

Original Research Article

Cutaneous manifestations in renal transplant recipients

Nekram Baghel, Sankalp Awasthi, Sweta S. Kumar*

Department of Dermatology, Uttar Pradesh University of Medical Sciences, Saifai, Etawah, Uttar Pradesh, India

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***Correspondence:**

Dr. Sweta S. Kumar,

E-mail: medicosweta.88@gmail.com

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ABSTRACT

Background: Skin lesions both benign and malignant occur frequently in renal transplant recipients receiving long term immunosuppressive drugs. Aim was to study cutaneous manifestations in renal transplant recipients (RTRs).

Methods: Thirty two patients with chronic kidney diseases who underwent renal transplant were included in the study. All of the patients were fully examined for cutaneous, hair, nail and mucosal changes. Diagnostic measures such as scraping and biopsy of the lesions was carried out, where necessary.

Results: Out of 32 patients, 23 (71.8%) were male and 9 (28.1%) were females. Skin infections occurred in 84.3% of the patients and most of them were fungal infections (37.5%), followed by viral infection in (31.2%) patients. Oral mucosal changes, hair and nail comprising of (34.3%), (71.8%), (43.7%) patients respectively. Only malignancy seen in one patient was basal cell carcinoma. Drug induced cutaneous manifestations were acneiform eruptions (18.75%), hirsutism (15.6%), hypertrichosis (9.3%), striae (6.25%), gingival hyperplasia (3.12%) and skin atrophy (3.12%).

Conclusions: Skin lesions are a significant problem in renal transplant recipients. A careful monitoring of these patients is recommended for early diagnosis and treatment.

Keywords: Gingival hyperplasia, Immune-suppressants, Renal transplant recipients

INTRODUCTION

Kidney transplant recipients are at the risk of a broad spectrum of skin diseases. Various cutaneous infections such as bacterial, viral and fungal infections as well as increased chances of skin cancers have been observed in organ transplant recipients.¹⁻⁴ The incidence of malignancy increases after renal transplantation. Skin cancer is the most frequent amongst malignancies, and is seen in 3-10% of renal transplant recipients.⁵⁻⁷

These cancers include squamous cell carcinomas (SCC), basal cell carcinoma (BCC), Bowen's disease, Kaposi sarcoma, and probably malignant melanoma.⁸ In organ transplant recipients skin cancers are usually multiple and invasive and have greater risk of recurrence after treatment. The risk of metastasis is also high in skin cancers of these patients.^{7,9,10} Drug-related lesions including hypertrichosis, gingival hyperplasia, acneiform

eruptions, cushingoid features, and striae frequently occur as a result of the immunosuppressive administration.

METHODS

All renal transplant recipients (RTRs) who underwent regular clinical follow up every month by nephrologist. Beyond scheduled visit patients were referred for dermatological consultation when skin lesions were noted by patients or by the nephrologist, these patients were enrolled for study. The period of study was from January 2012 to August 2016. In addition to dermatological examination, a standardized questionnaire was administered to all patients to obtain a detailed personal history, including information on age, occupation, cause of renal failure, date of renal transplant, and current immunosuppressive drug regimen. Specific investigations like skin biopsy, culture and sensitivity for bacterial infections, Gram's stain, potassium hydroxide mount and

fungal culture were done where indicated, after informed consent.

Statistical analysis

The percentage of various skin lesions occurring in RTR such as infections, neoplasms and miscellaneous lesions were calculated and the significance in difference, if any, was established using the Mann-Whitney U test. A p-value less than 0.05 was considered significant.

RESULTS

Out of 32 patients in this group, 23 (71.8%) were male and 9 (28.1%) were females. The mean age group was 37.9 years. The most important manifestation was infections seen in 84.3% (Table 1).

Table 1: Cutaneous manifestations in renal transplant patients.

