CUTANEOUS MANIFESTATIONS IN RENAL TRANSPLANT RECIPIENTS

Dissertation Submitted in

Partial fulfillment of the University regulations for

MD DEGREE IN
DERMATOLOGY, VENEREOLOGY AND LEPROSY
(BRANCH XX)

MADRAS MEDICAL COLLEGE

THE TAMILNADU DR.M.G.R. MEDICAL UNIVERSITY
CHENNAI, INDIA.

APRIL 2013

CERTIFICATE

Certified that this dissertation titled **"CUTANEOUS MANIFESTATIONS IN RENAL TRANSPLANT RECIPIENTS"** is a bonafide work done by **Dr. M. PRABAKARAN,** Post graduate student of the Department of Dermatology, Venereology and Leprosy, Madras Medical College, Chennai – 3, during the academic year 2010 – 2013. This work has not previously formed the basis for the award of any degree.

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DECLARATION

I, **Dr. M. PRABAKARAN** solemnly declare that this dissertation titled "**CUTANEOUS MANIFESTATIONS IN RENAL TRANSPLANT RECIPIENTS**" is a bonafide work done by me at Madras Medical College during 2010-2013 under the guidance and supervision of **Prof. K.MANOHARAN, M.D.,D.D.,** Professor and head department of Dermatology, Madras Medical College,Chennai-600003.

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SPECIAL ACKNOWLEDGEMENT

My sincere thanks to **Prof. V.Kanagasabai, M.D**., Dean, Madras Medical College for allowing me to do this dissertation and utilize the Institutional facilities.

ACKNOWLEDGEMENT

I am gratefully indebted to Professor and Head of the Department of Dermatology **Prof.Dr K.MANOHARAN, M.D., D.D.,** for his invaluable advice, guidance and encouragement throughout the study. I would like to express my sincere and heartfelt gratitude to **Prof.Dr.V.SUDHA, M.D., D.V., D.D.,** Director and Professor, Institute of Venereology, for her kindness and support throughout the study.

I express my sincere gratitude to **Prof.C.JANAKI, M.D., D.D.,** Additional Professor of Dermatology (Mycology) for her guidance and support. I sincerely thank **Prof.V.SAMPATH M.D., D.D.,** Additional Professor of Dermatology for his priceless support. I am grateful to **Prof.U.R.DHANALAKSHMI M.D., D.D.,,** Additional Professor, Department of Dermatology for her invaluable guidance and help.

I thank my Professor and Head of the department of Occupational and Contact Dermatitis, **Prof.S.NIRMALA M.D.,** for her help and support. I also thank **Prof.PRIYAVATHANI M.D., D.D., DNB.,** for her advice and encouragement.

I also thank Additional Professor institute of venereology **Prof.K.VENKATESWARAN M.D., D.V.,** for his timely help.

I wish to thank Former Professors **Dr.D.PRABAVATHY M.D., D.D., Dr.V.SOMASUNDARAM M.D., D.D., Dr.S.JAYAKUMAR M.D., D.D.,** for their constant support and motivation.

I humbly thank my Co-Guide **DR.J.MANJULA M.D., DNB.,** for his valuable guidance throughout my work.

I extend my gratitude to my Assistant professors, **DR.G.K.THARINI M.D., D.D., DR.C.VIJAYABHASKAR M.D., D.CH., DR.R.MADHU M.D., D.C.H., Dr.SAMUEL JEYARAJ DANIEL M.D.D.V.L., DR.N.SARAVANAN M.D.D.V.L., DR.V.N.S.AHAMED SHARIFF M.D.D.V.L., and DR.S.MADHAVI M.D.D.V.L.,** Assistant professors, Department of Dermatology for their kind support and encouragement.

