Section: DVL

Original Research Article

CLINICAL SPECTRUM AND TEMPORAL PATTERN OF DERMATOLOGICAL MANIFESTATIONS IN RENAL TRANSPLANT RECIPIENTS RECEIVING TACROLIMUS, PREDNISOLONE, AND MYCOPHENOLATE MOFETIL: A RETROSPECTIVE OBSERVATIONAL STUDY

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ABSTRACT

Background: Renal transplant recipients require prolonged immunosuppressive therapy, which increases their susceptibility to infectious, inflammatory, drug-related, and neoplastic dermatological disorders. Timely dermatological assessment is therefore important for early diagnosis and management. **Aim:** To evaluate the spectrum and frequency of dermatological and mucocutaneous manifestations among renal transplant recipients. **Materials and Methods:** This retrospective observational study included 72 renal transplant recipients attending or referred to the dermatology service at a tertiary care teaching hospital in Bhopal, India. Demographic details, duration since transplantation, immunosuppressive therapy, and dermatological findings were reviewed. Manifestations were categorized as infectious and non-infectious. Associations with post-transplant duration were assessed using appropriate statistical tests, with $p<0.05$ considered statistically significant. **Results:** The mean age was 43.2±11.7 years, and 75.0% were males. Infectious dermatoses were observed in 59.7% of patients, while non-infectious manifestations occurred in 69.4%. Fungal infections were the most common infectious group (43.1%), with dermatophytosis predominating. Xerosis (25.0%) and acneiform eruptions (22.2%) were frequent non-infectious findings. Multiple dermatological manifestations occurred in 47.2% of patients. Infectious dermatoses were significantly more common during the first post-transplant year, whereas non-infectious and multiple manifestations increased with longer transplant duration. **Conclusion:** Among dermatology-referred renal transplant recipients, a broad spectrum of dermatological disorders was observed. Early infectious complications and later cumulative non-infectious changes highlight the need for regular dermatological surveillance and close coordination between dermatologists and nephrologists.

INTRODUCTION

Kidney transplantation is the preferred renal replacement therapy for eligible patients with end-stage kidney disease because it offers better long-term survival and quality of life than maintenance dialysis. Sustained graft function, however, depends on lifelong immunosuppression. Contemporary maintenance regimens commonly combine a calcineurin inhibitor such as tacrolimus with an antimetabolite such as mycophenolate mofetil, with corticosteroids retained in many recipients according to immunological risk and institutional practice.[1] Although these agents reduce acute rejection, chronic immunosuppression alters cutaneous host defense

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and creates a broad spectrum of dermatological morbidity.[1,2]

Post-transplant dermatological manifestations may involve skin, hair, nails, and oral or genital mucosa. Infectious disorders include dermatophytosis, candidiasis, pityriasis versicolor, onychomycosis, bacterial folliculitis and pyoderma, viral warts, herpes simplex, herpes zoster, molluscum contagiosum, and parasitic infestations such as scabies.[2-4] Fungal disease is particularly important in kidney-transplant recipients because impaired cell-mediated immunity, metabolic comorbidity, antimicrobial exposure, and the intensity of immunosuppression increase susceptibility to superficial as well as invasive mycoses.[3]

Non-infectious manifestations are equally diverse and include acneiform eruptions, xerosis, pruritus, striae, skin atrophy, ecchymosis, pigmentary changes, alopecia, hypertrichosis, gingival changes, aphthous ulceration, eczematous disorders, seborrheic dermatitis, and other drug-related reactions.[2] Long-term immunosuppression also increases the risk of actinic keratosis, squamous cell carcinoma, basal cell carcinoma, and other cutaneous malignancies, making structured dermatological surveillance clinically important.[5,6] The present study therefore aimed to characterize the complete spectrum and frequency of dermatological and mucocutaneous manifestations among renal-transplant recipients receiving tacrolimus, prednisolone, and mycophenolate mofetil.

MATERIALS AND METHODS

Study Design and Setting

This retrospective observational study was conducted in the Department of Dermatology at a tertiary care teaching hospital in Bhopal, Madhya Pradesh, India. The study protocol was approved by the Institutional Ethics Committee of RKDF Medical College Hospital & Research Center, Bhopal (Registration number: IECRKDFMCRC/49/2023; dated 01 August 2023). The retrospective study reviewed hospital data of patients registered between 01 January 2022 to 01 July 2023.

