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Mucocutaneous lesions in renal transplant recipients in Erbil City

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Abstract

Background & objectives: Cutaneous manifestations may appear after kidney transplantation such as skin cancer and skin infections. Long-term use of the immunosuppressive drug could be a reason for developing and/or increasing incidence of the skin manifestations. The aim of this study is to describe the prevalence of skin and mucosal lesions in renal transplanted patients and evaluating the effect of immunosuppression on the skin.

Methods: a cross-sectional study was performed on 122 kidney transplant recipients of different ages of both sexes. A thorough examination performed by a dermatologist to detect and describe the lesions, then a diagnosis was based on the clinical and morphological features.

Results: Of 122 patients, 121 (99.2%) suffered from at least one skin disease. The most common diseases were the infections which include: - folliculitis 13 (10.7%) patients, wart 26 (21.3%) patients, tinea pedis 17 (13.9%) patients and scabies 1 (0.8%) patient. Among the evaluated patients, 26.2% of patients had premalignant and malignant diseases. Cutaneous side effects of immunosuppressive drugs were observed in 103 (84.4%) of patients. The most common drug-related lesion was hypertrichosis in 44 (36.1) patients. Nail changes were seen in 35 (28.7%) patients, the most common nail changes were absent lanula 11 (9.0%) and onychomycosis 9 (7.4%) patients.

Conclusions: Majority of kidney transplanted patents have skin manifestation. Skin lesions are a major problem for patients after kidney transplantation due to a secondary effect of immunosuppressive drugs.

Keywords: Cutaneous diseases; kidney transplantation; skin diseases and lesions; infections.

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Introduction

The ongoing advancement in surgical techniques and upgrades in immunosuppressive brought an increase of both number of organ transplants world-wide and long-term survival after transplantation respectively[1]. In spite of the importance of immunosuppressive drugs for graft functioning immunosuppressant but often cause negative knock-on influences that impair immune system functioning which in turn lead to complications such as infections and malignancies[1,2]. Various types of skin lesions, viral, fungal, and bacterial infections as well as an elevated number of non-melanoma skin cancers (NMSC), are most frequently occurring in renal transplant recipients compared to the general population, mainly related to post-transplant immunosuppression[1-3]. Several factors such as gender, age, ethnic group, skin type and geographical location are considered as main cause of different skin lesions[3,4,5]. For instance, gingival hypertrophy and hirsutism as a side-effect of immunosuppressive therapy represented more in Asians compared to Caucasian patients[4]. Some drugs have prominent side effects on the skin and mucosa such as cyclosporine-related hypertrichosis, gingival hypertrophy, steroid-induced acneiform eruption and striae[3,6]. Squamous-cell carcinoma is the most common skin cancers in transplant recipients, occurring 65 to 250 times more often in the general population while the basal-cell carcinoma 5-10 times greater[1,7,8]. Non-melanoma skin cancers characterized by emergence at an early age and behave more aggressively, with greater local invasiveness and a greater tendency to metastasize[9].The objective of the study is to assess skin and mucosal lesions that are associated or related to renal transplant patients.

Material and methods

This cross-sectional study was conducted in Hawler Teaching Hospital/Erbil city from July to November 2019 among renal transplant recipients. One hundred twenty two patients enrolled in the current study to collect data from both genders (male and female) of different ages with transplanted kidney for at least one year. Detailed medical history from each patient was obtained which is relevant to, a thorough dermatological examination (skin, mucosa, nail and hair) was done and the diagnosis made based on clinical and morphological features of the lesions. For premalignant and

malignant lesions, necessary work such as using Dermatoscope and biopsy has been considered for the purpose of diagnosis. In addition to dermatological examinations, a standardized questionnaire was administered verbally to all patients to obtain a detailed personal history, including information on age, profession, cause of renal failure, time period of the kidney that has been transplanted, age of recipient at the time of transplantation, and current immunosuppressive drug regimen. Each patient has been informed about conducting study therefore verbal consent obtained from each one who enrolled in the study after a detailed explanation about the aim of the study. An acceptance and approval of proposal of the study obtained from ethical committee of the Kurdistan Board for Medical Specialties. The statistical package for social science (SPSS) version 25 used for data analysis. Descriptive analysis (Frequencies and Descriptive section of the SPPS) has been used for analysis of data.

