Dermatological Manifestations Among Patients on Maintenance Hemodialysis

Akram Beheshti, MD; Malihe Charkhchian, MD; Amir Abdollah Zangivand, MD; Afsaneh Sedighi, MD; Golnoosh Amri, MD

Abstract: Introduction. Patients with chronic kidney disease on hemodialysis (HD) undergo many dermatological signs and symptoms during treatment. The aim of this study was to investigate the prevalence of skin manifestations among the patients on maintenance HD in the HD center of Boo Ali-Sina Hospital (Qazvin, Iran) and compare them with the general population. Methods. From June 2012 to July 2012 a case-controlled study was performed with 149 patients with end-stage renal disease undergoing regular HD (HD group) and 150 individuals who were randomly selected (control group) from healthy hospital staff at Boo Ali-Sina Hospital. A dermatologist examined all individuals in both groups to assess of skin, hair, nail, and mucosal tissues. Results. Overall, 108 of the patients in the HD group and 54 of the individuals in the control group were found to have at least 1 cutaneous and mucosal manifestation. Pruritus, skin discoloration, ecchymosis, drying and hair fragility, leukonychia, absent lunula, and half and half nails were more frequent in the HD group than compared to the control group (P < 0.05). Although no significant correlation between dermatological manifestations and age ≥ 65 or diabetes mellitus were made, multiple logistic regression analysis indicated that male sex, hypertension, and long-term HD were associated with dermatological manifestations. Discussion. In the present study, cutaneous and mucosal manifestations ranged from 36% in the control group to 72.4% in the HD group. The results also indicate a relationship between cutaneous and mucosal manifestations, and male sex, hypertension, and duration of dialysis in HD patients.
the fifth stage of CKD, and can lead to uremic syndrome, which can cause death in patients with this condition if toxins accumulate in the body.³

Patients with CKD on hemodialysis (HD) experience many dermatological symptoms during treatment. Since these symptoms are only detected in advanced cases of the disease, they are not valuable in the diagnosis of kidney failure.⁴ Complete and precise examination of skin, hair, nails, and mucosal membranes may reveal a wide variety of the following symptoms including hyperpigmentation, xerosis, ichthyosis, pruritus, onychomycosis, onycholyis, splinter hemorrhages, subungual hyperkeratosis, brittle hair, and sparse body scalp hair.⁵⁻⁸

These diseases are sometimes related to underlying renal illness but are more often associated, directly or indirectly, with uremia in its broadest sense. With a nearly 100% prevalence in dialysis populations, skin disorders are frequently the subject of patients’ complaints.⁶ Studies from different regions of the world have revealed different cutaneous manifestations in patients on HD.⁶⁻¹¹ However, few of these were controlled studies conducted to compare the prevalence of these disorders in patients undergoing dialysis with healthy individuals in the general population.¹²⁻¹³ Therefore, in the present study the aim was to compare the prevalence of skin manifestations among patients on maintenance HD in Boo Ali-Sina Hospital, Qazvin, Iran, to the general population of the city.

**Keypoints**

- Studies from different regions of the world have revealed different cutaneous manifestations in patients on hemodialysis.⁶⁻¹¹
- Few of these were controlled studies conducted to compare the prevalence of these disorders in patients undergoing dialysis with healthy individuals in the general population.¹²⁻¹³
- In the present study the aim was to compare the prevalence of skin manifestations among patients on maintenance HD in Boo Ali-Sina Hospital, Qazvin, Iran, to the general population of the city.

**Materials and Methods**

**Patients.** From June 2012 to July 2012 a case-controlled study was performed. One hundred and forty-nine patients with CRF undergoing HD (HD group), and 150 individuals who were randomly selected from healthy hospital staff (control group) were examined for cutaneous, mucosal, nail, and hair manifestations at Boo Ali-Sina Hospital in Qazvin, Iran. Patients had undergone HD for a renal transplant failure. Those who had undergone peritoneal dialysis were not included. Approval was obtained from the ethics committee of the Qazvin University of Medical Sciences prior to initiating the study, and the protocols used conformed to the ethical guidelines of the 1975 Helsinki Declaration. All participants were informed about the study protocols and written consent was obtained from each one.

