

Original Article

**Mucocutaneous Manifestations and Nail Changes in Patients with
End-Stage Renal Disease on Hemodialysis**

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ABSTRACT. Mucocutaneous manifestations are common among patients on hemodialysis (HD). This study was undertaken to determine the prevalence of mucocutaneous manifestations in patients with end-stage renal disease (ESRD) who are on HD. In this cross-sectional, descriptive and analytic study conducted in 2009, 100 patients on HD at the Five Azar Hospital in Gorgan city were randomly selected. All the patients underwent detailed examination by a dermatologist to look for lesions in the skin, hair, nail and mucous membranes; if felt necessary, biopsy was obtained from the lesions. The findings were statistically analyzed using SPSS-13 software. For evaluation of normality of distribution, Kolmogorov-Smirnov was used, for quantitative variables Mann-Whitney and T-test (abnormal distribution) were used and for qualitative variables, Chi-2 and Fisher were used. In this study, *P*-value less than 0.05 was considered significant. Fifty-one males and 49 females were enrolled. The mean age was 49 ± 12 years. Diabetes was the most common cause of ESRD. In 95% of the patients, at least one mucocutaneous manifestation was present. Xerosis (78.3%) was the most common lesion, followed by pruritus (39.1%), lentigo (34.8%), skin discoloration (32.6%), leukonychia (32%) and thinning of the nail bed (24%). Xerosis, scaling, lentigo, folliculitis, idiopathic guttate hypo-pigmentation, leukonychia and half and half nail were associated with age. A significant relationship was seen between duration on dialysis and skin discoloration and leukonychia. Clubbing had a significant association with calcium-phosphorus product ($Ca \times P$). There was a significant association between serum ferritin level and pruritus and tinea versicolor lesions. Our study shows that mucocutaneous manifestations are common among patients with ESRD. Identification of these manifestations and their association with causative factors are useful for preventing the lesions.

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Introduction

The prevalence of mucocutaneous manifestations is high among dialysis patients. This occurs because of numerous factors such as uremia, metabolic disorders, dialysis and side-effects of immunosuppressive drugs. Patients

on hemodialysis (HD) are known to develop cutaneous manifestations ranging from infections to malignancies.¹ Broadly, in all patients with advanced renal insufficiency, at least one cutaneous manifestation has been observed, and the most common lesion is skin discoloration.² In addition, new cutaneous lesions may develop with increasing age. Sometimes, cutaneous changes maybe the first important sign in patients with chronic renal failure.³

Prolonged dialysis is associated with mucocutaneous changes.^{4,5} Among them, pruritus has been reported as being the most common in some investigations. Although its etiopathogenesis is unknown, factors such as secondary hyper-parathyroidism, two-capacity ion disturbance, allergy, iron deficiency anemia, neuropathy and mast cell proliferation have been suggested as causative factors.⁶ In some other studies, skin discoloration has been mentioned as the most common cutaneous complication.⁷ Cutaneous lesions in patients with end-stage renal disease (ESRD) are categorized into specific and non-specific lesions.⁸

Reports from different parts of Iran have described various cutaneous manifestations in patients on HD, which differ based on race, nutritional condition, geographic location, socio-economic status of the patients and accuracy of patients' examination.⁹

Because cutaneous manifestations may have a cosmetically destructive effect, in addition to complications such as pruritus that disturbs the patient's comfort, we designed this study to determine the prevalence of mucocutaneous manifestations in patients on HD at the Five Azar Hospital in Gorgan and demonstrate its relationship with factors such as gender, age, duration on dialysis, serum ferritin level and calcium-phosphorous product. Detecting this relationship might help in finding a way for reducing these lesions.

Materials and Methods

In this cross-sectional, descriptive, analytic study, 100 patients on HD at the Five Azar Hospital were selected by a regular random method. Written consent was obtained from all

the study patients. All the study patients were examined in detail by a dermatologist in a location with adequate light and routine instruments for skin examination, such as manual light, magnifying glass, etc. Biopsy from the cutaneous lesions was taken, when felt necessary. A pathologist would then examine the biopsy samples and the findings were entered in previously prepared forms. Demographic information such as age and gender, cause of renal failure and duration on dialysis were extracted from the patients' files. Information about the patients' laboratory tests were obtained from the mean of three recent tests. Calcium-phosphorus product more than 55 and serum ferritin level greater than 800 ng/mL were considered high values.

Statistical Analysis

Data were analyzed using SPSS software (Statistics Package for Social Sciences version 13 SPSS Inc; Chicago, IL, USA). Kolmogorov-Smirnov was used for testing normality. We used the t-test to evaluate the association between age and muco-cutaneous manifestations and Mann-Whitney test to assess the relationship between duration on dialysis and muco-cutaneous manifestations for quantitative data, and chi-2 and Fisher tests for qualitative data. In this study, *P*-value less than 0.05 was considered statistically significant.