Results

Of the 122 patients, 75 (61.5%) were men and 47 (38.5%) were women. The mean age of them was 38.4 years (ranges from 9 to 67 years), mean of duration of transplantation was 66.2 months (ranges from 12 to 192 months). At the time of the study several immunosuppressant regimes used by kidney recipients. The most used regime was prednisolone, mycophenolate mofetil and cyclosporine which was 93 (76.3%) and the least used regime was prednisolone 1 (0.8%), Table(1).

Table (1): Immunosuppressant regime during study

Immunosuppressant regime	Number (%)
Prednisolone, mycophenolate mofetil and cyclosporine	93 (76.3%)
Prednisolone, mycophenolate mofetil and tacrolimus	14 (11.5%)
Prednisolone and mycophenolate mofetil	6 (4.9%)
Prednisolone, mycophenolate mofetil and sirolimus	4 (3.3%)
Prednisolone and cyclosporine	2 (1.6%)
Prednisolone and tacrolimus	2 (1.6%)
Prednisolone	1 (0.8%)

Skin lesions were observed in 121 (99.2%) patients. On physical examination, 11.5% had bacterial infections, 27.8% viral infections, 18.0% fungal infections and 0.8% parasitic infections, Table (2). Folliculitis in bacterial infection, viral wart

and Tinea pedis in fungal infections were the most common with a great difference comparing to other less frequent types

Table (2): Skin infections in kidney transplant recipient

Infection	Number (%)
Bacterial infections	
• Folliculitis • Acute paronychia	13 (10.7%) 1 (0.8%)
Viral infections	
• Wart • Herpes zoster • Molluscum contagiosum • Herpes simplex	26 (21.3%) 5 (4.1%) 2 (1.6%) 1 (0.8%)
Fungal infections	
• Tinea pedis • Pityriasis versicolor • Oral candidiasis	17 (13.9%) 3 (2.5%) 1 (0.8%)
Parasitic infections	
• Scabies	1 (0.8%)

A diagnosis of premalignant and malignant conditions was made in 32 (26.2%) patients based on dermoscopic and histopathological examination, Table (3).

Table (3): Premalignant and malignant skin infections in Kidney Transplant Recipient

Infection	Number (%)
Premalignant	
• Actinic keratosis	28 (23%)
Malignant	
• Basal cell carcinoma • Kaposi sarcoma	2 (1.6%) 2 (1.6%)

Regarding non-melanoma skin cancers there are two cases of Kaposi sarcoma, one of them had the lesion on the hard palate, the other one on the face and upper extremities, Figure 1.Basal cell carcinoma dermoscopically confirmed in two patients, Figure (2).

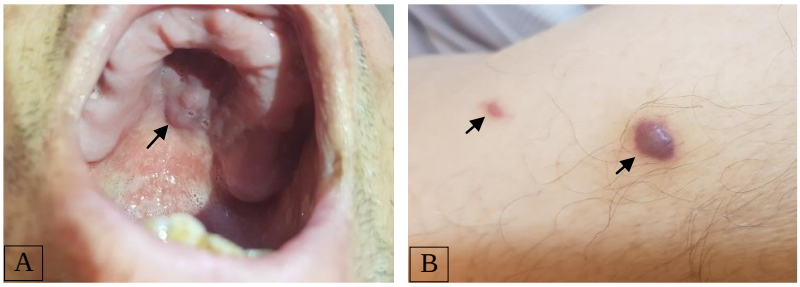

Figure (1): Kaposi sarcoma in (A) violaceous lamp on the hard palate and (B) violaceous nodule on the upper arm

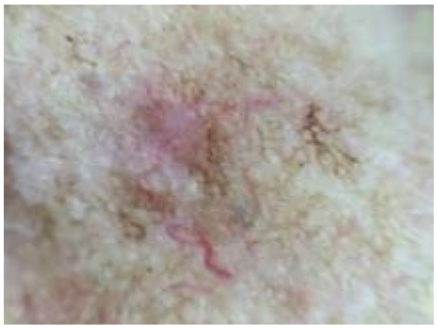

Figure (2): Dermoscopy of basal cell carcinoma on the cheek

Cutaneous side effects of immunosuppressive drugs were observed in 103 (84.4%) of patients. Among drug-related skin lesions, hypertrichosis was the most common, followed by cushingoid features, gum hypertrophy, sebaceous hyperplasia, purpura ecchymosis with acne being the least common, Table (4).