Clinical features	Total patients	Percentage
Infections	27	84.38%
Purpura	4	12.5%
Pallor	4	12.5%
Seborrheic dermatitis	3	9.37%
Perioral dermatitis	1	3.12%
Cutaneous malignancies	1	3.12%
Hair changes	23	71.8%
Oral changes	11	34.3%
Nail changes	14	43.7%
Manifestations of immunosuppressive drugs	18	56.2%

Table 2: Various infections in renal transplant patients.

Infections/Infestations	Total patients	Percentage
Viral		
<i>Herpes zoster</i>	2	6.25%
<i>Herpes simplex</i>	1	3.12%
Concomitant CMV and herpes simplex infection	1	3.12%
<i>Verruca vulgaris</i>	3	9.3%
<i>Molluscum contagiosum</i>	2	6.25%
<i>Varicella zoster</i>	1	3.12%
Bacterial		
Folliculitis	1	3.12%
Furuncles	2	6.25%
Fungal		
Dermatophyte	4	12.5%
<i>Pityriasis versicolor</i>	5	15.6%
Candidiasis	3	9.3%
Parasitic infections		
Scabies	2	6.25%

Among infections predominant was fungal infection seen in (37.5%) patients (Figure 1), followed by viral infection

in (31.2%), bacterial infection (9.3%), parasitic infestations (6.25%) patients (Table 2).



Figure 1: Extensive tinea corporis in renal transplant patient.

Among viral infections most common was verruca vulgaris (9.3%) (Figure 2) followed by molluscum contagiosum (6.2%) (Figure 3).



Figure 2: Verruca vulgaris in renal transplant patient.

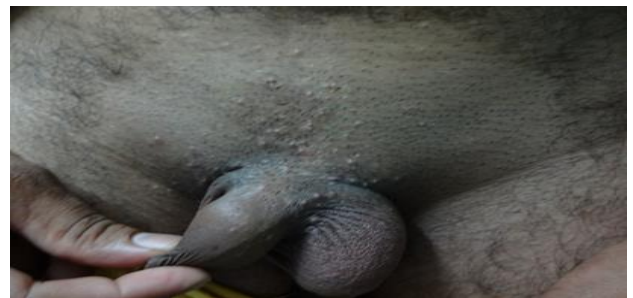


Figure 3: Molluscum contagiosum in renal transplant patient.



Figure 4: Basal cell carcinoma in renal transplant patient.

Oral mucosal, hair and nail changes comprising of (34.3%), (71.8%), (43.7%) patients respectively. Among oral changes most common was candidiasis (9.3%). Diffuse alopecia (28.12%) was most common among hair changes followed by brittle and lusterless hair in (18.75%) patients. Onychomycosis (18.75%) was common in nail changes. Only malignancy seen in one (3.12%) patient was basal cell carcinoma (Figure 4) 12 years post-transplant.

Table 3: Manifestations of immunosuppressive drugs.

Clinical features	Total patients	Percentage
Acneiform eruptions	6	18.75%
Hypertrichosis	3	9.3%
Gingival hyperplasia	1	3.12%
Striae	2	6.25%
Hirsutism	5	15.6%
Skin atrophy	1	3.12%

All renal transplant patients were on one or two immunosuppressive drugs like prednisolone, azathioprine, cyclosporine and tacrolimus. Drug induced cutaneous manifestations were acneiform eruptions (18.75%) (Figure 4), hirsutism (15.6%), hypertrichosis (9.3%) (Figure 5), striae (6.25%), skin atrophy (3.12%) and gingival hyperplasia in (3.12%) (Figure 6) (Table 3). One unique finding in present study was concomitant HSV and CMV infection which was not seen in previous studies.



Figure 5: Hypertrichosis in renal transplant patient on oral cyclosporine.



Figure 6: Gingival hyperplasia to cyclosporine.

Table 4: Cutaneous manifestations based on duration since renal transplant.

