

Original Research Article

A clinical study of cutaneous manifestations in renal transplant recipients

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ABSTRACT

Background: Chronic renal failure is becoming common entity with increased incidence of diabetes mellitus and resulting diabetic nephropathy. With the availability of renal transplantation services in many centers, increased availability of donors, improved surgical technique and availability of better drugs, the survival of renal transplant recipients has increased. The objective of the study was to study the cutaneous manifestations in renal transplant recipients.

Methods: Fifty consenting, consecutive renal transplant recipients attending the OPD and in-patients at Command Hospital Air Force, Bangalore during July 2001 to March 2003 were included in the study. Detailed history was taken and clinical examination was carried out with special emphasis on the Dermatological examination. Relevant investigations were carried out.

Results: A total of 50 renal transplant recipients were studied of which 42 (84%) were males and 8 (16%) were females. The age of patients ranged from 16 years to 60 years. Infections were the most common finding, encountered in 38 (76%) patients, followed by drug induced manifestations in 24 (48%) patients. Cellulitis was noted in 1 (2%) patient, viral infections were seen in 18 (36%) patients, fungal infection was the commonest in this study, encountered in 38 (76%) patients. Monomorphic acne was seen in 13 (26%) patients. Hypertrichosis/hirsutism were the commonest drug induced manifestation in this study, seen in 16 (32%) patients.

Conclusions: In patients with renal transplantation, superficial fungal infections and viral infections of the skin are seen more commonly. Monomorphic acne and hypertrichosis due to immunosuppressive are also seen frequently. These changes are moderately influenced by the immunosuppressive regimen used.

Keywords: Transplantation, Fungal infections, Monomorphic acne

INTRODUCTION

In contrast to the remarkable capacity of the kidney to regain function following the various forms of acute renal injury, renal injury of a more sustained nature is often not reversible but leads, instead to progressive destruction of nephron mass. This permanent nephron loss progresses inexorably to chronic renal failure.¹

Over the past five decades, dialysis and transplantations have become effective in prolonging the lives of patients with renal insufficiency. These modes of management are associated with many adverse effects. Skin is one of the important target organs for the manifestation of these adverse effects.²

Patients who undergo renal transplantation are required to be put on immunosuppressive agents to prevent rejection.

Most commonly corticosteroids, azathioprine, cyclosporine mycophenolate mofetil and OKT₃ are used. Various cutaneous manifestations of renal transplantations can be grouped as drug related manifestations, skin infections – viral, bacterial, fungal, pre-malignant and malignant skin lesions and other skin diseases associated with renal transplantation.³

Drug related manifestations are hypertrichosis, telangiectasias, moon facies, facial erythema, gingival hyperplasia, acne, seborrhea, purpura, keratosis pilaris, striae distensae, sebaceous hyperplasia, epidermal cysts. Viral skin infections associated with renal transplantations are verruca vulgaris, verruca filiformis, verruca plana, and epidermodysplasia verruciformis like syndrome, herpes simplex labialis, herpes zoster and Kaposi's sarcoma. Bacterial skin infections associated with renal transplantations are folliculitis, cellulitis, ecthyma and furuncle. Fungal infections associated with renal transplantations are-pityriasis versicolor, Tinea unguium, Tinea pedis, Tinea cruris, Tinea corporis and mucocutaneous candidiasis. Apart from these infections, infestations like scabies and pediculosis are also common among renal transplant recipients.⁴

Pre-malignant and malignant skin lesions in renal transplant recipients are actinic keratosis, basal cell carcinoma, squamous cell carcinoma and Kaposi's sarcoma. A number of other conditions like xerosis, rosacea, vitiligo, plantar hyper keratosis, xanthoma, pityriasis simplex, pruritus, lichen planus, Terry's Nail etc are also associated with renal transplantation. With the availability of renal transplantation services in many centers, increased availability of donors, improved surgical technique and availability of better drugs, the survival of renal transplant recipients has increased. There are only few Indian studies carried out to study the cutaneous manifestations in renal transplant recipients. Hence there is a need to undertake such studies and therefore the present study has been done.

METHODS

The study has been carried out on 50 CRF patients who have undergone renal transplantation attending nephrology OPD as well as admitted patients at nephrology ward of Command Hospital, Air Force, Bangalore. Patients with acute renal failure are excluded from the study. Diagnosis of CRF was made by the nephrologist depending on the clinical, biochemical, radiological and histopathological findings as per the requirement.

Complete clinical examination was carried out. Clinical photographs were taken as and when cutaneous manifestations were encountered. Routine investigations were carried out in all patients. Special investigations including Tzanck smear to look for multinucleated giant cells, wet mount preparations from the scraping and microscopy, skin biopsy for histopathology, when the

diagnosis was in doubt, nail clipping for fungal culture, skin scraping for fungal culture, pus swab for culture and sensitivity were carried out at the beginning of the study and during follow up period wherever required. All patients were followed up after 1 month, 6 months and 1 year intervals.