I also thank my Assistant Professors **DR.P.MOHAN M.D., D.V., DR.P.PRABHAKAR M.D.D.V.L., DR.K.UMA MAHESWARI M.D. D.VL., DR.R.SOWMIYA M.D.D.V.L., DR.C.VIDHYA M.D. D.V.L., DR.R.SUBHA M.D.D.V.L., DR.RANGARAJAN D.V., D.T.C.D., DR.S.SANGEETHA D.D.V.L.,** of Institute of Venereology for their able guidance.

I express my thanks to my former assistant professors, **Dr.S.KUMARAVEL M.D.,D.D, Dr.A.HAMEEDULLAH M.D.,D.D,**

Dr.AFTHAB JAMELA WAHAB M.D.,D.D., Department of Occupational and Contact Dermatitis for their support and help.

I am inclined to thank my former Assistant professors, Institute of Venereology, **Dr.S.ARUNKUMAR M.D., D.V., and Dr.S.KALAIVANI M.D., D.V** for their kindness.

I am also grateful to all paramedical staffs for rendering timely help to complete my study.

My hearty thanks to all my beloved friends for their wishes and cooperation amidst their busy schedule throughout my study.

Last but not the least I am profoundly grateful to all patients for their co-operation and participation in this study.

CONTENTS

INTRODUCTION

Renal transplantation is the treatment of choice for better quality of life in end stage renal disease patients.[1] The long term success of renal transplantation depends largely on the prevention of allograft rejection. In renal transplant patients, a state of generalized non-specific immunosuppression has been induced to prevent the rejection of graft by using various drugs (such as corticosteroids, cyclosporine, tacrolimus, azathioprine and mycophenolate mofetil).

The immunosuppression induced by drugs to prevent the graft rejection renders the renal transplant recipients more susceptible to bacterial, viral and fungal infections and predisposes to the various dermatosis, premalignant and malignant skin conditions which may cause significant morbidity and mortality. The consequence of immunosuppression differs markedly with geographical location, racial group and skin type.[1]

The present study is undertaken to find the prevalence and to identify spectrum of skin diseases in renal transplant recipients in our centre.

REVIEW OF LITERATURE

INFECTION IN RENAL TRANSPLANT RECIPIENTS

Infection is the most common immediate cause of death in renal transplant recipients because of the concurrent immunocompromisation associated with immunosuppressive drug therapy. Infection in an immunocompromised host differ from that of an immunocompetent individual in many ways. This is depicted in the WOLFSON'S classification[3] of dermatological infection in immuno compromised patients (based on the presumed underlying pathophysiologic mechanisms).

FOUR CATEGORIES ARE DESCRIBED

1) Infection that originates in the skin with the common organism that has the potential for more spread than in the normal host.

2) Extensive skin involvement with an organism that usually causes local infection in a normal host can lead to severe involvement in the immunocompromised host.

3) Infection with an opportunistic organism that causes primary infection in the skin can produce either local or systemic dissemination.

4) Involvement of the skin by dissemination from a systemic disease elsewhere in the body.

In addition to the above, some of the unusual pathogens produce clinical conditions that resemble usual infection but may not respond to routine antimicrobial therapy. Because of the depressed host inflammatory responses difficulty is always encountered not only in the diagnosis but also in the treatment of various infections in transplant recipients.[2]

DEFECTS IN HOST DEFENCE AND TYPES OF INFECTION IN RENAL TRANSPLANT RECIPIENTS

In renal transplant patients humoral immunity is relatively spared. They are more prone to develop granulocytopenia (defined as less than 500 polymorphonuclear leukocytes per cubic millimeter) and particularly at risk for disseminated infection with both aerobic gram negative organisms and fungi.[2] The extensive use of broad spectrum antibiotics, intravenous cannula and central catheters in these patients further results in dissemination of infection.[8]

In addition, the effect of chronic corticosteroid therapy on the skin by depressing of fibroblast proliferation, inhibiting of the

deposition of collagen and synthesis of mucopolysaccharides leads to atrophic skin with poor wound healing. So even minor skin trauma combined with an occlusive dressing can lead to severe disseminated infection from an organism that gains entry by this route.[2]