**Data collection and variable definition.** The patients’ history consisted of age, sex, primary and secondary diagnoses, medications, type of kidney disease, duration of renal failure and HD, and changes in nails were noted. The quality of HD was assessed during the study period by calculating Kt/V using the Daugirdas formula, as described in the Dialysis Outcomes Quality Initiative guidelines.¹¹ All individuals in both groups were examined by a dermatologist for assessment of the skin, hair, nail, and mucosal tissues.

**Statistical analysis.** The collected data were analyzed using the SPSS software (Statistical Package for the Social Sciences, version 11.0, SPSS Inc, Chicago, IL). The Fisher’s exact chi-square test and the Student t test were used to assess statistical relationships between variables. The authors elaborated demographic characteristic, medical data in a multivariate analysis. Continuous data were demonstrated as mean ± standard deviation. P-value less than 0.05 was considered significant.

**Results**

Of the 149 patients in the HD group, 96 (64.4%) were men and 53 (35.6%) were women. Mean age was 55.9 ± 16.1 years (range 13 years - 91 years) and the mean dialysis duration was 40.85 ± 42.64 months (range 3 months - 228 months). In the control group, 88 (59.8%) were men and 59 (40.1%) were women. Mean age was 55.7 ± 17.9 years (range 8 year -75 years). The causes of ESRD in the patient cohort are shown in Figure 1.

Overall, 108 of the patients in the HD group and 54 of the individuals in the control group were found to have at least 1 cutaneous or mucosal manifestation. The prevalence rates of the different types of manifestations
Table 1. The prevalence rates of cutaneous and mucosal manifestations in case and control groups.

<table>
<thead>
<tr>
<th>Manifestation</th>
<th>Control group (n = 150)</th>
<th>Case group (n = 149)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pruritus</td>
<td>83</td>
<td>23</td>
<td>0.000*</td>
</tr>
<tr>
<td>Skin discoloration</td>
<td>61</td>
<td>23</td>
<td>0.000*</td>
</tr>
<tr>
<td>Ecchymosis</td>
<td>15</td>
<td>4</td>
<td>0.008*</td>
</tr>
<tr>
<td>Xerosis</td>
<td>11</td>
<td>4</td>
<td>0.061</td>
</tr>
<tr>
<td>Pigmented purpura dermatitis</td>
<td>3</td>
<td>0</td>
<td>0.080</td>
</tr>
<tr>
<td>Acne</td>
<td>6</td>
<td>6</td>
<td>0.991</td>
</tr>
<tr>
<td>Vitiligo</td>
<td>4</td>
<td>3</td>
<td>0.696</td>
</tr>
<tr>
<td>Bulla and folliculitis</td>
<td>3</td>
<td>4</td>
<td>0.709</td>
</tr>
<tr>
<td>Necrotic excoriation</td>
<td>2</td>
<td>0</td>
<td>0.155</td>
</tr>
<tr>
<td>Ichtus</td>
<td>2</td>
<td>0</td>
<td>0.155</td>
</tr>
<tr>
<td>Eczema</td>
<td>6</td>
<td>2</td>
<td>0.148</td>
</tr>
<tr>
<td>Seborrheic dermatitis</td>
<td>1</td>
<td>2</td>
<td>0.565</td>
</tr>
<tr>
<td>Seborrheic keratoses</td>
<td>1</td>
<td>1</td>
<td>0.996</td>
</tr>
<tr>
<td>Telangiectasia</td>
<td>1</td>
<td>0</td>
<td>0.316</td>
</tr>
<tr>
<td>Puritic nodule</td>
<td>1</td>
<td>1</td>
<td>0.996</td>
</tr>
<tr>
<td>Drying and hair fragility</td>
<td>8</td>
<td>1</td>
<td>0.017*</td>
</tr>
<tr>
<td>Scalp hair loss</td>
<td>6</td>
<td>8</td>
<td>0.593</td>
</tr>
<tr>
<td>Hair discoloration</td>
<td>4</td>
<td>3</td>
<td>0.696</td>
</tr>
<tr>
<td>Aphthous stomatitis</td>
<td>6</td>
<td>1</td>
<td>0.054</td>
</tr>
<tr>
<td>Scrotal tongue</td>
<td>3</td>
<td>1</td>
<td>0.311</td>
</tr>
<tr>
<td>Furred tongue</td>
<td>3</td>
<td>2</td>
<td>0.647</td>
</tr>
<tr>
<td>Herpes simplex</td>
<td>2</td>
<td>3</td>
<td>0.657</td>
</tr>
<tr>
<td>Leukonychia</td>
<td>25</td>
<td>8</td>
<td>0.001*</td>
</tr>
<tr>
<td>Half and half nails</td>
<td>9</td>
<td>1</td>
<td>0.009*</td>
</tr>
<tr>
<td>Onycholysis</td>
<td>9</td>
<td>3</td>
<td>0.074</td>
</tr>
<tr>
<td>Subungual hyperkeratosis</td>
<td>3</td>
<td>0</td>
<td>0.080</td>
</tr>
<tr>
<td>Pitting</td>
<td>5</td>
<td>4</td>
<td>0.727</td>
</tr>
<tr>
<td>Undiagnosable lesion</td>
<td>3</td>
<td>1</td>
<td>0.311</td>
</tr>
<tr>
<td>Thin nail</td>
<td>3</td>
<td>3</td>
<td>0.993</td>
</tr>
<tr>
<td>Cyanosis</td>
<td>2</td>
<td>2</td>
<td>0.995</td>
</tr>
<tr>
<td>Pincer nail</td>
<td>2</td>
<td>0</td>
<td>0.155</td>
</tr>
<tr>
<td>Melasma</td>
<td>1</td>
<td>0</td>
<td>0.316</td>
</tr>
<tr>
<td>Clubbing</td>
<td>1</td>
<td>2</td>
<td>0.565</td>
</tr>
</tbody>
</table>