Cutaneous manifestations	<5years of duration	5-10 years of duration	>10 years of duration
Infections	20 (62.5%)	05 (15.6%)	02 (6.25%)
Purpura	1 (3.12%)	02 (6.25%)	01 (3.12%)
Pallor	2 (6.25%)	01 (3.12%)	01 (3.12%)
Seborrheic dermatitis	2 (6.25%)	-	-
Perioral dermatitis	-	01 (3.12%)	-
Cutaneous malignancies	-	-	01 (3.12%)
Hair changes	18 (56.25%)	04 (12.5%)	01 (3.12%)
Nail changes	10 (31.25%)	03 (9.3%)	01 (3.12%)
Mucosal changes	8 (25%)	02 (6.25%)	01 (3.12%)
Acneiform eruptions	4 (12.5%)	02 (6.25%)	-
Hypertrichosis	1 (3.12%)	02 (6.25%)	-
Striae	1 (3.12%)	01 (3.12%)	-
Hirsutism	1 (3.12%)	02(6.25%)	02 (6.25%)
Skin atrophy	-	01(3.12%)	-

On the basis of duration since transplant patients were classified into three groups- less than 5 years of duration (22 patients), 5-10 years (7 patients), more than 10 years (3 patients). Cutaneous manifestations in these groups were compared (Table 4).In patients having renal transplant for less 5 years; infections were most common;

seen in 20 patients (62.5%), followed by hair changes in 18 patients (56.25%), nail changes in 10 patients (31.25%). Drug related changes like hypertrichosis in 2 patients (6.25%), striae in 1 (3.12%) and skin atrophy in 1 patient (3.12%) were predominantly seen in 5-10 years duration since renal transplant patients. Basal cell

carcinoma was seen in one patient having duration of renal transplant more than 10 years. Miscellaneous changes that are not related to renal transplant like melasma, keloid, acute urticaria were also seen in 17 patients (Table 5).

Table 5: Miscellaneous conditions.

Miscellaneous conditions	Total patients
Keloids	2
Achrocordons	4
Melasma	3
Acute urticaria	2
Psoriasis vulgaris	2
Fixed drug eruption	1
Vasculitis	2
Prurigonodularis	1

DISCUSSION

Skin lesions are a significant problem in renal transplant patients and this study has been conducted to highlight the spectrum of dermatological lesions seen in RTR. We studied the prevalence of skin lesions in patients who had already undergone a renal transplant and prospectively studied the time profile of skin lesions in a group of patients who were followed up from after transplant.

Cutaneous infections

The incidence of infections were 84.3%, with dermatophytic infection in 12.5% patients, viral in 31.25% patients, bacterial infections in 9.3% patients and parasitic infestations in 6.25% patients. Infections were the most common cutaneous manifestation similar to studies done by Lugo-Janer and co-workers and Benicini and colleagues.¹¹ Rafi et al, observed skin lesions in 90% of renal transplant patient, out of which cutaneous infections were present in nearly half of them.¹² The higher incidence of infections can be explained because of long term use of immunosuppressive drugs. The cutaneous infections were more common in patients having duration of transplant less than five years than those with duration of transplant more than ten years. This could be due to high dose of immunosuppressant drugs required immediately after transplant, given to prevent chance of rejection. Among fungal infections, pityriasis versicolor was the commonest infection in renal transplant patients, seen in 18.5% patients. Gluec et al from Turkey reported pityriasis versicolor in 36.3% patients as compared to 13.3% in some of the studies in India and 18% in West in renal transplant patients.¹³⁻¹⁵ Dermatophytosis accounted for 42% of total infection in a study done by Selvi et al, which is similar to present study.¹⁶ Deep fungal infections are very rare in these patients. There was no case seen in present study.

