

## Original Article

# Dermatological problems in kidney recipients in Yazd Province, Iran

P. Kafaie\*, F. Najafi\*\*, M.T. Noorbala\*

\* Department of Dermatology, Shahid Sadoughi Medical Science University, Yazd, Iran

\*\* Department of Nephrology, Shahid Sadoughi Medical Science University, Yazd, Iran

**Abstract** *Background* Kidney transplantation is one of the effective methods to treat kidney disease. In a kidney transplant, due to the use of many immunosuppressive drugs, the body is often subjected to various benign, premalignant and malignant dermatoses. The early diagnosis and effective treatment of such conditions can potentially reduce morbidity and mortality.

*Objective* To determine the distribution of dermatoses in patients who have received kidney transplants.

*Patients and methods* This cross-sectional study was performed on 120 kidney transplant recipients in Yazd University Hospitals in two years. The patients were examined by a dermatologist and diagnosis was made on the basis of clinical observations. Biopsies and scraping of the lesions were taken whenever necessary.

*Results* 120 evaluable patients included 84 males and 36 females with mean age of 32 years. A total of 116 patients developed dermatological symptoms, which included: hypertrichosis (78.3%), photosensitivity (70%), cushingoid face (60%), gingival hyperplasia (43.3%), warts (40%), pityriasis versicolor (33.3%), steroidal acne (26.6%), herpes simplex (13.3%), herpes zoster (10%), nonmelanoma cancer (10%), oral candidiasis (6.6%), striae (6.6%), actinic keratosis (6.6%) and sebaceous hyperplasia (3.3%).

*Conclusion* Skin lesions are a significant problem in kidney transplant recipients. A careful monitoring of these patients is recommended in order to detect these lesions in early stages and treat them.

### Key words

Kidney transplant, dermatological side-effects, immunosuppressive drugs.

## Introduction

Although many patients suffering from the last phase of kidney disease could achieve better living conditions through dialysis, yet most of them are affected by insufficient alteration of kidney performance. Kidney transplantation is an appropriate treatment for patients affected with kidney failure, and it may give them a long life. Now, more than one million people around the world are living with a renal transplant that indicates the importance of paying due attention

to the problems and complications of kidney transplantation.

Intensive immunosuppressive therapy is generally warranted to prevent rejection of a kidney allograft and provide a long-term graft survival. Immunosuppressive therapy, as presently available, generally suppresses all immune responses including those to bacteria, fungi, and even tumors. The frequency of internal organs malignancies, common in the general population, is not increased in transplanted patients; however, a variety of uncommon cancers are more frequent.<sup>1,2,3</sup> Kidney transplant recipients are at risk of a broad spectrum of skin diseases. The most

---

### Address for correspondence

Dr. M.T. Noorbala  
Department of Dermatology,  
Shahid Sadoughi Medical Science University,  
Yazd - Iran  
E mail: mtnoorbala@gmail.com

important lesions are skin and lip cancers, actinic keratosis, squamous cell carcinoma (SCC), basal cell carcinoma (BCC), and malignant melanoma.<sup>4-10</sup>

Immunosuppressive therapy may predispose these patients to various skin infections e.g. herpes simplex, herpes zoster, pityriasis versicolor etc.<sup>11</sup> Drug-related lesions including hypertrichosis, gingival hyperplasia, acne, cushingoid features, and striae frequently occur as a result of the immunosuppressives. Additionally, there are miscellaneous skin disorders that may be detected in kidney allograft recipients. Kidney transplantation has been performed in Iran since years ago, but associated skin diseases have not been assessed adequately.

The goal of this study was to determine frequency and types of skin lesions in patients receiving kidney transplant who were referred to Yazd medical science university hospitals.

### Patients and methods

This cross-sectional study was performed on a total of 120 patients who had undergone kidney transplantation in Yazd University Hospitals. They were visited by a nephrologist and a dermatologist during their monthly follow-ups. A thorough physical examination for skin lesions was done. Skin biopsies and scrapings were taken whenever necessary. Diagnosis of the skin diseases was made on clinical basis and pathological studies.

### Results

During two years, from March 2006 to March 2008, 120 patients underwent kidney transplant with average age of 32 years. Among them 84 patients were men and 36 were women. The

**Table 1** Skin lesions in kidney recipients (n=120)

<i>Skin lesions</i>	<i>Number (%)</i>
<i>Drug-related lesions</i>	
Hypertrichosis	94 (78.3%)
Photosensitivity	84 (70%)
Cushingoid features	72 (60%)
Gingival hyperplasia	52 (43.3%)
Acne	32 (26.6%)
Striae	8 (6.6%)
Sebaceous hyperplasia	4 (3.3%)
<i>Infectious lesions</i>	
Warts	48 (40%)
Pityriasis versicolor	40 (33.3%)
Herpes simplex	16 (13.3%)
Herpes zoster	12 (10%)
Mucosal candidiasis	8 (6.6%)
<i>Premalignant/malignant lesions</i>	
Actinic keratosis	8 (6.6%)
Squamous cell carcinoma	8 (6.6%)
Basal cell carcinoma	4 (3.3%)

patients' therapeutic plan included prednisone + azathioprine + cyclosporine in 56 (46%), prednisone + mycophenolate + cyclosporine in 56 (46%) and prednisone + cyclosporine in 8 (6%) patients.

