

Skin Infections in 401 Renal Transplant Recipients in Southern Turkey

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Abstract

Objectives: Renal transplant recipients are predisposed to the development of a variety of skin infections that can result from graft-preserving immunosuppressive therapy. In this study, we aimed to determine the prevalence of skin infections in a group of renal transplant recipients in the Mediterranean region of Turkey.

Materials and Methods: The medical records of 401 patients followed up by the Transplantation Center at Akdeniz University in Antalya, Turkey, were used in a retrospective analysis. The prevalence of skin infections was calculated, and the effects of age, sex, and time after transplant on skin infections were evaluated.

Results: Of the patients studied, 220 (54.9%) had a skin infection. Of 280 infections identified in those individuals, 180 (64.3%) were fungal, 77 (27.5%) were viral, and 23 (8.2%) were bacterial. Pityriasis versicolor was present in 95 patients (23.7%), human papillomavirus infection in 44 (11%), onychomycosis in 23 (5.7%), and fungal toe-web infection in 20 (5%). The duration of immunosuppression significantly affected the prevalence of skin infections, and the mean interval for the development of fungal infections after transplant was earlier than that for viral or bacterial infections (25.8 ± 29.3 , 50.7 ± 36.7 , and 52.1 ± 47.9 months, respectively).

Conclusions: In this study, pityriasis versicolor was the most common skin infection in renal transplant

recipients in our region. Except for the higher prevalence of superficial fungal infections, the overall results in our population agree with those of other similar series.

Key words: Renal transplant recipients, Skin infections, Fungal infections, Pityriasis versicolor, Immunosuppression

Because of their treatment with graft-preserving immunosuppressive therapy, renal transplant recipients have an increased risk of skin infections. Factors such as climate and skin type have been implicated as modifiers of those infections (1-6). In this study, we aimed to determine the prevalence of skin infections in renal transplant recipients in Antalya, Turkey. The effects of common demographic parameters in those individuals and the time after transplant on skin infections were evaluated.

Materials and Methods

The study subjects (401 consecutive renal transplant recipients who were monitored for 14 years by the Transplantation Center of the Akdeniz University Faculty of Medicine) were retrospectively evaluated. Data on all patients were obtained from their medical records, dermatologic consultations, and follow-up notes. The age, sex, cause of chronic renal failure, date of transplant, and graft survey time for each patient were recorded. The graft survey time was defined as the time from the date of transplant until the initiation of the study. For patients who died, graft survey time was defined as the interval between the transplant and death.

Immunosuppression varied considerably according to the combinations of drugs given during the study. Forty-nine (12.2%) patients were treated with prednisolone and azathioprine; 11 (2.7%) with

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prednisolone and mycophenolate mofetil; 23 (5.7%) with prednisolone and tacrolimus; 41 (10.2%) with prednisolone and cyclosporine; 111 (27.7%) with prednisolone, azathioprine, and cyclosporine; 3 (0.7%) with prednisolone, azathioprine, and tacrolimus; 70 (17.5%) with prednisolone, mycophenolate mofetil, and cyclosporine; and 93 (23.2%) with prednisolone, mycophenolate mofetil, and tacrolimus. In all regimens, the dosage of prednisolone was tapered from 1 g to a maintenance dosage of 5 mg daily. The dosage of azathioprine ranged from 1 to 3 mg/kg/d, and the dosage of mycophenolate mofetil was 2 g/d. The dosage of cyclosporine ranged from 5 to 10 mg/kg/d, and the dose of tacrolimus ranged from 0.1 to 0.3 mg/kg/d, depending on the tissue trough level.

The type and time of occurrence of various skin infections were noted. The prevalence of the skin infections was calculated by counting the infections per patient and was expressed as a percentage of the total group of patients. If a patient experienced multiple skin infections of 1 type, only the first infection of that type was calculated. For statistical analysis, the paired *t* test and the chi-square test were used. A *P* value of < .05 was considered statistically significant.

Results

The ages of recipients at the initiation of the study ranged from 14 to 59 years (mean $\pm$ SD, 34.3 $\pm$ 14.9 years), and 269 men (67.1%) and 132 women (32.9 %) were studied. The cause of renal failure was diabetes mellitus in 17 patients (4.2%). The mean graft survey time was 75.5 $\pm$ 65.5 months (range, 1-292 months). Of 401 renal transplant recipients, 220 (54.9%) were found to have a skin infection. Three major categories (fungal, viral, and bacterial) of skin infections were identified. Of 280 infections in 220 patients, 180 (64.3%) were fungal, 77 (27.5%) were viral, and 23 (8.2%) were bacterial. The prevalence, numbers, and types of skin infections in the renal transplant recipients studied are presented in Table 1.