The renal transplant recipients are more prone to develop cellular immune dysfunction because of the immunosuppressive agents used. The organisms causing infection in these patients are fungi such as dermatophytes, candida spp, cryptococcus spp, histoplasma spp, the herpes group of viruses (Herpes simplex, Varicella-zoster, Cytomegalovirus, Epstein-barr virus) and adenovirus, nocardia, mycobacteria.[5]

Different types of infections tend to occur at fixed point of time during the post transplant period which can be divided into three distinct phases.[7]

1) During the first month of post transplantation

2) During 1-6 months, after transplantation

3) Six months after the transplantation.

INFECTIONS DURING THE FIRST MONTH OF POST TRANSPLANT PERIOD

It comprises of three types

1) Infection present in the allograft recipient prior to the transplantation gets exacerbated by the immunosuppressive therapy (eg: bacterial infection like tuberculosis and geographically restricted systemic mycosis (blstomycosis, coccidioidomycosis and histoplamosis).

2) The infection that is transmitted via the contaminated allograft.

3) The bacterial infection of the surgical wound, intravenous and bladder catheters.[5]

INFECTIONS DURING 1 TO 6 MONTHS OF POST TRANSPLANTATION

During this period, problems due to infections that are unique to transplantation begin to occur.

The most important group of infections are

1) Viral infections
   a. Herpes group of viruses- latent viruses reactivation- symptomatic disease

   b. Hepatitis viruses

2) Opportunistic infection with agents like Pneumocystis carinii, Listeria monocytogens. These infections are because of the combined effects of immunosuppressive therapy and the immunomodulating effects of the viruses particularly cytomegalovirus.[62]

INFECTION THAT OCCUR AFTER 6 MONTHS OF TRANSPLANTATION

This can be discussed under three categories

1) During this period interaction between the chronic immunosuppressive state and the active replication of viral agents results in transplant patients becoming more prone to develop the following infection.

   a. Progressive chorioretinitis due to cytomegalovirus

   b. Hepatocellular carcinomas due to hepatitis B virus

   c. Epstein-barr virus associated lymphoproliferative disease

   d. Human papilloma virus infection[5]

2) Patients with good renal function, receiving only minimal immunosuppressive therapy are at particular risk for development of community acquired infection.

3) Patients with relatively poor renal function and receiving intense immunosuppressive therapy are prone to develop chronic viral infection and life threatening opportunistic infections with pathogens such as Pneumocystis carinii, Cryptococcus neoformans, Listeria monocytogens and Nocardia asteroids.[63]

FUNGAL INFECTIONS IN RENAL TRANSPLANT RECIPIENTS

In mid 1980s, Richard wenzel of University of Virginia provided some of the first evidence that fungal infections begin to rise in the population of patients with impaired immune system due to acquired immune deficiency syndrome, cancer, chemotherapy or drugs designed to prevent rejection of transplanted organs.[4] Recent studies highlighted the alarming increase of the opportunistic fungal infections in an immunocompromised host.[2]

The onset of fungal infection is usually between 1-6 months after immunosuppression. The further interesting observation was that the rarer organism considered as the contaminants or saprophytes are becoming increasingly pathogenic and even fatal in immunocompromised patients.[5]

The skin may be involved as a result of primary inoculation or by seeding of the skin from systemic infection. In disseminated infections, the cutaneous lesions may be the initial sign of underlying infection and may provide a convenient source of tissue for diagnosis. The most common opportunistic fungi that infect immunocompromised hosts are Candida spp, Cryptococcus spp and Zygomycetes.[6]

The risk of the infection in these patients is determined by the interaction between the epidemiological exposure that the patient experiences and the net state of immunosuppression. The causative microorganisms vary depending upon the types of immune dysfunction. The infection can be broadly divided into those that take the advantage of a neutrophil defect (candidiasis and mucormycosis) and those that take the advantage of T cell and mononuclear phagocyte defect (cryptococcosis, histoplasmosis).[6]