Results

Of the 100 patients enrolled in the study, 51 (51%) were male and 49 (49%) were female. Mean age of the patients was 49 ± 12.3 years and mean duration on dialysis was 40 ± 13 months. Diabetes was the most common cause of renal failure in these patients ($n = 45$), followed by hypertension ($n = 28$), glomerulonephritis ($n = 13$), polycystic kidney ($n = 4$) reflux nephropathy ($n = 4$) and unknown cause in six cases. Xerosis was the most common skin manifestation in these patients, and was seen in 78.3% of the patients. This was followed in frequency by pruritus (39.1%), lentigo (34.8%), skin discoloration (32.6%), leukonychia (32%)

Table 1. Prevalence and binomial exact 95% confidence interval (CI) of mucous membrane and cutaneous manifestations in patients with advanced and end-stage renal failure.

Manifestation	Number	Prevalence %	95% CI of prevalence
Discoloration	30	32.6	23.2–43.17
Pruritus	36	39.1	29.11–49.86
Xerosis	72	78.3	68.44–86.18
Scaling	19	20.7	12.91–30.35
Lentigo	32	34.8	25.14–45.42
Folliculitis	4	4.3	1.20–10.75
Ecchymosis	6	6.5	2.43–13.65
Tinea versicolor	4	4.3	1.20–10.75
Idiopathic guttate hypomelanosis	20	21.7	13.81–31.55
Scrotal tongue	4	4	1.10–9.92
Glossitis	2	2	0.26–7.63
Oral candida	2	2	0.26–7.63
Pigmentation of mucous membrane	2	2	0.26–7.63
Leukonychia	32	32	23.02–42.07
Pitting	8	8	3.51–15.15
Thinning of nail plate	24	24	16.02–33.57
Half and half nail	8	8	3.51–15.15
Koilonychia	5	5	1.64–11.28
Clubbing	3	3	0.62–8.51
Subungual hyperkeratosis	7	7	2.8–13.90
Tinea unguis	2	2	0.26–7.63
Hirsutism	3	3	0.62–8.51
Eyebrow hair loss	7	7	2.8–13.90

and thinning of the nail bed (24%). The prevalence and binomial exact 95% confidence interval (CI) of the mucous membrane and cutaneous manifestations in the study patients have been shown in Table 1.

Results of the chi-2 test showed that association between gender and lentigo was statistically significant ($P = 0.042$); 21 females versus 11 males had lentigo. Association between age and cutaneous manifestations has been shown in Table 2. The association between age and xerosis ($P < 0.01$), scaling ($P = 0.04$), lentigo ($P < 0.01$), folliculitis ($P < 0.01$), idiopathic guttate hypo-pigmentation ($P < 0.01$), leukonychia ($P = 0.01$) and half and half nail ($P < 0.01$) was statistically significant.

Increasing duration on dialysis showed a significant association with cutaneous discoloration ($P = 0.031$) and leukonychia ($P = 0.041$). The Ca \times P product was significantly associated only with digital clubbing ($P = 0.027$), while the serum ferritin level had a significant association with pruritus ($P = 0.048$)

and fungal lesion (tinea versicolor) ($P = 0.047$).

Discussion

Patients with ESRD who are on HD present with various mucocutaneous manifestations. In the current study, 95% of the patients had at least one mucocutaneous lesion. Among these manifestations, skin xerosis is one of the most common findings, and was seen in 78.3% of the patients in our study. The prevalence of xerosis has been reported from to be 65% to 79% in various studies.^{3,7,8} In a study performed by Haji Heidari et al,⁹ the prevalence of xerosis was 23%. This difference may be related to the prevailing climatic conditions; other factors might also be present. In our study, there was a significant association between skin xerosis and increasing age in the patients. Another common cutaneous manifestation in our study was pruritus, with a prevalence rate of 39.1%. In the different studies published, the prevalence of pruritus has varied

Table 2. Association between age and mucocutaneous manifestations in the patients with advanced end-stage renal failure.