* P-value < 0.05 as determined by t test
detected in the patients on HD and in the controls are shown in Table 1. The patients in the HD group had different rates of various types of dermatologic disorders compared to the control group.

Pruritus, skin discoloration, ecchymosis, drying and hair fragility, leukonychia, absent lunula, and half and half nails were the most frequent disorders in patients. Compared to the control group the HD group had a significantly higher rate of these disorders (P < 0.05). The disorders often were seen in patients with diabetes mellitus or hypertension (Table 2). Of the 108 cases of HD patients found to have at least 1 cutaneous or mucosal manifestation, 72 patients were male, 36 patients were ≥ 65 years of age, 39 patients had diabetes mellitus, 46 patients had hypertension, and 38 patients had long-term HD (> 8 years). These results were shown to be statistically related to gender, hypertension and duration of HD. (Table 3) In this study dermatologic disorders such as xerosis, eczema, aphthous stomatitis, splinter hemorrhage, and onycholysis were more common in the HD group then in the control group but the difference was not statistically significant.

Discussion

In the present study, cutaneous and mucosal manifestations ranged from 36% (54/150) in the control group to 72.4% (108/149) in HD group; however, previously conducted studies have reported values ranging from 52% to 88% for dermatological manifestations.6,11,15-18 This variation between results in this study and other studies6,11,15-18 may stem from lack of education, genetic factors, occupation and/or chance, in association with different physical and chemical agents in the studied population.

Although the authors didn’t find significant correlation between the cutaneous and mucosal manifestations and age ≥ 65 (OR = 0.781, 95% CI 0.371-1.644), or diabetes mellitus (OR = 1.090, 95% CI 0.512-2.320), multiple logistic regression analysis indicated that male sex (OR = 2.556, 95% CI 1.225-5.331), hypertension (OR = 2.300, 95% CI 1.025-5.162), and long-term dialysis (OR = 2.637, 95% CI 1.067-6.513) were associated with cutaneous and mucosal manifestations.