Study Population

Medical and dermatology records of renal transplant recipients attending or referred to the dermatology service were reviewed. A total of 72 eligible renal transplant recipients fulfilling the study criteria were included in the final analysis. All included patients were receiving maintenance triple immunosuppressive therapy comprising oral tacrolimus, prednisolone, and mycophenolate mofetil. As this was a retrospective record-based study, all eligible patients with adequate clinical documentation available for review were included. Therefore, consecutive sampling was used, and the final available sample comprised 72 patients.

Inclusion Criteria

Patients were included if they:

1. had undergone renal transplantation;
2. were receiving maintenance immunosuppressive therapy with tacrolimus, prednisolone, and mycophenolate mofetil;
3. had attended or been referred to the dermatology department for a cutaneous, mucosal, hair, or nail-related complaint; and
4. had adequate medical and dermatological records to establish the diagnosis and clinical characteristics of the dermatological manifestation.

Exclusion Criteria

Patients were excluded if they had incomplete clinical records, inadequate information regarding renal transplantation or immunosuppressive treatment, or insufficient documentation to establish a dermatological diagnosis. Dermatological conditions clearly documented as having been present before renal transplantation were excluded from the post-transplant dermatological spectrum wherever such information was available. Patients receiving an immunosuppressive regimen other than the predefined combination of tacrolimus, prednisolone, and mycophenolate mofetil were also excluded from the final analysis.

Data Collection

Data were extracted retrospectively from hospital medical records, renal transplant follow-up records, dermatology consultation sheets, laboratory reports, and histopathology records wherever available.

The following variables were recorded:

- age and sex;
- duration since renal transplantation;
- duration of immunosuppressive therapy;
- maintenance immunosuppressive regimen;
- associated comorbidities;
- presenting dermatological complaints;
- number of dermatological manifestations per patient;
- anatomical site of involvement;
- clinical dermatological diagnosis;
- relevant laboratory or microbiological investigations;
- mucosal, hair, and nail abnormalities;
- drug-related dermatological adverse effects;
- premalignant or malignant cutaneous lesions; and
- treatment provided for the dermatological condition.

A patient could have more than one dermatological diagnosis. Therefore, the frequency of each major dermatological category was described as the proportion of included recipients affected. At the same time, individual manifestations were recorded separately when multiple disorders occurred in the same patient. Because this was a dermatology-referred cohort, these proportions should not be interpreted as population prevalence among all renal transplant recipients.

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Dermatological Assessment

Dermatological diagnoses documented in the clinical records were classified into infectious and non-infectious manifestations.

Infectious dermatoses were further classified as:

- fungal;
- bacterial;
- viral; and
- parasitic.

Fungal manifestations included dermatophytosis such as tinea corporis, tinea cruris, tinea faciei, tinea pedis and tinea barbae, as well as candidiasis, pityriasis versicolor, and onychomycosis.

Viral manifestations included viral warts, herpes simplex, herpes zoster, and molluscum contagiosum. Bacterial disorders included folliculitis, furunculosis, impetigo, and other clinically documented pyogenic infections. Scabies and other documented infestations were classified as parasitic dermatoses.

Non-infectious manifestations were grouped into:

- drug- or immunosuppression-related cutaneous changes;
- inflammatory and eczematous disorders;
- hair disorders;
- nail abnormalities;
- oral and mucosal lesions;
- pigmentary disorders; and
- premalignant and malignant cutaneous lesions.

Drug- and immunosuppression-related manifestations included acneiform eruptions, xerosis, striae, skin atrophy, easy bruising or ecchymosis, alopecia, hypertrichosis, and other clinically documented treatment-associated changes.

Diagnostic Evaluation

The diagnosis of most dermatological conditions was based on clinical examination documented by the treating dermatologist. Where fungal infection was suspected and investigations were clinically indicated, potassium hydroxide microscopic findings were reviewed. Bacterial, viral, and parasitic disorders were diagnosed based on characteristic clinical findings, supplemented by appropriate laboratory investigations where available. Histopathological examination was considered for clinically uncertain, premalignant, or malignant lesions whenever documented in the patient records.