Informed consent for inclusion into the study, photography and relevant investigations were taken from the patients. Clearance has been taken from the ethical committee of command hospital air force, Bangalore for the present study.

RESULTS

A total of 50 renal transplant recipients were studied of which 42 (84%) were males and 8 (16%) were females. The age of patients ranged from 16 years to 60 years. 3 (6%) patients were in the age group of 10-20 years, 4 (8%) in the age group of 20 to 30 years, 22 (44%) in the age group of 30-40 years, 12 (24%) in the age group of 40-50 years, and 9 (18%) patients were in the age group of 50-60 years (Table 1).

Table 1: Age and sex distribution of the study subjects.

	Number	%
Sex		
Male	42	84
Female	08	16
Age (in years)		
10-20	3	6
20-30	4	8
30-40	22	44
40-50	12	24
50-60	9	18

Table 2: Distribution of study subjects as per characteristics of renal transplants undergone.

Characteristics	Number	%
Number of transplants		
One	43	86
Two	06	12
Three	01	02
Cause of CRF		
Chronic glomerulonephritis	39	78
chronic interstitial nephritis	8	16
diabetic nephropathy	3	6
Type of graft		
Allograft from living donors	48	96
Allograft from cadaver	2	4

Cause of CRF was chronic glomerulonephritis in 39 (78%) patients, chronic interstitial nephritis in 8 (16%) patients and diabetic nephropathy in 3 (6%) patients. Duration of transplantation varied between 3 days to 10 years, with 2 (4%) patients in 0-8 week period, 6 (12%)

patients in 8 weeks to 6 months period, 12 (24%) of patients in 6 months to 2 years period, 23 (46%) patients in 2-5 years period and 7 (14%) patients in more than 5 years period. 48 (96%) were allograft from living donors and 2 (4%) were cadaver grafts. 43 (86%) patients had

one transplantation, 06 (12%) patients had 2 transplantations, and 01 (2%) patient had 3 transplantations. One (2%) patient had hyper acute rejection, 4 (8%) patients had acute rejection and 3 (6%) patients had chronic rejection (Table 2).

Table 3: Cutaneous manifestations in renal transplant recipients on different immunosuppressant regimens.

Regimen used	Total no. of patients	Patients developing infections	Patients developing drug induced manifestations
CSA+AZA+P	28	19	12
CSA+MM+P	13	9	11
MM+P	2	0	2
CSA+P+MM+AZA	2	1	2
AZA+P	5	2	4

*There is overlapping of manifestation. Some patient has developed infections as well as drug induced manifestation. Hence totaling figures in 3rd and 4th columns may not tally with figures in 2nd columns. (CSA-Cyclosporine A, AZA-Azathioprine, P-Prednisolone, MM-Mycophenolate mofetil).

Infections were the most common finding, encountered in 38 (76%) patients, followed by drug induced manifestations in 24 (48%) patients. Twenty eight (56%) patients were treated with cyclosporine + azathioprine + prednisolone posttransplant. In this group 12 (42.9%) patients had drug induced manifestations, 19 (67.9%) patients had infections. Thirteen (26%) patients were treated with cyclosporine + mycophenolate mofetil + prednisolone posttransplant. In this group 11 (84.61%) patients had infections, 9 (69.23%) patients had drug induced manifestations. Two (4%) patients were treated with mycophenolate mofetil and prednisolone posttransplant. In this group, 2 (100%) patients developed infections. Two (4%) patients were treated with cyclosporine + azathioprine + mycophenolate mofetil + prednisolone posttransplant and in this group 2 (100%) patients developed infections and 1 (50%) patient developed drug induced manifestations. Five (10%) patients were treated with azathioprine and prednisolone posttransplant and in this group 4 (80%) patients developed infections and 2 (40%) patients developed drug induced manifestations (Table 3).

Cellulitis was seen in one (2%) patient. Viral infections were seen in 18 (36%) patients and among these, herpes labialis was seen in 9 (18%) patients, herpes genitalis in one (2%) patient herpes zoster in 1(2%) patient, chicken pox in 3 (6%) patients, out of these 3, 2 (4%) patients had persistent varicella infection. Verruca vulgaris was seen in 4 (8%) patients out of these, one (2%) patient developed Buschke-Lowenstein tumor for which all conservative modalities of treatment failed and he was subjected to partial amputation of penis. This patient also had extensive verrucous nodular lesions of wart measuring about 3-5 cm over legs and pubic region. This patient had undergone transplantation in 1992. Fungal infection was the commonest in this study, encountered in 38 (76%) patients. Among the fungal infections, pityriasis versicolor was the commonest, seen in 16 (32%) patients, followed by tinea cruris et corporis in 8 (16%) patients, onychomycosis in 5 (10%) patients, oral candidiasis in 10 (20%) patients (Table 4).