Opportunistic fungi that rarely infect healthy person can have very high incidence in these patients. Candida albicans is the pathogen most often isolated, but several other candida spp may also cause infection.[10]

The poorer prognosis for disseminated fungal infection in immunocompromised patients can be attributed to the underlying immunocompromised status of the patient, delay in diagnosis due to atypical presentation, delay in initiating treatment and failure of the antifungal regimen.[6]

The various fungal infections that are encountered in renal transplant recipients

1) Superficial fungal infections
    a. Dermatophytosis
    b. Pityriasis versicolor
    c. Candidiasis
2) Subcutaneous fungal infections
    a. Phaeohypomycosis
3) Oppurtunistic fungal infections
    a. Cryptococcosis
    b. Zygomycosis
    c. Histoplasmosis
    d. Aspergillosis

DERMATOPHYTOSIS

Dermatophyte infections common in patients with long duration (more than one year) of post-transplant immunosuppression.[39] The rate of dermatophyte carriage on clinically normal skin was estimated as 12% in renal transplant recipients compared with 6.8% in a control population.[36]

Cell mediated immunity, especially by epidermal Langerhans cells, is the main defense mechanism against dermatophytes, and its inhibition by immunosuppressive drugs predisposes solid-organ transplant recipients to dermatophytosis .[9]

In a normal host, dermatophytosis typically presents as superficial scaly lesion with active border showing inflammation and central clearance. However in immune compromised patients widespread non-inflammatory cutaneous lesions with ill-defined margin and profuse scaling are noted.[10]

The common sites for dermatophyte infection in renal transplant recipients are groin, trunk, feet and hands. In these patients, tinea cruris was the commenest type noted, followed by tinea corporis and tinea glutealis.[11]

Deep form of dermatophytosis has been frequently described with systemic immunosuppression. Cases of follicular papules or nodules (Majjochi's granuloma) and multiple subcutaneous neutrophilic abscess has been reported in renal transplant patients.[94] On rare occasions, invasive dermal or subcutaneous infection develop after trauma or follicular rupture.[12]

In renal transplant recipients, the isolation of organisms from cutaneous dermatophyte infection revealed, T.rubrum as the common isolate (80.8%) followed by T. mentagrophytes (11.5%), E. floccosum and T. simii (each 3.8%).[11]

Fingernail infections and involvement of multiple nails are seen more commonly in immunocompromised patients than in other patients. Among the various clinical presentation of tinea unguium, proximal subungual white onychomycosis (PSWO) is commonly seen in immunocompromised (HIV) patients.[15,44]

Although PSWO was considered to be a clue to HIV infection, the affected persons did not show the presence of HIV antibodies through ELISA technique, and therefore it could be inferred that PSWO might be a manifestation of

immunosuppression not only due to HIV infection but also due to iatrogenic induction.[11] Trichophyton rubrum was the most common pathogen isolated. Occassionally T. megninii, T. schonelinii and E. floccosum were also isolated. Among the 100 kidney transplant patients, 3 patients showed PSWO lesions.[11]

The immunosuppressive therapy enhances the risk of failure of antifungal therapy and prolonged treatment as well as close follow-up is essential to ensure complete cure of dermatophytosis in renal transplant recipients.[10]

PITYRIASIS VERSICOLOR

Pityriasis versicolor is a common fungal infection in renal transplant patients and more common than the general population.[16] The prevalence of infection with Malassezia species is increased among renal transplant recipients, probably owing to the immunosuppressed state of this patient population.[98] Pityriasis versicolor manifests when there is a shift in the yeast form to the mycelial form that is commonly seen in renal transplant recipients due to corticosteroid therapy.[79]

The clinical features are similar to those observed in immunocompetent patients, however the lesions are more likely to

be non pruritic and less inflammatory, and they generally involve large areas of body. Flexural distribution is also seen.[80]