Assessment According to Duration After Transplantation

To evaluate the relationship between duration of immunosuppression and dermatological morbidity, patients were categorized according to time elapsed since renal transplantation into:

- less than 1 year;
- 1–5 years; and
- more than 5 years.

The occurrence of infectious dermatoses, fungal infections, non-infectious manifestations, and multiple dermatological disorders was compared across these groups.

Assessment of Multiple Dermatological Manifestations

The number of dermatological manifestations per patient was recorded. Patients were categorized as having:

- one manifestation;
- two manifestations; or
- three or more manifestations.

Multiple dermatological manifestations were defined as the occurrence of two or more distinct dermatological diagnoses in the same renal transplant recipient.

Outcome Measures

The primary outcome was the frequency and clinical spectrum of dermatological and mucocutaneous manifestations among renal transplant recipients receiving tacrolimus, prednisolone, and mycophenolate mofetil.

Secondary outcomes included:

1. frequency of infectious and non-infectious dermatoses;
2. distribution of fungal, bacterial, viral, and parasitic infections;
3. spectrum of drug- and immunosuppression-related cutaneous manifestations;
4. frequency of hair, nail, oral, mucosal, inflammatory, and pigmentary abnormalities;
5. occurrence of premalignant and malignant cutaneous lesions;
6. frequency of multiple dermatological manifestations; and
7. association of dermatological manifestations with duration since renal transplantation.

Statistical Analysis

Data were entered into a structured database and checked for completeness and internal consistency before analysis. Continuous variables were summarized as mean ± standard deviation (SD) when approximately normally distributed and as median with interquartile range (IQR) when the distribution was skewed. Categorical variables were expressed as frequency and percentage. The frequency of major dermatological manifestations was calculated using the total study population of 72 patients as the denominator. Because an individual patient could have more than one dermatological disorder, percentages for individual manifestations were not required to total 100%. Selected proportions were reported with 95% confidence intervals (95% CI). Associations between categorical variables were assessed using the Pearson chi-square test. Fisher's exact test was used when expected cell frequencies were small. Dermatological manifestations were compared according to duration since transplantation (<1 year, 1–5 years, and >5 years). A two-sided p-value <0.05 was considered statistically significant.

RESULTS

A total of 72 renal transplant recipients receiving maintenance immunosuppression with tacrolimus,

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prednisolone, and mycophenolate mofetil were included in the analysis. The mean age of the study population was 43.2 ± 11.7 years. The largest proportion of patients belonged to the 41–50-year age group (31.9%). There was a clear male predominance, with 54 (75.0%) males and 18 (25.0%) females, giving a male-to-female ratio of 3:1.

The median duration since renal transplantation was 3.8 years (IQR: 1.4–6.7 years). Eighteen patients (25.0%) were within the first year following transplantation, 34 (47.2%) were between 1 and 5 years after transplantation, and 20 (27.8%) had undergone transplantation more than 5 years previously. All patients were receiving tacrolimus, prednisolone, and mycophenolate mofetil as maintenance immunosuppressive therapy.

Table 1: Baseline demographic and clinical characteristics of the study population (n=72)

Characteristic	n (%) / Summary value
Age, years, mean ± SD	43.2 ± 11.7
≤30 years	11 (15.3)
31–40 years	20 (27.8)
41–50 years	23 (31.9)
>50 years	18 (25.0)
Male	54 (75.0)
Female	18 (25.0)
Male: female ratio	3:1
Duration since transplant, median (IQR), years	3.8 (1.4–6.7)
<1 year after transplant	18 (25.0)
1–5 years after transplant	34 (47.2)
>5 years after transplant	20 (27.8)
Tacrolimus	72 (100.0)
Prednisolone	72 (100.0)
Mycophenolate mofetil	72 (100.0)

Infectious dermatoses were identified in 43 (59.7%) recipients, with fungal infection being the most common infectious category [31 (43.1%)]. Non-infectious manifestations were recorded in 50 (69.4%) recipients, while drug/immunosuppression-related changes occurred in 28 (38.9%) patients. [Table 2]

Table 2: Major categories of dermatological manifestations among renal transplant recipients