Table 2. The prevalence rates of common cutaneous and mucosal manifestations in case groups due to ESRD.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>HTN</th>
<th>DM</th>
<th>GN</th>
<th>Stone and obstructive uropathy</th>
<th>ATN</th>
<th>Infection</th>
<th>Malignancy</th>
<th>Unknown</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pruritus</td>
<td>29</td>
<td>44</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>5</td>
<td>83</td>
</tr>
<tr>
<td>Skin discoloration</td>
<td>14</td>
<td>34</td>
<td>6</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>61</td>
</tr>
<tr>
<td>Ecchymosis</td>
<td>6</td>
<td>3</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>16</td>
</tr>
<tr>
<td>Drying and hair fragility</td>
<td>2</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>8</td>
</tr>
<tr>
<td>Leukonychia</td>
<td>4</td>
<td>11</td>
<td>1</td>
<td>0</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>4</td>
<td>25</td>
</tr>
<tr>
<td>Absent lunula</td>
<td>1</td>
<td>4</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>10</td>
</tr>
<tr>
<td>Half and half nails</td>
<td>2</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>0</td>
<td>1</td>
<td>9</td>
</tr>
<tr>
<td>Total</td>
<td>58</td>
<td>102</td>
<td>15</td>
<td>3</td>
<td>8</td>
<td>7</td>
<td>4</td>
<td>15</td>
<td>212</td>
</tr>
</tbody>
</table>

Figure 1. The causes of ESRD in the patients of the present study.
ATN= acute tubular necrosis, DM= diabetes mellitus, GN= glomerulonephritis, HTN= hypertension, UTI= urinary tract infections
DO NOT DUPLICATE

The etiology of pruritus in CRF is unknown; however, it has been associated with the degree of renal insufficiency (urine output of < 500 mL), dry skin, retention of middle molecules (molecular weight range 300 daltons - 12,000 daltons) such as beta-2 microglobulin, advanced glycosylation end products, and parathyroid hormone that is thought to cause pruritic symptoms in CRF patients. A study by Chou et al revealed that a higher calcium-phosphorus product was associated with a greater degree of pruritus after parathyroidectomy. Neurogenic theory is also considered a probable cause for CRF pruritus. There is an abnormal pattern of cutaneous innervation in ESRF and this led to the neurogenic hypothesis of uremic pruritus. Another suggested cause of uremic pruritus is increased serum histamine levels, which may be due to allergic sensitization to diverse dialyzer membrane components as well as impairing renal excretion of histamine. Other possible causes of pruritus are composed of increasing serum levels of magnesium, albumin (due to inadequate excretion), and iron deficiency anemia that are present in CRF patients. Skin discoloration in this study ranged from 40.9% in the HD group to 15.3% in the control group. Skin discoloration was often a form of hyper-pigmentation and pallor in the patients. In the current study, pallor was often seen in the face and hyperpigmentation seen in legs. Diffuse hyperpigmentation on sun-exposed areas is attributed to an increase in melanin in the basal layer and superficial dermis, which is due to failure of the kidneys to excrete beta-melanocyte stimulating hormone (\( \beta \)-MSH). It has been shown that the prevalence of hyperpigmentation increases with duration of HD. However, Pico and colleagues reported reduction of disseminated pigmentation with increase in term of dialysis. They thought reduction of exposure to the sunlight as well as chronic nature of the disease could have been the cause of this phenomenon. Pallor is due to anemia, which was reported as the hallmark of CRF. Anemia is primarily the result of inadequate erythropoietin production by failing kidneys. Other contributory factors to anemia include iron deficiency, folic acid or vitamin B12 deficiency, and diminished erythrocyte survival. Ecchymosis was seen in 10% of patients in the HD group in the current study, while only 4 cases (7.3%) in the control group had this problem. The causes may be related to defects in primary hemostasis such as increased vascular fragility, platelet dysfunction, and the usage of heparin during dialysis. Also in this study, the prevalence of leukonychia and half and half nails have been reported as the most common nail disorder, respectively (16.7%, 6% in the HD group and 5.3%, 0.6% in the control group). In other studies, frequency of leukonychia, or discoloration of the nail plate, was reported at 17% to 31%. The nail plate has a normal surface but loses its transparency and appears white in color because of the presence of parakeratotic cells within its ventral portion. Parakeratotic cells have immature large nuclei containing keratohyalin. The cells containing keratohyalin reflect the light, and as a result, the nail appears white. This disorder has multiple subtypes. True leukonychia is attributable to matrix dysfunction. Apparent leukonychia is due to changes in the underlying tissue. Pseudoleukonychia is used when the nail plate alternation has an external origin, such as in onychomycosis, or in keratin granulations observed after nail enamel applications. Leukonychia can be congenital or acquired. Congenital leukonychia can be an isolated phenomenon or can develop in conjunction with other diseases. Acquired leukonychia may have various causes such as Addison disease, cardiac failure, systemic lupus.