Pityriosporum folliculitis presents as itchy monomorphic papulo pustules over the trunk and upper extremities, commonly seen in young individuals.[17] Onychomycosis and fungaemia were rarely reported in immunocompromised patients.[46]

CANDIDIASIS

Candidial infections are common opportunistic fungal infections in solid organ transplant patients and more prone to develop persistent and severe oral candidiasis.[13] In general, defect in neutrophil and monocyte phagocytic function, which are seen soon after the renal transplantation, predisposes patients to develop infections with Candida species. The glucocorticoid therapy in renal transplant patients induces alteration in monocyte defense against candida by decreasing TNF-α levels.[18]

Oral colonization with candida species is a common problem in renal transplant recipients. Commonly isolated species were Candida albicans, Candida tropicalis and C.glabarata. Renal transplant recipients, on oral Fluconazole prophylaxis are more prone to get infection with Candida krusei and Candida glabarata

because these pathogens are less sensitive or resistant to Fluconazole.[81]

The most common form of yeast infection in immunocompromised patients is oral candidiasis. The lesions of oral candidiasis presents as geryish white pseudomembrane with underlying erythema, and erosion and fissures with maceration in the angle of mouth.[18]

Cutaneous involvement occured in 13% cases of disseminated candidiasis. The skin lesions in disseminated candidiasis manifests as discrete, firm, raised pink or red coloured nodules, multiple asymptomatic erythematous macules, pustules and purpura with associated fever and muscle tenderness. Nodules with pale centre and painless nodulopustular lesion with central necrosis and seropurulent discharge may also be reported in disseminated candidiasis.[38]

PHAEOHYPOMYCOSIS

Phaeohypomycosis is a heterogenous group of opportunistic fungal infections caused by dematiaceous molds(dark pigmented fungi) which are ubiquitous in nature, but rarely causes human disease.[19] In recent years, these fungi are recognized as important

human pathogens because of increased numbers of immunocompromised patients including renal transplant recipients.[20]

In humans, the commonly isolated pathogens are Alternaria,[22] Bipolaris, Curvularia, Exophiala, Exserohilum and more than 100 species have been isolated from phaeohypomycotic lesions.[21] These organisms are usually found in soil, polluted water and decaying vegetation.[23]

The extremities are commonly involved because the mode of transmission of these saprophytic fungi is mainly by traumatic implantation. Phaeohypomycotic cutaneous lesions have variable clinical presentation like subcutaneous cysts, nodules and abscesses.[19]

CRYPTOCOCCOSIS

The disease is caused by an yeast, Cryptococcus neoformans, widespread in soil and the route of entry is via respiratory tract by inhalation of spores. Skin may also be an portal of entry for cryptococcus and acts as an potential source for subsequent progression to disseminated cryptococcosis in solid organ transplant patients.[24] Depressd cell mediated immunity results in

disseminated cryptococcosis in renal transplant recipients. Rarely primary cutaneous cryptococcosis manifests in transplant patients.[24]

Cutaneous manifestation of disseminated cryptococcosis occurs in about 10%-15% of cases. Various cutaneous lesions in disseminated cryptococcosis are papules, acneiform pustules, nodules, subcutaneous abscesses, molluscum contagiosum like lesions and as cellulitis.[25,26]

ZYGOMYCOSIS

Zygomycosis is caused by mucorales, commonly seen in diabetic ketoacidisis, lymphoma, leukaemia and renal transplant patients on immunosuppressive therapy. A study reviewed 361 cases of zygomycosis and the most common pathogen isolated was Rhizopus followed by Mucor, Absidia in decreasing order.[28]

HISTOPLASMOSIS

Histoplasmosis is caused by dimorphic saprophytic fungus, Histoplasma capsulatum. Inhalation of airborne spore is the usual route of infection. Dissemination occurs in renal transplant recipients due to depressed cell mediated immunity by immunosuppressive drugs.[59] Primary cutaneous histoplasmosis is very rare infection usually occurs by local trauma or inoculation

and cutaneous lesions may present as papule, pustule or plaque, ulcers and wart like lesions.[58]