Dermatological category	n (%)	95% CI
Any infectious dermatosis	43 (59.7)	48.2–70.3
Fungal infection	31 (43.1)	32.3–54.6
Viral infection	13 (18.1)	10.9–28.5
Bacterial infection	10 (13.9)	7.7–23.7
Parasitic infestation	6 (8.3)	3.9–17.0
Any non-infectious manifestation	50 (69.4)	58.0–78.9
Drug/immunosuppression-related changes	28 (38.9)	28.5–50.4
Inflammatory/eczematous disorders	20 (27.8)	18.8–39.0
Hair disorders	15 (20.8)	13.1–31.6
Oral/mucosal manifestations	12 (16.7)	9.8–26.9
Nail disorders	10 (13.9)	7.7–23.7
Pigmentary disorders	8 (11.1)	5.7–20.4

Table 3: Detailed spectrum of infectious dermatoses

Manifestation	n (%)
Fungal manifestations	
Tinea corporis	15 (20.8)
Tinea cruris	11 (15.3)
Oral candidiasis	8 (11.1)
Pityriasis versicolor	6 (8.3)
Tinea faciei	5 (6.9)
Onychomycosis	5 (6.9)
Tinea pedis	4 (5.6)
Tinea barbae	2 (2.8)
Cutaneous candidiasis	2 (2.8)
Viral manifestations	
Viral warts	9 (12.5)
Herpes zoster	4 (5.6)
Herpes simplex	3 (4.2)
Molluscum contagiosum	2 (2.8)
Bacterial manifestations	
Folliculitis	7 (9.7)
Furunculosis	3 (4.2)
Impetigo/pyoderma	2 (2.8)
Parasitic manifestation	

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Manifestation	n (%)
Scabies	6 (8.3)

Note: Patients could have more than one infectious manifestation; therefore, percentages do not total 100%.

Table 4: Detailed spectrum of non-infectious dermatological manifestations

Manifestation	n (%)
Xerosis	18 (25.0)
Acne/acneiform eruption	16 (22.2)
Pruritus	12 (16.7)
Striae	10 (13.9)
Seborrhoeic dermatitis	8 (11.1)
Diffuse alopecia/hair loss	8 (11.1)
Skin atrophy	6 (8.3)
Contact dermatitis	6 (8.3)
Nail dystrophy/brittle nails	6 (8.3)
Hyperpigmentation	6 (8.3)
Ecchymosis/easy bruising	5 (6.9)
Eczema	5 (6.9)
Androgenetic alopecia	5 (6.9)
Urticaria	4 (5.6)
Telogen effluvium	4 (5.6)
Aphthous oral ulceration	4 (5.6)
Xerostomia	4 (5.6)
Facial erythema	4 (5.6)
Psoriasis/psoriasiform lesions	2 (2.8)
Hypopigmentation	2 (2.8)

Note: Patients could have more than one non-infectious manifestation; therefore, percentages do not total 100%.

Among individual manifestations, tinea corporis (20.8%) and tinea cruris (15.3%) were the leading dermatophyte infections (Table 3). Xerosis (25.0%) and acne/acneiform eruption (22.2%) were the most frequent non-infectious findings. [Table 4]

Table 5: Association between duration since renal transplantation and dermatological manifestations

Manifestation	<1 year (n=18)	1–5 years (n=34)	>5 years (n=20)	χ^2	p-value
Any infectious dermatosis	14 (77.8%)	22 (64.7%)	7 (35.0%)	7.87	**0.020**
Fungal infection	12 (66.7%)	14 (41.2%)	5 (25.0%)	6.80	**0.033**
Any non-infectious manifestation	8 (44.4%)	24 (70.6%)	18 (90.0%)	9.31	**0.010**
Multiple dermatological manifestations	4 (22.2%)	16 (47.1%)	14 (70.0%)	8.68	**0.013**

A significant temporal pattern was observed. Infectious dermatoses decreased from 77.8% within the first post-transplant year to 35.0% beyond 5 years (p=0.020), and fungal infections decreased from 66.7% to 25.0% (p=0.033). In contrast, non-infectious manifestations increased from 44.4% to 90.0% (p=0.010), while multiple dermatological manifestations increased from 22.2% to 70.0% (p=0.013). [Table 5]

Table 6: Number of dermatological manifestations per patient

Number of manifestations	n (%)
One	38 (52.8)
Two	20 (27.8)
Three or more	14 (19.4)
Any multiple manifestations	34 (47.2)

Overall, 34 (47.2%) recipients had two or more dermatological manifestations, including 14 (19.4%) with three or more manifestations (Table 6). Representative clinical manifestations are shown in Figures 1-3.