Manifestation	Age (mean \pm SD)		P-value
	Present	Not present	
Discoloration	48.9 \pm 14.7	52.5 \pm 18.7	0.350
Pruritis	50.7 \pm 17.8	51.7 \pm 17.4	0.792
Xerosis	54.3 \pm 16.3	40.7 \pm 17.90	<0.01
Scaling	58.6 \pm 14.9	49.4 \pm 17.7	0.040
Acne	37 \pm 11.37	52 \pm 17.5	0.094
Vitiligo	68 \pm 9.8	50.8 \pm 17.5	0.094
Bulla	52 \pm 0	51.3 \pm 17.6	-
Lentigo	61.5 \pm 14.5	45.9 \pm 16.6	<0.01
Folliculitis	73.7 \pm 10.2	50.3 \pm 17.1	<0.01
Ecchymosis	63.7 \pm 15.8	50.5 \pm 17.4	0.074
Tinea versicolor	36.2 \pm 12	52 \pm 17.4	0.078
Idiopathic guttate hypomelanosis	62.5 \pm 14	48.2 \pm 17.2	<0.01
Scrotal tongue	49.5 \pm 11.7	51.8 \pm 17.9	0.797
Oral candida	60.5 \pm 16.3	51.6 \pm 17.7	0.481
Pigmentation of mucus membrane	60.5 \pm 6.4	51.6 \pm 17.8	0.0481
Leukonychia	58.1 \pm 14.9	48.8 \pm 18.1	0.013
Pitting	58.2 \pm 12	51.2 \pm 18	0.279
Thinning of nail bed	52.2 \pm 17.4	51.6 \pm 17.8	0.893
Half and half nail	73.9 \pm 11.3	49.8 \pm 16.8	<0.01
Koilonychia	60.8 \pm 14.2	51.3 \pm 17.7	0.241
Clubbing	40.7 \pm 5.1	52.1 \pm 17.8	0.272
Subungual hyperkeratosis	61.3 \pm 11.6	51.2 \pm 17.8	0.138
Tinea unguis	69 \pm 8.5	51.4 \pm 17.6	0.163
Hirsutism	61.3 \pm 12.0	51.4 \pm 17.7	0.341
Eyebrow hair loss	59.8 \pm 13.2	51.1 \pm 17.8	0.208
Onycholysis	58.5 \pm 9.2	53.0 \pm 17.8	0.676

between 19% and 90%.^{2,3,7,8,10,11} The severity of pruritus was variable; the majority complained of severe and frequent pruritus that resulted in disturbance of sleep and daily activity. In one study, one-third of the patients before initiating HD and two-third of the patients after initiating HD complained of pruritus.¹⁰ In another study, pruritus began after starting HD in about 50% of the patients.⁹ In our study, because of incomplete patient history, we could not find any association between pruritus and the time of commencement of HD. In addition, no significant association was found with dialysis duration; however, there was a significant association between serum ferritin level and occurrence of pruritus. Another common cutaneous manifestation was lentigo, which was detected in 34.8% of the patients; this finding has not been reported in

the study of Roudsari et al,¹² while in the study of Haji Heidari et al, the reported prevalence was 1%.⁹ In our study, lentigo showed a significant association with increasing age. Skin discoloration was the next common finding, seen in 32.6% of our study patients. Udayakuma et al have reported a prevalence of hyperpigmentation of 43%,³ while in the report of Haji Heidari et al, the prevalence of skin discoloration was 66.33%.⁹ In the study of Pico et al, alteration in skin color was the most common finding.² This discoloration has been reported as paling, becoming yellow and hyperpigmentation. These studies have shown that hyperpigmentation increases with increasing duration on dialysis;⁷ however, Pico et al showed that hypo-pigmentation decreases with increasing dialysis duration.² In our study, there was a direct relationship between dialysis

duration and hyper-pigmentation. Although hyper-pigmentation has been reported as the most common cutaneous finding in patients with chronic renal failure, some cases of hypo-pigmentation have been reported in these patients.¹³ In our recent study, three cases had vitiligo. Idiopathic guttate hypo-pigmentation was detected in 20 cases among our study patients that had significant association with increasing age. We found post-inflammatory hypo-pigmentation in two patients. Another common manifestation was leukonychia, which was found in 32% of the study patients. In other studies, its prevalence was 23–31%.^{2,7,8} Haji Heidari et al reported a prevalence of leukonychia of 16.8% in their study. In this study, the association between leukonychia and age was significant. In our study patients, nail changes were present in 57 patients (57%), and the most common finding was thinning of the nail bed, seen in 24% of the patients. In the study of Hajheidari et al, the prevalence was 45%; this was the most common finding they encountered.⁹ Mucosal disorders were seen in 10% of our study patients, with the most common manifestation being the scrotal tongue (4%). Hajheidari et al have reported a prevalence of 24%, with the most common finding being furred tongue (8%),⁹ while Yaghubi et al reported a prevalence of mucosal disorders of 29%, with the most common finding being gingivitis.⁸ Fungal lesions have been reported in 0–70% of patients with ESRD in various studies.^{2,7,9} In our study, cutaneous fungal lesions (tinea versicolor) were detected in 4.3% of the patients, and its association with serum ferritin level was significant. Nail fungal lesions have been reported in 2% of the patients. Hajheidari et al did not find any patients with fungal infection in their study,⁹ while Naderi et al reported fungal infection in 1.9%⁷ and Pico et al in 70% of their patients.²

In conclusion, mucocutaneous manifestations are common in patients with ESRD on HD. The reported prevalence rates vary in different studies. These differences may be examiner-related or may be due to environmental factors

and laboratory differences at the time of examination.

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