Among 120 investigated patients, 116 patients (96.6%) were suffering from at least a skin problem (Table 1).

### Discussion

Skin lesions are a significant problem in transplant patients. Rafi *et al.*<sup>12</sup> performed a cross sectional study on 60 kidney transplant recipients in Saudi Arabia. They observed skin lesions in 90% of the patients including infectious lesions in nearly half of them. Pityriasis versicolor was the most common skin infection (36%), followed by folliculitis (8%) and warts (6%). In a similar study in Puerto Rico, the frequency of skin diseases was reported to be 95% in transplant patients.<sup>13</sup> In the study performed by Bencini *et al.*<sup>14</sup> on 105 patients, the frequency of skin diseases was 97% and premalignant / malignant skin lesions were

seen in 12% of these patients with the preponderance of SCC. Reports from Saudi Arabia, Italy, and India agree with our results.<sup>12,15,16</sup>

Skin lesions in kidney transplant recipients can be divided into 5 groups i.e. drug related, infectious, premalignant, malignant, and miscellaneous.<sup>13,15</sup>

Certain miscellaneous skin disorders are related to neither the renal condition nor the immunosuppression. These include pigmented nevi, skin tags, ichthyosis, and seborrheic dermatitis.<sup>13</sup>

Drug-related, infectious, and premalignant/malignant lesions were seen in our patients, as in **Table 1**. These frequencies agree with the report from India.<sup>16</sup>

Lugo-Janer *et al.*<sup>13</sup> and Bencini *et al.*<sup>14</sup> reported infectious lesions as the most common skin manifestation in transplant recipients. We found that the risk of infectious lesions increased in proportion to the time elapsed since transplantation. Plane warts were detected in 40% of the cases and were considered as the most common infection in the present study, while the prevalence of warts has been reported from 6.6% to 48% in the previous studies.<sup>12,17,18</sup> These differences may be due to the different duration of follow-ups. For example, human papillomavirus infections may develop much later and a longer follow-up period is required.

Pityriasis versicolor is a common fungal infection in transplant patients and more common than the general population.<sup>19</sup> Pityriasis versicolor was reported in 33.3% of the patients in this study, 36% in Saudi Arabia, 13.3% in India, 27.4% in Italy, and 36.3% in Turkey.<sup>12,16,19,20</sup>

Hepburn *et al.*<sup>17</sup> performed a study on 52 kidney transplant recipients in New Zealand and reported malignancies in 9 (17.3%) and actinic keratosis in 20 (38.46%) patients occurring in the exposed areas to sunlight. They showed that SCC was more frequent than BCC. Frequency of skin cancers is higher in transplant patients and correlates with the post-transplant duration of follow-up and immunosuppressive therapy. In this study SCC was the most common skin malignancy. In a 23-year follow-up study on 793 transplant recipients in Spain, tumors occurred in at least 10% of these patients and included cancers in the skin (46%) and other parts (56%). This study showed that malignancy was an important cause of morbidity and mortality in transplant recipients.<sup>21</sup> In the study by Cohen *et al.*<sup>22</sup> on 580 transplant patients, 59 out of 170 skin lesion biopsies showed malignancy on pathologic examination. Half of these lesions were SCC and they mostly occurred in sun-exposed areas.<sup>23</sup> The frequency of malignancies is influenced by age, sex (more frequent in men), duration of the follow-up, immunosuppression with cyclosporine A, color of patient's eyes (more frequent in those with light colors), pre-transplant SCC or actinic keratosis, place of residency (tropical areas), smoking, and childhood sunburn.<sup>24-26</sup> Bunney *et al.*<sup>27</sup> reported no difference between the dermatological effects of two immunosuppressive regimens with azathioprine and cyclosporine A in kidney transplant patients except for hypertrichosis. In the present study, it was concluded that the type of immunosuppressive regimens had no influence on the prevalence of skin disease in these patients.