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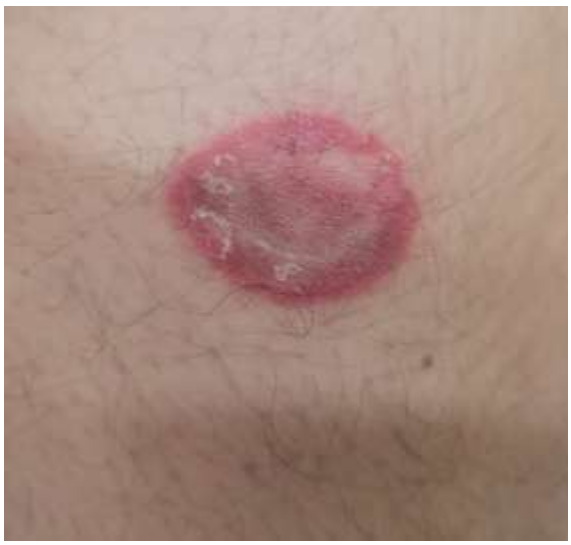

Figure 1: Tinea corporis in a renal transplant recipient

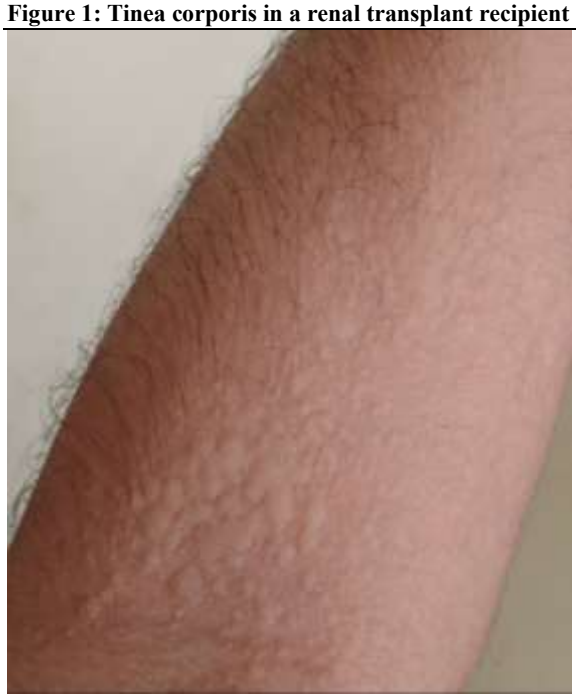

Figure 2: Urticaria in a renal transplant recipient

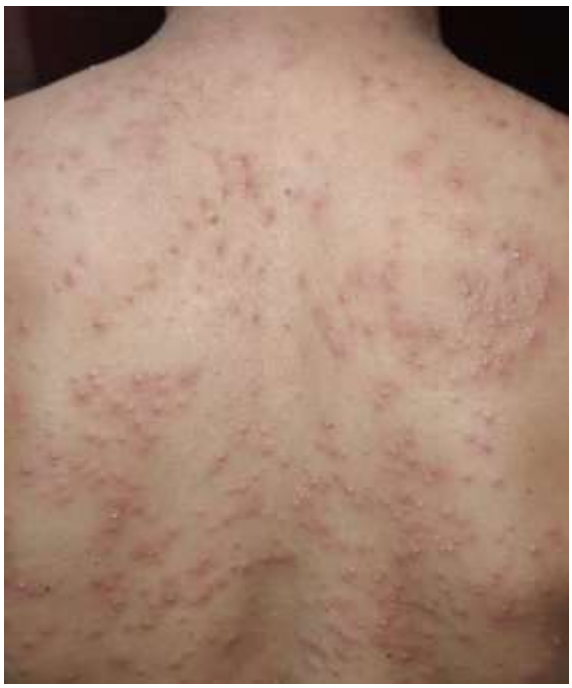

Figure 3: Acneiform eruption in a renal transplant recipient

DISCUSSION

Renal transplant recipients experience a broad range of dermatological disorders because long-term immunosuppression changes host immune defense. At the same time, individual immunosuppressive drugs can themselves produce cutaneous, mucosal, hair, and nail abnormalities. In the present study, infectious dermatoses were identified in 59.7% of recipients, while non-infectious manifestations occurred in 69.4%. Nearly half of the patients had more than one dermatological disorder. This mixed pattern supports the concept that dermatological morbidity after renal transplantation is determined by both immunosuppression-related susceptibility to infection and the cumulative adverse effects of long-term treatment.[2]