The most common skin infections identified in the study subjects were pityriasis versicolor (23.7% of patients), human papillomavirus infection (11%), dermatomycosis (9.5%), and onychomycosis (5.7%). The types and numbers of fungal, viral, and bacterial skin infections recorded in the renal transplant recipients studied are presented in Table 2. We noted

Table 1. Prevalence, numbers, and types of skin infections in the renal transplant recipients studied.

Variables	Number of patients n = 220	Number of infections n = 280
Type of infection	n (%)	n (%)
Fungal	131 (32.7)	180 (64.3)
Pityriasis versicolor	95 (23.7)	95 (33.9)
Dermatomycosis	38 (9.5)	47 (16.8)
Onychomycosis	23 (5.7)	23 (8.2)
Mucocutaneous candidiasis	15 (3.7)	15 (5.4)
Viral	68 (17)	77 (27.5)
Warts	44 (11)	44 (15.7)
Herpes simplex	16 (4)	16 (5.7)
Herpes zoster	15 (3.7)	15 (5.4)
Molluscum contagiosum	2 (0.5)	2 (0.7)
Bacterial	21 (5.2)	23 (8.2)
Cellulitis	8 (2)	8 (2.9)
Folliculitis	6 (1.5)	6 (2.1)
Furuncle	4 (1)	4 (1.4)
Impetigo	2 (0.5)	2 (0.7)
Paronychia	2 (0.5)	2 (0.7)
Ecchyma	1 (0.2)	1 (0.4)

Table 2. Types and numbers of fungal, viral, and bacterial skin infections in the study subjects.

Fungal infections	n
PV	72
PV and onychomycosis	3
Dermatomycosis	14
PV and candidiasis	4
PV and dermatomycosis	7
PV, onychomycosis, and dermatomycosis	8
PV, dermatomycosis, and candidiasis	1
Onychomycosis and dermatomycosis	7
Onychomycosis	5
Candidiasis and dermatomycosis	1
Candidiasis	9
Total	131
Viral infections	n
Warts	37
Warts and herpes simplex	2
Warts and herpes zoster	3
Herpes simplex	12
Herpes zoster	11
Warts and molluscum contagiosum	1
Warts, molluscum contagiosum, and herpes simplex	1
Herpes simplex and herpes zoster	1
Total	68
Bacterial infections	n
Cellulitis	8
Folliculitis	6
Furuncle	3
Furuncle and paronychia	1
Impetigo	2
Ecchyma and paronychia	1
Total	21

47 dermatophyte infections (other than nail involvement) in 38 patients. Some of the patients were found to have more than 1 type of dermatophyte infection. The most commonly seen dermatomycosis was tinea pedis, which was identified in 20 patients (5%). Other types of dermatomycosis in our subjects consisted of tinea corporis (17 patients, 4.2%), tinea cruris (8 patients,

2.0%), and tinea manum (2 patients, 0.5%). Human papillomavirus infection accounted for most of the viral skin infections identified.

The mean interval for the development of fungal infections after transplant was earlier than that for viral and bacterial infections (25.8 ± 29.3 , 50.7 ± 36.7 , and 52.1 ± 47.9 months, respectively). Further analysis showed that the duration of immunosuppression did significantly affect the prevalence of fungal, viral, and bacterial skin infections ($P < .0001$, $P < .0001$, and $P < .008$, respectively). However, development of skin infections was not found to be statistically associated with age or underlying diseases such as diabetes mellitus. Sex was significantly associated with the risk of fungal skin infections. Prevalence was higher in men than in women (98 of 171 men vs 33 of 99 women) ($P < .05$) (Table 3). We also found pityriasis versicolor more often in men (75 men vs 20 women) ($\chi^2 = 7936$, $P < .005$). The sex of the subjects was not significantly associated with the prevalence of viral or bacterial infection.

Table 3. Effects of clinical variables on the prevalence of skin infections in the renal transplant recipients studied.

Type of Infection	Age (y)*	P Value	Sex (F/M)	χ^2/P Values	Graft Survey* Time (mo)	P Value
Fungal						
Positive (n = 131)	33.1 $\pm$ 11.0	.35	33/98	5.260 / .022	93.0 $\pm$ 61.1	< .0001
Negative (n = 270)	34.2 $\pm$ 10.5		99/171		67.0 $\pm$ 66.0	
Viral						
Positive (n = 68)	32.5 $\pm$ 11.6	.26	23/45	0.030 / .861	107 $\pm$ 61.6	< .0001
Negative (n = 333)	34.1 $\pm$ 10.4		109/224		68.9 $\pm$ 64.4	
Bacterial						
Positive (n = 21)	32.7 $\pm$ 11.3	.26	4/17	1.930 / .164	112.4 $\pm$ 73.2	< .008
Negative (n = 380)	33.7 $\pm$ 10.7		128/252		73.4 $\pm$ 64.5	

*Mean $\pm$ SD.

