

Cutaneous and Mucosal Manifestations in Patients on Maintenance Hemodialysis

A Study of 101 Patients in Sari, Iran

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Introduction. Cutaneous and mucosal disorders are of the common problems in patients on long-term hemodialysis. The aim of this study was to evaluate the frequency of dermatologic problems among patients with end-stage renal disease (ESRD) who receive maintenance hemodialysis.

Materials and Methods. One hundred and one patients with ESRD on hemodialysis were studied. All of patients were fully examined for cutaneous, nail, hair, and mucosal changes by a single dermatologist. Complementary diagnostic measures such as biopsy of the lesions were carried out, where necessary.

Results. The patients were 43 (42.6%) women and 58 (57.4%) men with a mean age of 50.0 ± 12.3 years. The duration of hemodialysis was 36.0 ± 11.0 months. Dermatologic examination revealed that 95 patients (94.1%) suffered from cutaneous problems. Skin discoloration (66.3%) was the most common skin lesion. Pruritus was seen in 38.6% of the patients. Hair, mucous membrane, and nail problems were present in 37.6%, 23.8%, and 43.6% of the patients, respectively. There was a significant association of the number of cutaneous manifestations with the age of the patients ($P = .001$), but not with hemodialysis duration. The most common hair disorder was hair loss in 9.9% of the patients and the most common oral mucosal problem was furred tongue (7.9%). Of the nail disorders, nail bed paleness (16.8%) was the most common.

Conclusions. Cutaneous and mucosal lesions in patients with ESRD can vary from each patient population to another. Factors such as diagnostic accuracy, climate, and early treatment influence some disorders such as pruritus, xerosis, and infections.

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INTRODUCTION

The effects of chronic kidney disease (CKD) are complex as it causes dysfunction of multiple organs. The disease may be followed by different symptoms such as skin manifestations, and sometimes these symptoms may be the first important sign of CKD.¹ In almost all patients with progressive kidney failure, at least one of the cutaneous involvements can be observed.² Treatment of all manifestations is not necessary, but therapeutic

management will be required for some diseases such as penetrating dermatosis, calcified disorders, and bullous diseases.³ Likewise, although many of the patients with end-stage renal disease (ESRD) can improve their quality of life by hemodialysis, in case of denying kidney transplantation, prolonged hemodialysis itself will be associated with certain cutaneous and mucosal complications or changes in the type of dermatologic involvement and manifestations.^{4,5}

The cutaneous manifestations of ESRD are divided into 2 specific and nonspecific groups.³ Studies from different regions of Iran have revealed different cutaneous manifestations in patients on hemodialysis,^{6,7} which may depend on the race of the patients, nutrition, geographic and economic conditions, accuracy of the examinations, and the light of the environment in which dermatologic examinations have been done. The aim of our study was to evaluate cutaneous and mucosal manifestations in the patients on maintenance hemodialysis at the clinical centers of Mazandaran Province, Iran.

MATERIALS AND METHODS

This cross-sectional study was done on 101 patients at hemodialysis centers of Mazandaran province, Iran, in 2005. They were patients with ESRD who were on maintenance hemodialysis for at least 3 months. Informed consent was obtained from all of the enrolled patients.

Data of the patients on age, sex, predisposing factors, underlying cause of ESRD, and duration of hemodialysis treatment were collected. A dermatologist examined all of the patients for examination of the skin, hair, nail, and mucosal tissues. Culture and biopsy of the lesions were done if needed. Pathologic examinations were done on specimens with hematoxylin-eosin staining. The collected data were analyzed using the SPSS software (Statistical Package for the Social Sciences, version 11.0, SPSS Inc, Chicago, Ill, USA), and the Spearman rho test was used to evaluate correlations between the variables. Continuous data were demonstrated as mean \pm standard deviation. A *P* value less than .05 was considered significant.

RESULTS

Of the 101 studied patients, 43 (42.6%) were women and 58 (57.4%) were men with a mean age of 50.0 ± 12.3 years. The duration of hemodialysis was 36.0 ± 11.0 months. None of the patients had a history of peritoneal dialysis. The most common causes of ESRD in the patients were hypertension in 30 (29.7%), diabetes mellitus in 12 (11.9%), diabetes mellitus with hypertension in 14 (13.9%); and unknown causes in 14 (13.9%). It was found that 18 patients (17.8%) were infected with hepatitis C virus, 12 (11.9%) with hepatitis B virus, and 2 (1.9%) with both of the viruses. None of the patients were positive for human immunodeficiency virus.