The burden of dermatological abnormalities reported among renal transplant recipients varies widely between studies. George et al. evaluated 365 renal transplant recipients in India and identified skin lesions in 94.7% of patients. Drug-related lesions of aesthetic interest accounted for 62.3% of lesions, whereas infections accounted for 27.3%.[7] Chugh et al., in another Indian study conducted in a tropical environment, also demonstrated a high frequency of both immunosuppression-related cutaneous changes and infections.[8] Direct comparison of overall prevalence with the present study should be made cautiously because the current population was selected from renal transplant recipients attending or referred to dermatology services. Therefore, the present findings describe the spectrum and relative burden of dermatological disease rather than the population prevalence of dermatoses among all renal transplant recipients.

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Fungal infections were the major infectious category in the present study, affecting 43.1% of patients. Dermatophytic infections, particularly tinea corporis and tinea cruris, formed an important part of this burden. This finding is consistent with previous studies from tropical and subtropical settings. Chugh et al. reported cutaneous mycoses in 82.6% of renal allograft recipients with infectious manifestations, with tinea corporis and tinea cruris being particularly frequent.[8] George et al. similarly found that fungal disorders comprised 58.7% of infections among Indian renal transplant recipients.[7] The predominance of dermatophytosis in Indian transplant recipients may reflect the combined effects of impaired cell-mediated immunity, warm and humid climatic conditions, sweating, occlusion, and repeated community exposure to dermatophytes.

The frequency of fungal disease also agrees with evidence from studies outside India. Güleç et al. evaluated 102 renal transplant recipients and found superficial fungal infections in 63.7%, compared with 30.7% among healthy controls. Pityriasis versicolor was the commonest fungal disorder in their population, followed by cutaneous or oral candidiasis.[9] Imko-Walczuk et al. subsequently reported superficial fungal infection in approximately 60% of 223 renal transplant recipients, compared with 27% of controls.[10] Differences in the specific fungal spectrum between studies probably reflect geographic variation, immunosuppressive regimens, duration following transplantation, local antifungal use, and differences in active microbiological screening. In the present study, special attention was given to systemic antifungal therapy because azole antifungal agents may inhibit CYP3A-mediated tacrolimus metabolism and increase tacrolimus exposure. Terbinafine and topical antifungal treatment was preferred where clinically appropriate. When systemic azole therapy such as fluconazole or itraconazole was required, treatment was undertaken in coordination with the nephrology team. Tacrolimus dose adjustment and therapeutic drug monitoring were performed or advised where clinically indicated.

An important observation in the present study was the higher frequency of infectious disease during the earlier post-transplant period. Infectious dermatoses occurred in 77.8% of patients within the first year, compared with 35.0% among those more than five years after transplantation. Fungal infections showed a similar decline, from 66.7% during the first year to 25.0% over five years. The association between early transplantation and superficial fungal infection has also been reported by Imko-Walczuk et al., who observed a particularly high frequency of fungal infection during the first year after renal transplantation.[10] Contemporary reviews similarly recognize the early post-transplant period as an important phase of infection risk because immunosuppression is generally more intense during this period.[3] The present findings therefore suggest that dermatological surveillance for opportunistic and superficial infections may be particularly valuable during the initial period following transplantation.

However, the relationship between fungal disease and duration of immunosuppression is not uniform across all studies. Güleç et al. did not identify duration of immunosuppression as a significant determinant of superficial fungal infection.[9] Such differences may arise from variations in study populations, immunosuppressive protocols, prophylactic therapy, climatic conditions, and methods used to diagnose fungal disease. Therefore, the temporal association observed in the present study should not be interpreted as indicating that infection risk invariably decreases with time in every transplant recipient.