## References

1. Penn I. Tumors of the immunocompromised patient. *Annu Rev Mee* 1988; **39**: 63-73.

2. Penn I. Cancers complicating organ transplantation. *N Engl J Med* 1990; **323**: 1767-9.
3. Carpenter CB, Milford EL, Sayegh MH. Transplantation in the treatment of renal failure. In: Kasper DL, Braunwald E, Fauci AS *et al*, editors. *Harrison's principles of internal medicine*. 16<sup>th</sup> edn. New York: Mc Graw- Hill; 2005. P.1668-74.
4. Berg D, Otley CC. Skin cancer in organ transplant recipients: epidemiology, pathogenesis, and management. *J Am Acad Dermatol* 2002; **47**: 1-17.
5. Jensen P, Hansen S, Moller B *et al*. Skin cancer in kidney and heart transplant recipients and different long term immunosuppressive therapy regimens. *J Am Acad Dermatol* 1999; **40**: 177-86.
6. Boyle J, Mackie RM, Briggs JD *et al*. Cancer, warts, and sunshine in renal transplant patients. A case-control study. *Lancet* 1984; **1**: 703-5.
7. Mclelland J, Ressa A, Williams G, Chu T. The incidence of immunosuppression-related skin disease in long-term transplant patients. *Transplantation* 1998; **46**: 871-4.
8. Gupta AK, Cardella CJ, Haberman HF. Cutaneous malignant neoplasms in patients with renal transplants. *Arch Dermatol* 1986; **122**: 1288-93.
9. Hintner H, Fritsch P. Skin neoplasia in the immunodeficient host. The clinical spectrum: Kaposi's sarcoma, lymphoma, skin cancer and melanoma. *Curr Probl Dermatol* 1989; **18**: 210-7.
10. Greene MH, Young TI, Clark WH Jr. Malignant melanoma in renal transplant recipients. *Lancet* 1981; **1**: 1196-9.
11. Spencer ES, Andersen HK. Viral infections in renal allograft recipients treated with long-term immunosuppression. *Br Med J* 1979; **2**: 829-30.
12. Rafi A, Ghacha R, Sinha A *et al*. Spectrum of skin diseases in renal transplant recipients. *Dia Transplant* 2001; **30**: 282-5.
13. Lugo-Janer G, Sanchez JL, Santiago-Delpin E. Prevalence and clinical spectrum of skin diseases in kidney transplant recipients. *J Am Acad Dermatol* 1991; **24**: 410-4.
14. Bencini PL, Montagnino G, Sala F *et al*. Cutaneous lesions in 67 cyclosporin-treated renal transplant recipients. *Dermatologica* 1986; **172**: 24-30.
15. Lesnoni La Parola I, Citterio F *et al*. Skin manifestations in 140 kidney transplants. *Recenti Prog Med* 1992; **83**: 61-3. [Italian].
16. Chugh KS, Sharma SC, Singh V *et al*. Spectrum of dermatological lesions in renal allograft recipients in a tropical environment. *Dermatology* 1994; **188**: 108-12.
17. Hepburn DJ, Divakar D, Bailey RR, Macdonald KJ. Cutaneous manifestations of renal transplantation in a New Zealand population. *N Z Med J* 1994; **107**: 497-9.
18. Rudlinger R, Smith IW, Bunney MH, Hunter JA. Human papillomavirus infections in a group of renal transplant recipients. *Br J Dermatol* 1986; **115**: 681-92.
19. Virgili A, Zampino MR, La Malfa V *et al*. Prevalence of superficial dermatomycoses in 73 renal transplant recipients. *Dermatology* 1999; **199**: 31-4.
20. Gulec AT, Demirbilek M, Seckin D *et al*. Superficial fungal infections in 102 renal transplant recipients: a case – control study. *J Am Acad Dermatol* 2003; **49**: 187-92.
21. Dreno B. Skin cancers after transplantation. *Nephrol Dial Transplant* 2003; **18**: 1052-8.
22. Cohen EB, Komorowski RA, Clowry LJ. Cutaneous complications in renal transplant recipients. *Am J Clin Pathol* 1987; **88**: 32-7.
23. Bordea C, Wojnarowska F, Millard PR *et al*. Skin cancers in renal-transplant recipients occur more frequently than previously recognized in a temperate climate. *Transplantation* 2004; **77**: 574-9.
24. Marcen R, Pascual J, Tato AM *et al*. Influence of immunosuppression on the prevalence of cancer after kidney transplantation. *Transplant Proc* 2003; **35**: 1714-6.
25. Lindelof B, Granath F, Dal H *et al*. Sun habits in kidney transplant recipients with skin cancer: a case- control study of possible causative factors. *Acta Derm Venereol* 2003; **83**: 189-93.
26. Ramsay HM, Fryer AA, Hawley CM *et al*. Factors associated with nonmelanoma skin cancer following renal transplantation in Queensland, Australia. *J Am Acad Dermatol* 2003; **49**: 397-406.
27. Bunney MH, Benton EC, Barr BB *et al*. The prevalence of skin disorders in renal allograft recipients receiving cyclosporine. A compared with those receiving azathioprine. *Nephrol Dial Transplant* 1990; **5**: 379-82.