The incidence of viral infection in present study in second group was 31.25%, which is similar to study done

by Benici et al, 35%, while Chugh et al, found 29%, Koranda et al, 43%. Among infections the incidence of verruca vulgaris was 9.3%, herpes zoster 6.25%, molluscum contagiosum 6.25%, varicella zoster 3.12%, herpes simplex 3.12% and cytomegalovirus infection 3.12%.^{11,14,15} In present study warts and pityriasis versicolor were more common after one year of transplantation, but HSV infections and candidiasis were more common in the early period (less than 6 months) after transplantation which agrees with Benici et al.¹¹ Warts were found to be numerous and of greater proportion in the late recipients, as they are more related to the duration of immunosuppression rather than the degree of immunosuppression.^{17,18}

One unique finding in present study was concomitant HSV and CMV infection which was not seen in previous studies. The incidence of bacterial infection reported in second group was 11.11% patients which is similar to other study in India by Lien George et al, in 11% patient, Chugh et al, in 8.9% patients and Barba et al, in 3.5% patients.^{3,14,19}

Cutaneous malignancies

In present study only one patient having malignancy in second group. Malignancies are well-recognized complication of renal transplantation. Cutaneous malignancies are more common in developed countries, than in developing countries. This is because of geographic and ethnic variations.²⁰ Skin cancers are the most common malignancy seen in organ transplant recipients and the risk of them is related to the degree of immunosuppression caused by long-term immunosuppressive therapy.²¹⁻²² In normal population basal cell carcinoma (BCC) to squamous cell carcinoma (SCC) ratio is 4:1 but in organ transplant recipients the incidence of SCC increases and this ratio reverses. Hepburn and colleagues reported malignancy in 17.3% patients which has occurred in areas exposed to sunlight. They found that SCC is more frequent than BCC.²³ In present study only patient who had malignancy was having basal cell carcinoma. He was on immunosuppressants for twelve years. Basal cell carcinoma in present study noted after twelve years of renal transplant, that is different with other previous study done by Ramsay et al study the mean duration between transplantation and development of malignancy was five years.²⁴ UV radiations have an important role in developing epithelial skin cancer (lesion situated on face). One of most important factor for decreasing the risk of skin cancers in organ transplant recipients is sun avoidance.

Cutaneous manifestations due to immunosuppressive drugs

In present study cutaneous manifestations due to immunosuppressive drugs were seen in 56.2% renal transplant patients. Most common being acneiform

eruption seen in 33.3% patients which is similar to other studies done by Chug et al, and Benici et al.^{11,14} Acneiform eruptions predominantly involved face, chest and back and were resistant to anti acne treatment. Hirsutism was seen in 15.6% patients. The incidence was 6.25% in patients with mean duration of renal transplant more than 10 years and 5-10 years and 3.12% in patients having duration less than 5 years. This could be due to long term use of steroids and cyclosporine. Striae were seen in two patients 6.25% as compared to 0.9% in one previous study done by Abbas Z et al.²⁵ Hypertrichosis was seen in 9.3% patients as compared to Chug et al who found it in 41.1% patients.¹⁴

Nail changes

Nail changes were seen in 43.75% patients. The most common being onychomycosis seen in 18.75% patients. This was again because of long term immunosuppressive drug intake.

Hair changes

Most important was diffuse alopecia seen in 28.12%, followed by brittle and lustreless hairs seen in 18.75% patients. Although hypertrichosis was lower (9.3% vs. 41.1%) compared to data by Chugh et al.¹⁴

Oral mucosal changes

Oral changes were seen in 34.3% patients, candidiasis being the commonest. Other unique finding was gingival hyperplasia seen in one patient, which was due to long term use of cyclosporine.

Miscellaneous changes

Prurigo nodularis, vasculitis, achrochordons and seborrheic dermatitis were seen that were unrelated to renal transplant.

CONCLUSION

Transplant patients are at increased risk of cutaneous lesions such as infections, cutaneous malignancies and cutaneous manifestations secondary to immunosuppressive drugs, which is an important cause of morbidity and mortality among these patients. Therefore, careful and regular examination of kidney recipients by a dermatologist is mandatory.

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