### Table 3. Multivariate logistic regression analysis for overall nail disorder.

<table>
<thead>
<tr>
<th>Factor</th>
<th>HD patients with (n = 108) &amp; without (n = 41) positive cutaneous and mucosal manifestations</th>
<th>OR (95% CI)</th>
<th>( P )-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>2.556 (1.225-5.331)</td>
<td>&lt; 0.05*</td>
<td></td>
</tr>
<tr>
<td>DM</td>
<td>1.090 (0.512-2.320)</td>
<td>0.609</td>
<td></td>
</tr>
<tr>
<td>HTN</td>
<td>2.300 (1.025-5.162)</td>
<td>&lt; 0.05*</td>
<td></td>
</tr>
<tr>
<td>Age ≥ 65</td>
<td>0.781 (0.371-1.644)</td>
<td>0.521</td>
<td></td>
</tr>
<tr>
<td>Long term hemodialysis</td>
<td>2.637 (1.067-6.513)</td>
<td>&lt; 0.05*</td>
<td></td>
</tr>
</tbody>
</table>

* \( P \)-value < 0.05 as determined by test
erythematous, after treatment with antimetabolites, arsenic poisoning, exfoliative dermatitis, Hodgkin disease, infectious fever, menstruation, myocardial infarct, leprosy, malaria, pneumonia, pellagra, thallium poisoning, trauma, herpes zoster, fungal infections, tuberculosis, zinc deficiency, and trichinosis. Half and half nails were the second most common disorder in HD patients in the present study (6%), and were found in a much smaller number (0.6%) in the control group. In other publications, half and half nails have been reported as representing the most common nail disorder in CRF patients on HD, varying from 7.7% to 50.6%. Half and half nails, the white appearance of proximal half of the nail, is due to nail bed edema associated with a dilated capillary despite the fact that the other half of the nail bed appears normal. The etiology of this nail disorder remains unknown. In this study, the prevalence of hair disorders in HD patients was not considerable. Among the 149 patients in the HD group, 8 patients had drying and lusterless hair, 6 patients reported scalp hair loss, and 4 patients experienced hair discoloration. Scalp hair loss was more common in the control group (8 cases), although the difference between the 2 groups was not significant. In another study, sparse body hair and diffuse alopecia with dry, lusterless hair has been reported. The most common hair disorder among HD patients is diffuse hair loss from the scalp. Sparse body hair and discoloration and dryness of hair are other changes experienced by patients with CRF. Nutritional supplementation is absolutely required, along with treatment of xerosis and pruritus to prevent hair loss. In mucosal examination, the results of this study showed variable disorders, such as scrotal tongue, furred tongue, herpes simplex, aphthous stomatitis and gingivitis, that did not have a statistically significant difference in prevalence between the HD group and the control group. However, oral mucosal changes have been reported in up to 90% of patients with CRF in a previous study.

Conclusion

In this study, at least 1 cutaneous manifestation was found in 72.4% of CRF patients. The most prevalent findings were pruritus, skin discoloration (hyperpigmentation and pallor), ecchymosis, drying and hair fragility, leukonychia, and half and half nails. Hemodialysis increases the life expectancy of these patients, but also increases the time that other cutaneous changes have to manifest. Many of these disorders can reduce the quality of life of patients. More attention to, and follow-up treatment of cutaneous manifestations will be required in patients undergoing HD, especially those with long-term HD, hypertension, and who are male.

Acknowledgement

This work was supported by a grant from Qazvin University of Medical Sciences, Qazvin, Iran. The authors are grateful for its financial support.

References