Table 4: Cutaneous manifestations in post-transplant patients.

Cutaneous manifestations	Number	%
Herpes labialis	9	18
Herpes genitalis	1	2
Herpes zoster	1	2
Chicken pox	2	4
Wart	4	8
Pityriasis versicolor	16	32
Dermatophytosis	8	16
Onychomycosis	5	10
Candidiasis	10	20
Moon facies/buffalo hump	3	6
Acne	13	26
Hypertrichosis/hirsutism	16	32
Diffuse hyperpigmentation of sun exposed area	5	10
Xerosis	14	28
Cellulitis	14	28
Facial erythema	2	4
Gingival hypertrophy	2	4
Keratinosis pilaris	1	2

DISCUSSION

Infections were the most common cutaneous findings encountered in this study observed in 38 (76%) patients. Among infections, fungal infections were the commonest, encountered in 38 (76%) patients. In the decreasing order of frequency, pityriasis versicolor in 16 (32%) patients, oral candidiasis in 10 (20%) patients, tinea cruris et corporis in 8 (16%) patients and onychomycosis in 5 (10%) patients. This is in accordance with other studies in which the frequency of pityriasis versicolor has been reported to be 14.5% and 25%, tinea cruris (4%), onychomycosis (29%) and oral candidiasis (8%).^{3,4,6}

Koranda et al recorded herpes simplex in 35%, herpes zoster in 13% and warts in 43%.⁵ In the present study,

herpes labialis was observed in 9 (18%) patients, herpes genitalis in one (2%) patients, herpes zoster in 1 (2%) patient, chicken pox in 3 (6%) patients in the early transplant period (within 6 months posttransplant) and verruca vulgaris in 4 (8%) patients, including one (2%) patient with extensive verruca vulgaris with Buschke-Lowenstein tumor.

Among bacterial infections, cellulitis was seen in only one (2%) patient. This is in accordance with the study of Koranda et al who did not find any case of staphylococcal or streptococcal skin infections in 200 renal transplant recipients.⁵

Among the drug induced manifestations, hypertrichosis/hirsutism was the commonest finding, noted in 16 (32%) patients, followed by monomorphic acne in 13 (26%) patients and moon facies and buffalo hump in 3 (6%) patients and facial erythema in 2 (4%) patients. All these findings were noted within 6 months of transplantation. Lugo-Janer et al observed in their series of 82 patients of renal transplant recipients, acne in 31% and hypertrichosis in 61% of patients.⁶ However, Koranda et al observed acne in 63% of patients, hypertrichosis/hirsutism in 49% of patients and facial erythema in 70% of patients.⁵

Xerosis was observed in 14 (28%) patients and diffuse hyper pigmentation of sun exposed skin was observed in 5 (10%) patients. Koranda et al observed xerosis in 66% of patients and diffuse hyper pigmentation in 2% of their series of 200 renal transplant recipients.⁵

Gingival hyperplasia was observed in 2 (4%) patients. This may be due to the adverse effect of cyclosporine or diltiazem used for control of hypertension or due to both. Keratosis pilaris was noted in one (2%) patient. Reported frequency of gingival hyperplasia is 8-70% and that of keratosis pilaris is 55%.^{5,7}

Both pre malignant and malignant lesions have been reported to increase with greater time after renal transplantation and may be related to sun exposure and skin type.⁶ For skin malignancy, the average time of diagnosis is 5 years posttransplant.^{8,9} Only 7 patients included in this study crossed 5 years posttransplant period and all patients included in the study are Indian patients (skin type 4/5). This could possibly explain the absence of premalignant and malignant skin lesions observed in this study.

Half and half nail was noted in 4 (8%) patients, pediculosis pubis was noted in 1 (2%) patient and one (2%) patient had Kyrle's disease that was also found to be diabetic. Another interesting observation made in this study includes the increased prevalence of infections in those patients whose immunosuppressive regimen included mycophenolate mofetil in addition to other

immunosuppressant. 17 (34%) patients were treated with mycophenolate mofetil in addition to other immunosuppressive drugs (prednisolone ± cyclosporine ± azathioprine). Out of these 17 patients, 15 (88.23%) patients developed infections, predominantly fungal (pityriasis versicolor and oral candidiasis) in comparison to those 33 (66%) patients who were treated with a non-mycophenolate mofetil regimen out of which 23 (69.69%) patients developed infections. This could be due to the more potent immunosuppressive potential of mycophenolate mofetil.

CONCLUSION

In renal transplant recipients, the cutaneous manifestations are mainly related to infections and drug induced manifestations and these changes are moderately influenced by the immunosuppressive regimen used.

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Ethical approval: The study was approved by the institutional ethics committee

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