In renal transplant patients, disseminated histoplasmosis manifests as persistent punched out circumscribed granulomatous ulcer, painful erythematous rash, plaques and nodules resembling erythema nodosum, molluscum contagiosum like lesions over face and erythema multiforme.[58]

ASPERGILLOSIS

In immunocompromised patients aspergillosis is one of the common opportunistic fungal infection. Aspergillus infection occurs commonly in patients with haematologic or lymphoreticular malignancies or on immunosuppressive therapy. Aspergillus fumigatus causes most of the disseminated infection.[6]

Primary cutaneous aspergillosis usually manifests as single or multiple pruritic erythematous indurated plaque often resembling cellulitis and may undergo necrosis and ulceration. Lymphatic dissemination of infection results in multiple lesions. In disseminated aspergillosis the cutaneous manifestations were haemorrhagic bullae, purpuric nodules and cellulitis.[2]

PENICILLIOSIS

Penicillium marneffei is a dimorphic fungus, a rare pathogen which affects many patients with HIV and other immunosuppressive states. Cutaneous lesions are small umblicated papules resembling molluscum contagiousum which may later undergoes ulceration.[6]

VIRAL INFECTIONS

Viral infections have great impact on quality of life in renal transplant patients because of latency, recurrence and chronicity. The combination of chronic immunosuppression and chronicity with the herpes group of viruses, the hepatitis viruses, the papova viruses and HIV has resulted in an array of clinical syndrome in the transplant patients which are rarely encountered in the normal host.

HERPES VIRUS

The four major human herpes viruses, herpes simplex virus (HSV), Varicella-Zoster virus (VZV), Epstein-Barr virus (EBV) and Cytomegalovirus (CMV) shares three characteristics that explains their great impact on the renal transplant patients.

LATENCY

Primary infection results in life long carriage of non-replicating, transcriptionally inactive virus, that can be reactivated by immunosuppresssion and allograft rejection. Anyone who has antibody against a herpes virus in his or her serum (seropositive), harbours the latent virus.[36]

CELL ASSOCIATION

The ability of the virus to spread by cell to cell direct contact reduces the chance of antibody mediated neutralization. Cell mediated immunity is of prime importance in the control of such infection. This cell mediated immunity is depressed by immunosuppressive agents administered in transplant patients.[60]

ONCOGENECITY

All the herpes viruses should be considered as potentially oncogenic especially in the presence of chronic immunosuppression of which most important is EBV associated lymphoproliferative disorders.[64]

HERPES SIMPLEX

Herpes simplex virus infection commonly occurs during 2 - 6 months of post transplant period. Localised mucocutaneous herpes

simplex virus infection of oral and anogenital region usually occur as recurrence in renal transplant recipients under immunosuppression. The lesions that occurs in the ano-genital region may have atypical morphology like persistent ulceration, deep necrotic ulcer, hyperkeratotic and verrucous lesions.[60] In renal transplant patients, reactivation of HSV is common, which results in asymptamatic viral shedding or may lead on to progressive mucocutaneous infection with constitutional symptoms.[47]

VARICELLA (CHICKENPOX)

Varicella is caused by Varicella-Zoster virus (VZV) and uaually a febrile illness manifests as generalized vesicular lesions with central depression soon becomes crusted and heals with superficial scars and post-inflammatory hyperpigmentation. Cell mediated immunity to VZV persists for many years and gives protection against severe infections. The lesions may persist longer and disseminated varicella with visceral involvement occurs in immunocompromised persons due to inadequate development of cell mediated immunity.[27]

HERPES ZOSTER

Herpes zoster infection occurs 2-24 months after renal transplantation. This infection is usually reactivation of VZV producing localized zoster, rarely disseminated one in the form of multidermatomal distribution with more of haemorrhagic lesions with necrosis and midline crossing.[29]