Viral infections were less frequent than fungal infections in the present series. Viral warts were observed in 12.5% of patients, while herpes zoster, herpes simplex, and molluscum contagiosum occurred less frequently. Sandhu et al., in their study of mucocutaneous infections among renal transplant recipients, found viral infections to form a major component of infectious episodes.[11] Persistent human papillomavirus infection is particularly relevant in chronically immunosuppressed recipients because viral warts may become multiple, resistant to therapy, or recurrent. The comparatively lower viral burden in the present study may be related to differences in duration after transplantation, intensity of immunosuppression, demographic characteristics, or dermatological referral patterns.

Bacterial infections formed a relatively smaller group. Folliculitis was the predominant bacterial manifestation, followed by furunculosis and pyoderma. Sandhu et al. also documented bacterial infections among renal transplant recipients, although these were less frequent than viral and fungal infections.[11] The relatively modest bacterial burden in the present study may partly reflect easier clinical recognition, earlier use of antibacterial treatment, and the transient nature of many uncomplicated bacterial skin infections. Potential CYP3A4 drug interactions should be considered while treating infections, as drugs such as azithromycin and clarithromycin, which are CYP3A4 inhibitors, can increase tacrolimus levels, which can be detrimental for the patient. Drugs such as clarithromycin and azithromycin should be avoided.

Scabies was detected in 8.3% of the present population. Although parasitic infestations are usually less frequently reported than fungal or viral infections, they remain clinically relevant in immunosuppressed individuals. Immunosuppression can alter the appearance and severity of scabies, and unusual or extensive forms may occur. Household exposure, overcrowding, local community prevalence, and socioeconomic conditions can also influence its occurrence. Therefore, scabies should remain part of the differential diagnosis of pruritic eruptions in renal transplant recipients, particularly in settings where infestation is common.

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Non-infectious manifestations affected 69.4% of patients and became more frequent with longer post-transplant duration. Xerosis was the most common non-infectious manifestation, occurring in 25.0%, followed by acne or acneiform eruption in 22.2%, pruritus in 16.7%, and striae in 13.9%. These findings are clinically plausible in patients exposed to chronic corticosteroid and multidrug immunosuppressive therapy. Chugh et al. reported xerosis, striae, facial erythema, hypertrichosis, and skin fragility among common non-infectious changes following renal transplantation.[8] George et al. also identified drug-related aesthetic changes as the largest group of dermatological manifestations in their Indian cohort.[7]

Acneiform eruptions deserve particular attention because corticosteroid exposure can alter pilosebaceous activity and produce monomorphic acneiform lesions. George et al. identified acneiform eruptions among the common treatment-related manifestations in renal transplant recipients.[7] Differences in the frequency of acne, hypertrichosis, gingival enlargement, and alopecia between older and contemporary studies may partly reflect changes in immunosuppressive treatment. Many older transplant cohorts predominantly received cyclosporine and azathioprine, whereas the patients in the present study were receiving tacrolimus, mycophenolate mofetil, and prednisolone. Castello et al. also noted that changes in immunosuppressive protocols influence the spectrum of dermatological abnormalities observed after kidney transplantation.[12]

Hair disorders were identified in approximately one-fifth of patients. Diffuse hair loss, androgenetic alopecia, and telogen effluvium formed the observed spectrum. Hair loss in renal transplant recipients is likely multifactorial rather than attributable to a single medication. Tacrolimus exposure, physiological stress, nutritional disturbances, endocrine abnormalities, underlying genetic susceptibility, and recovery from chronic renal failure may all contribute. Consequently, temporal association with drug therapy and exclusion of other causes are important before attributing alopecia directly to immunosuppression.[1]

Oral and mucosal abnormalities were also observed, including aphthous ulceration and xerostomia. Oral ulceration is especially relevant in patients receiving mycophenolate mofetil. Tenório et al. described persistent oral ulcerations associated with MMF in a kidney transplant recipient, in whom lesions resolved after reduction of MMF exposure once infectious and malignant causes had been excluded.[13] Thus, persistent or atypical oral ulceration in transplant recipients should not automatically be considered drug-related. Infection, medication toxicity, inflammatory disease, and malignancy must be excluded before establishing the diagnosis.

