafiltration. So, a more stable hemodynamic status provides better and continuous tissue perfusion. More importantly, HD procedure itself may cause skin hypoxia. Previous studies showed that transdermal oxygen perfusion may decrease by as much as 15-20 mmHg during hemodialysis and dermal microcirculation may be distorted<sup>[26,27]</sup>. The type of the HD membrane used may be effective on this effect<sup>[28]</sup>. The involvement of skin, which is the most distal organ in



the body, is a predictable result of hypoxemia and tissue hypoxia. PD, with more stable hemodynamic status and better skin oxygenation, may allow lesions easy to cope with to be more frequent. On the other hand, exposure to high amount of glucose for a prolonged time may increase the frequency of fungal skin infections in both diabetic and nondiabetic PD patients.

Skin abnormalities are common in in PD patients. The spectrum of clinical presentation is different from HD patients based on recent reports. The most frequent skin pathologies are onychomycosis and tinea pedis which must not be overlooked.

## COMMENTS

### Background

Dermatologic abnormalities are common in chronic kidney disease and almost all patients have at least one of the cutaneous involvements. Some of these disorders are described specifically in end stage renal disease while the others are nonspecific findings that may be associated with various entities. Symptoms associated with skin disorders can lead to varying degrees of discomfort, anxiety, depression, sleeping disorders and can affect the quality of life leading to distorted mental and physical health.

### Research frontiers

The skin changes observed in hemodialysis patients have been studied previously. But, data about peritoneal dialysis patients regarding skin changes is lacking in the literature except for a few studies subjecting only skin color changes and xerosis. The authors aimed to examine all skin changes in peritoneal dialysis (PD) patients followed up in the authors' PD unit.

### Innovations and breakthroughs

Data about peritoneal dialysis patients regarding skin changes is limited in the literature. This study showed that skin abnormalities are common in PD patients. The spectrum of clinical presentation is different from hemodialysis patients based on recent reports. The most frequent skin pathologies are onychomycosis and tinea pedis which must not be overlooked.

### Terminology

Peritoneal dialysis is an option for patients with end stage renal disease. The most commonly encountered skin lesion in chronic kidney disease are xerosis and pruritus. Xerosis is abnormal dryness of the skin which also may cause pruritus.

### Peer-review

Skin abnormalities are common in in PD patients. The most frequent skin pathologies are onychomycosis and tinea pedis which must not be overlooked.

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