Abbreviation: F; female, M; male.

Discussion

Prior studies similar to ours usually investigated a broad spectrum of cutaneous manifestations in renal transplant recipients. Most of those manifestations were found to be infectious (1-11). However, the frequencies of various skin infections were extremely variable, probably because of diverse diagnostic criteria, different geographic and climatic conditions,

and variations in the duration of immunosuppression. Prior studies have shown that fungal infections (4-6,10) and human papillomavirus infection (1-3,7,8,11) were the most common types of skin infection. In our study, superficial fungal infections were the most frequent cutaneous infections identified. This higher frequency was similar to that reported by Lugo-Janer and colleagues (4) and Chugh and colleagues (6). Superficial cutaneous mycosis is more common in people who live in a hot, humid climate than in those who live in a temperate zone. Therefore, the higher prevalence of superficial fungal infections noted in our study may reflect prevailing environmental conditions. Among fungal infections, pityriasis versicolor was the most frequent clinical finding. The prevalence of pityriasis versicolor found in our study was similar to the rate of 20.3% reported by Prakash and colleagues (10) and the rates of 23% and 25%, respectively, that were published in 2 other studies from Turkey (8,11). In other series, the frequency of pityriasis versicolor has been reported to range from 13.3% to 48% in different geographic locations (1,4,6,7,12,13), particularly those in hot, humid climates (4).

Mucocutaneous candidal infections affect about 4% to 25.5% of renal transplant recipients (6,12). That type of infection was one of the less common fungal infections noted in our study; it afflicted only 3.7% of our subjects. The difference in the frequency of candidal infections may result from differences in methodology among studies.

Warts were the second most common infectious complication in our study. It has been reported that human papillomavirus infection affects 8% to 55% of renal transplant recipients, depending on the patient's characteristics (skin type, the time since transplant, immunosuppressive protocols) (1-8,11,14). Various types of warts were found in 11% of our subjects (a finding similar to that of Chugh and colleagues) (6).

In our study, the frequency of infection with the herpes simplex virus or the herpes zoster virus was lower than that reported by Koranda and colleagues (1) but well within the range (3.1%-10.8%) reported by other authors (4,6,8,10,11).

The prevalence of bacterial skin infections in renal transplant recipients varies in different series from 1.8% to 27.7 % (5,7,9,11,15). In our series, bacterial infections accounted for a small proportion of all

infections. This finding is comparable to that in several uncontrolled studies in which the overall frequency of bacterial infections in renal transplant recipients ranged from 3.2% to 6.8% (7,9,11). However, in a controlled study by Ada and colleagues (16), the number of microbiologically proven cutaneous bacterial infections was not increased in transplant patients. Those authors suggested that most of the lesions clinically mimicking folliculitis in renal transplant recipients could interfere with the folliculitis-like lesions because of direct systemic treatment such as corticosteroid administration.

Several previous studies have shown that skin infections are associated with the time since transplant, and that the spectrum of skin infections differs according to the posttransplant interval (3-6,8,13,15). We found that the duration of immunosuppression did significantly affect the prevalence of fungal, viral, and bacterial skin infections. We also noted that the mean interval for the development of fungal infections after transplant was shorter than that for viral and bacterial infections. In addition, we found that the prevalence of fungal skin infections, particularly pityriasis versicolor, was influenced significantly by sex. The prevalence of those infections was higher in men than in women. Pityriasis versicolor is known to be more prevalent in warm, humid areas, but there are few data on the prevalence of that infection according to sex. In 1 study of dermatologic outpatients in Greece, significantly more men than women were found to have that infection (17). This trend (which was similar to that noted in our study) was attributed to the preponderance of men in that geographic area who engage in physical exercise and/or manual labor (17).

Retrospective studies relying on data presented in medical records have some limitations, which are reflected in the results of our study. Minor skin infections can be overlooked by patients and clinicians. Nevertheless, our study includes a relatively large population of renal transplant recipients, and we suggest that some conclusions can be drawn.

In this study, we attempted to establish the prevalence of skin infections in our subjects, and we found that superficial fungal infections (especially pityriasis versicolor) are the most common type of skin infection in renal transplant recipients in our region. Except for the higher prevalence of superficial fungal infections, the overall results in our population confirm those of other series.

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