One important temporal observation in the present study was the progressive increase in non-infectious and multiple dermatological disorders with increasing duration after transplantation. Non-infectious manifestations increased from 44.4% within the first year to 90.0% over five years, while multiple dermatological conditions increased from 22.2% to 70.0%. This finding suggests a cumulative dermatological burden associated with prolonged survival and long-term exposure to immunosuppressive therapy. Castello et al. similarly found that prolonged immunosuppressive exposure was associated with important dermatological complications and that premalignant and malignant lesions were particularly associated with longer duration after transplantation.[12]

Premalignant and malignant lesions were not seen in the present study. Long-term immunosuppression substantially increases the risk of keratinocyte cancers, particularly squamous-cell carcinoma, among renal transplant recipients.[5,6] Thet et al. demonstrated a considerable burden of benign and malignant skin lesions among contemporary renal transplant recipients, with non-melanoma skin cancer representing an important long-term complication.[5] A systematic review by Olszewska et al. likewise highlighted the increased risk of non-melanoma skin cancer in kidney transplant recipients receiving calcineurin inhibitors.[6] The relatively small number of malignant lesions in the present study may reflect the sample size, younger mean age, skin type, duration of follow-up, sun exposure, and geographic characteristics of the study population.

The finding that multiple dermatoses were present in 47.2% of recipients is also clinically relevant. A patient may simultaneously develop an opportunistic infection, a chronic drug-related cutaneous change, a hair or nail disorder, and an inflammatory dermatosis. Consequently, evaluation should not stop after identification of the first lesion. A complete examination of the skin, oral mucosa, scalp, hair, and nails is more appropriate for this population. Previous studies have similarly demonstrated considerable heterogeneity and coexistence of dermatological abnormalities in kidney transplant recipients.[2,12]

Overall, the present findings suggest a temporal shift in dermatological morbidity after renal transplantation. Infectious and particularly fungal disorders appeared more prominent during the earlier period following transplantation, while non-infectious and multiple cutaneous disorders accumulated with longer post-transplant duration. This pattern is biologically plausible because the early period is characterized by relatively intense immunosuppression and susceptibility to opportunistic infection. In contrast, prolonged treatment increases cumulative drug-related, inflammatory, viral, premalignant, and malignant cutaneous morbidity.[1,3,6]

These findings support regular dermatological surveillance as part of long-term renal transplant care. Attention should be given to superficial fungal infection in the early post-transplant period, persistent viral lesions, unusual or treatment-resistant infections, chronic oral ulceration, and new or

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changing keratotic lesions. Collaboration between dermatologists and nephrologists is also important because treatment of dermatological disease may interact with transplant medications, and modification of immunosuppression should not be undertaken without consideration of graft function and rejection risk.

The present study has certain limitations. Its retrospective, single-center design limits the ability to establish causal relationships and may introduce referral and documentation bias. Patients were selected from those attending or referred to dermatology services; therefore, the findings cannot be interpreted as the prevalence of dermatological disease among all renal transplant recipients. The relatively small sample size also limits subgroup analysis, particularly for uncommon premalignant and malignant lesions. Microbiological or histopathological confirmation was not available for every lesion, and detailed cumulative doses or blood concentrations of individual immunosuppressive agents could not be correlated consistently with specific manifestations. Nevertheless, the study provides a clinically useful overview of the diverse infectious and non-infectious dermatological problems encountered among renal transplant recipients receiving a contemporary regimen comprising tacrolimus, prednisolone, and mycophenolate mofetil.

CONCLUSION

In this dermatology-referred cohort, renal transplant recipients receiving long-term immunosuppressive therapy with tacrolimus, prednisolone, and mycophenolate mofetil showed a wide spectrum of dermatological and mucocutaneous manifestations. Infectious disorders, particularly fungal infections and dermatophytosis, formed an important part of the early post-transplant dermatological burden. In contrast, non-infectious, drug-related, inflammatory, hair, nail, and mucosal abnormalities became increasingly relevant with longer duration after transplantation. The coexistence of multiple dermatological conditions in a substantial proportion of patients highlights the value of comprehensive skin examination rather than symptom-based assessment alone. Although premalignant and malignant lesions were not seen in this cohort, their potential long-term risk warrants continued surveillance. Regular dermatological screening, early recognition of infection, assessment of treatment-related adverse effects, and coordinated management with nephrology may help reduce morbidity while maintaining graft safety.

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