Dermatologic examination revealed that 95 patients (94.1%) suffered from at least 1 type of skin problems (Table). Pruritus was seen in

Frequency of Cutaneous and Mucosal Manifestations in Patients on Hemodialysis

| Lesion/Manifestation | Patients (%) |
|----------------------------------|--------------|
| Skin | |
| Skin discoloration | 67 (66.3) |
| Pruritus | 39 (38.6) |
| Ecchymosis | 30 (29.7) |
| Xerosis | 23 (22.8) |
| Scaling | 10 (9.9) |
| Pressure sore | 2 (2.0) |
| Stria | 2 (2.0) |
| Acne | 2 (1.0) |
| Vitiligo | 1 (1.0) |
| Lentigo | 1 (1.0) |
| Eccrine hidrocystoma | 1 (1.0) |
| Erythroderma | 1 (1.0) |
| Bulla and folliculitis | 1 (1.0) |
| Neurotic excoriation | 1 (1.0) |
| None | 6 (5.9) |
| Hair | |
| Scalp hair loss | 10 (9.9) |
| Whole body hair loss | 9 (8.9) |
| Low limbs hair loss | 8 (7.9) |
| Drying and hair fragility | 2 (2.0) |
| Hair discoloration | 2 (2.0) |
| Hair loss and hair dryness | 1 (1.0) |
| Hair loss and hair discoloration | 1 (1.0) |
| Hirsutism | 1 (1.0) |
| None | 63 (62.4) |
| Mucous membrane | |
| Furred tongue | 8 (7.9) |
| Scrotal Tongue | 6 (5.9) |
| Deficiency glossitis | 3 (3.0) |
| Herpes simplex | 3 (3.0) |
| Gingivitis | 2 (2.0) |
| Aphthous | 1 (1.0) |
| Angular chilitis | 1 (1.0) |
| None | 77 (76.2) |
| Nail | |
| Apparent leukonychia | 17 (16.8) |
| Half-and-half nail | 7 (6.9) |
| Koilonychia | 5 (5.0) |
| Subungual hyperkeratosis | 4 (4.0) |
| Onycholysis | 3 (3.0) |
| Undiagnosable lesion | 2 (2.0) |
| Onychogryposis | 2 (2.0) |
| Alternate | 1 (1.0) |
| White pinkish band | 1 (1.0) |
| Clubbing | 1 (1.0) |
| Anonychia | 1 (1.0) |
| Cyanosis | 1 (1.0) |
| None | 57 (56.4) |

38.6% of the patients. With dialysis, the severity of pruritus had increased in 18 patients, had not altered in 13, and had decreased in 8. Hair, mucous membranes, and nail problems were present in 38 (37.6%), 24 (23.8%), and 44 (43.6%) patients, respectively. Skin biopsy was taken from 3 patients and pathologic examination showed eccrine hidrocystoma, neurotic excoriation, and aphthous. There was a significant association of the number of cutaneous manifestations with the age of the patients ($P = .001$), but not with hemodialysis duration. The most common hair disorder was hair loss in 9.9% of the patients and the most common oral mucosal problem was furred tongue (7.9%). Of the nail disorders, nail bed paleness (16.8%) was the most common.

DISCUSSION

Of the total studied patients on maintenance hemodialysis, 95% had at least one skin lesion; 44%, one nail problem; 38%, hair problem; and 23% mucosal problem. Pruritus, an irritating problem in 39% of our patients, is one of the most common cutaneous complaints in patients with CKD.^{2, 8-10} Different reports indicate the prevalence of pruritus in the hemodialysis patients 19% to 90%.^{1,2,6,7,10-12} A potential explanation of the difference in the rate of pruritus between our study and the others' may be the relatively low frequency of xerosis in our patients, which is due to the geographic condition. Uremic pruritus can be localized or generalized. The severity of itching is variable and most of the patients experience severe and recurrent itching that disturbs during sleep and daily activities. One-third of the patients prior to dialysis and two-third after dialysis experience itching.¹⁰ In our study, the severity of pruritus had increased in nearly half of the patients since dialysis had been started.