Table (4): Drug-related skin lesions in Kidney Transplant Recipient

Skin lesions	Number (%)
Hypertrichosis	44 (36.1%)
Cushingoid features	36 (29.5%)
Gum hypertrophy	32 (26.2%)
Sebaceous hyperplasia	27 (22.1%)
Purpura and ecchymosis	26 (21.3%)
Acne	19 (15.6%)

Nail changes were seen in 35 (28.7%) patients who had more than one nail changes in some patients, Table (5). The most common type was absent lanula and Onychomycosis followed by both leukonychia and koilonychia in less frequent ending with melanonychia, brittle nail, half and half nail, terry's nail, beau's nail, muehrcke's line and green nail syndrome with least availability in the current study.

Table (5): Nail disorders in Kidney Transplant Recipient

Nail changes	Number (%)
Absent Lanula	11 (9.0%)
Onychomycosis	9 (7.4%)
Leukonychia	5 (4.1%)
Koilonychia	4 (3.3%)
Melanonychia	2 (1.6%)
Nail brittle	2 (1.6%)
Half and Half Nails s	2 (1.6%)
Terry's Nail	1 (0.8%)
Beau's Line	1 (0.8%)
Muehrcke's Line	1 (0.8%)
Green nail syndrome	1 (0.8%)
Nail pitting	1 (0.8%)

Discussion

Skin lesions appeared in renal transplant recipients were extraordinary problem and stressful for physician that they have to deal with[6]. In several studies conducted in different countries such as Saudi Arabia, Italy and India skin disease reported to be ranged between (90-97%)[6] were almost like to that found in our study, (99.2%) of skin lesions. Among skin infections, human papilloma virus needs to be treated in early stages because it has been expressed that human papilloma virus behave differently in immunocompromised patients in comparison to the general population[10]. Assumption had been made that few human papilloma virus serotypes might be oncogenic under immunosuppressed conditions, whereas they are not in normal conditions[10]. A patient with scabies treated with topical therapies but didn't respond therefore systemic ivermectin tablet provided for as stated by the weight which prompts absolute cure indicating that sometimes topical anti-scabetic therapy was not sufficient in the immunocompromised patient. The high prevalence of skin cancers in transplant patients relates to posttransplant duration and immunosuppressive therapy[6]. Numerous researches displayed that skin lesions seems to be appear 5 years after transplantation in old ages (more than 50 years) and 8-10 years in younger patients, therefore; occasional dermatologic evaluation of renal transplant recipients is crucial to scale back the danger of developing non-melanoma skin cancers[2]. Kaposi's sarcoma might be developed in renal transplant recipient in the first 13

months after transplantation or it may take 18 years to appear[5]. In the current study, two cases of Kaposi's sarcoma showed up in 9 and 12 months which might be slightly in advance.In a patient of our examine cyclosp orine brought about numerous cutaneous lesions of Kaposi's sarcoma. Replacement of cyclosporine with sirolimus produced complete clearance because there is an association of cyclosporine with rapid onset and higher incidence of Kaposi's sarcoma in the immunocompromised patient[11]. Hypertrichosis is the most common cutaneous change after renal transplantation (36.1%) which may be due to the synergistic effect of both cyclosporine and corticosteroids on the pilosebaceous unit[4]. Sebaceous hyperplasia is frequently seen in the current study and observed at a younger age compared to the normal population due to the lipophilic effect of cyclosporine that may accumulate in the sebaceous glands[12]. To our knowledge many previous studies didn't concentrate on nail changes and disorders in transplant recipients, this might be due to appearance of nail disorders before transplantation which will be gone after transplantation as a result of correction of uremic state as contrasted to skin lesions which appear after kidney transplantation mostly due to immunosuppressive therapy. The mechanism through which nail changes occur in renal transplant recipients has not been studied yet[13]. The absence of lunula was the most common nail change in the renal transplant recipient group probably due to metabolic change and anemia. Leukonychia was another pathology seen frequently (4.1%) in the present study. It has been found that the immunosuppressive state itself somehow leads to leukonychia or it is possible to have resulted from the interference of immunosuppressive treatment with the cornification process in the nail matrix[13.]

Conclusions

In the framework of this study, immunosuppressive was the main cause of skin manifestation in transplanted kidney specifically cyclosporine which was our major concern. Our study shed light on necessity and alerting of kidney recipients to accurately and annually examination by a dermatologist. The role of physician is to point out patients to take care of their skin from environmental hazards including excessive sun exposure, early detection, and

treatment of pre-cancerous lesions (Actinic keratosis,warts).

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Conflict of interests

The authors recorded no conflict of interests.

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