In 67 (66.33%) of the patients in our study, skin discoloration was observed. Udayakumar and colleagues reported hyperpigmentation in 43% of the patients,¹ and in some other studies, the frequency of skin discoloration was reported between 20% and 80%.^{2,6,7,13} Pico and coworkers studied 102 patients on hemodialysis, in whom skin discoloration was the most common finding.² Skin discoloration in the patients included pallor, yellowish, and hyperpigmentation of the skin in our patients. It has been shown that the prevalence

of hyperpigmentation increases with the term patients being under hemodialysis.⁷ However, Pico and colleagues reported reduction of disseminated pigmentation with increase in term of dialysis. They believed that reduction of exposure to the sun light and chronic condition of the disease could have been the cause of this phenomenon. Noteworthy is that evaluation of the skin color depends on the accuracy of the examiner's vision and the type and intensity of the environment light. Therefore, misdiagnosis is probable; hence, examination by a more accurate method such as color meter reflectance is recommended.¹¹ Although hyperpigmentation is known as the most common type of skin manifestation in the patients with CKD, there are some reports of hypopigmentation, too.⁸ In the present study, one case of vitiligo was observed.

Thirty percent of our patients had skin ecchymosis, generally, around the arteriovenous fistula. Ecchymosis reported by other investigators was present in about one-fifth of the patients.⁷ Twenty-three percent of our patients had xerosis. In some studies, xerosis was reported in 65% to 79% of the patients.^{1,6,7} The skin of patients on hemodialysis might be dry and xerotic, and in more severe cases, a dry scaled skin similar to ichthyosis is seen. Diagnosis of xerosis is clinically depended on the examiner's diagnostic skill, as well as the environmental condition such as the humidity and temperature. Therefore, the highly humid climate of our region, particularly of the summer temperature can cause this low frequency of xerosis in our patients.

More than half of the patients in the present study had at least 1 hair disorder, the most common of which were hair loss (10%) and disseminated hair loss of the entire body, particularly of the lower limbs (9%). Generally, it has been shown that long-term chronic diseases result in hair loss.¹⁴ Xerosis and pruritus are the reasons of hair loss. Mucosal disorders were observed in 24% of the patients. Furred tongue, scrotal tongue, and deficiency glossitis were seen in 8%, 6%, and 3% of the patients, respectively, and the frequency of herpes simplex and gingivitis were 3% and 2%, respectively. Yaghubi and colleagues reported mucosal disorders in 29% of their patients⁶; the most common disorders were gingivitis in 14 cases, hairy black tongue in 6, and scrotal tongue in 5.

Forty-five percent of our studied patients had changes in their nails. In the previous studies, the frequency of nail changes, excluding onychomycosis, was from 66% to 79%.^{2,6,7,15} In our study, the most common finding was apparent leukonychia (17%), while reports of other investigators indicated 23% to 31% frequency of leukonychia.^{2,6,7} Half-and-half nail in our study was observed in 6.9% of the patients, while others reported it in 7% to 39% of the patients.^{1,2,6,7,15}

In this study, there were 2 cases of acne and 1 case of neurotic excoriation. There was 1 case of skin infection (folliculitis and various furuncles). No fungal infection was observed in our patients. Naderi and associates⁷ reported fungal infections in 1.9% of the patients, and Pico and colleagues reported infections in 70% of the patients.² Absence of any fungal infection in our study may be due to early referring, early diagnosis, and treatment. Moreover, in this study, no case of metastatic calcification, bullous dermatosis, or acquired perforating dermatosis was observed. While, in other studies, 2% to 21% of the patients were found to have acquired perforating dermatosis.^{1,6,7} One of the causes of dermatosis is the trauma due to skin scratching. Lack of this symptom in our patients can be described by the lower frequency of pruritus. In addition, diabetes is one of the risk factors of this lesion which was seen less frequently in our patients.

Cutaneous disorders are common in patients with ESRD. Numerous factors influence the prevalence rate of these conditions and their diagnosis. In this study, we emphasized on the accuracy of our findings. The difference between our findings and the other similar studies on some specific cutaneous manifestations in patients on hemodialysis may be due to differences of climatic condition of the region, season the study was conducted, race, socioeconomic condition of patients, etc.

CONCLUSIONS

Further similar studies for more accurate determination of the cutaneous manifestation prevalence in patients with ESRD are necessary. Some common lesions such pruritus, skin infections, and xerosis were less frequent in our patients than expected. We suggest that some prophylactic procedures such as application of moisturizers for prevention of dryness, avoiding sun light

for prevention of pigmentation changes and malignancies, and mouth hygiene for prevention of oral lesions can help patients on hemodialysis to have better cutaneous and mucosal conditions.

CONFLICT OF INTEREST

None declared.

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