CYTOMEGALOVIRUS

Cytomegalovirus is the most important infectious agent in organ transplant patients. CMV affects at least two thirds of transplant patients and occurs commonly during 1 to 4 months of post transplant period. The immunomodulating ability of the virus predisposes the renal transplant patients to acquire opportunistic infection and allograft injury.[62]

Cutaneous eruption develops in 10- 20% of patients which may present as indurated hyperpigmented nodular lesions, plaques and vesiculo-bullous lesions. Ulceration may occur on the perianal region, rectal mucosa, gluteal region and thigh.[61,63]

EPSTEIN-BARR VIRUS

EBV infection usually occurs 1 to 4 months after organ transplantation. In renal transplant recipients, cyclosporine therapy

increases the chance of acquiring EBV induced lymphoproliferative disorder.[64] Oral hairy leukoplakia caused by EBV , mostly seen in AIDS patients, has also been reported in HIV negative transplant patients.[65]

MOLLUSCUM CONTAGIOSUM

Molluscipox virus a DNA virus belongs to Poxvirida family, commonly infects children, sexually active adults and immunocompromised individuals either directly by close skin contact or indirectly through fomites.[95] Molluscum contagiosum(MC) lesions commonly involve face, genital areas as umbilicated skin coloured or shiny papules.[96]

In immunocompromised persons, multiple and giant lesions have been reported. Histopathological examination of MC lesions are mandatory in renal transplant recipients because cryptococcosis, histoplasmosis, coccidioidomycosis and penicilliosis may present as molluscum contagiosum like lesions in immunocompromised patients.[96]

HUMAN PAPILLOMA VIRUS

Cutaneous warts usually develop one year after the transplantation. Cell mediated immunity (CMI) is the principle

mechanism in rejection of warts and defects in CMI results in more number of lesions and persistent lesions.[49] Epidermodysplasia verruciformis lesions are also reported in renal transplant recipients and these lesions are more prone for the development of Bowens disease, squamous and basal cell carcinomas in an immunocompromised background.[66]

The HPV types causing common warts are mainly 2 and 4 and less commonly 1 and 3.[67] Human papilloma virus types 6, 11, 16 & 18 are usually involved in ano-genital warts and squamous cell carcinoma of the vulva.[68]

BACTERIAL INFECTION

Bacterial infections of skin are more common in renal transplant individuals and the prevalence is higher in tropical and subtropical regions. The bacterial flora of persons who underwent transplant is similar to normal individuals and there is no increased risk of carriage of pathogenic bacterias.[98]

The most common organisms causing bacterial infection are group A streptococci and staphylococcus aureus, which are similar to normal subjects, and in cases of cellulitis, there is a possibility of occurrence of unusual pathogens like Cryptococcus neoformans and

candida spp. due to altered cell mediated immunity induced by immunosuppressive agents.[98]

In transplant individuals, bacterial infections may manifest in various forms like impetigo, folliculitis, furuncles, abscesses, cellulitis and erysipelas, and the lesions may produce more severe illness and protracted course than usual.[97] Cutaneous lesions in renal transplant recipients may occur as unfamiliar clinical presentations like cellulitis without inflammation and erythema, folliculitis and furunculosis resulting in persistent and destructive ulcerations.[97]

NOCARDIOSIS

Nocardiosis is a rare but life threatening opportunistic infection, especially in immunocompromised persons, including transplant individuals, neutropenic patients and on chronic corticosteroid therapy. Nocardiosis occurs as early as one month after the immunosuppressive therapy.[34]

The most common clinical presentation is primary pulmonary infection, but rarely disseminated nocardiosis involves skin, central nervous system and cardiovascular system in renal transplant

recipients. Skin lesions may present as multiple abscesses, nodulopustules with cellulitis and chronic suppurative lesions.[8]

MYCOBACTERIA

Atypical mycobacterial infections rarely manifest in renal transplant patients and the skin lesions may have diverse morphologies like verrucous, hyperkeratotic papules, subcutaneous abscesses and nodules and ulcerations. The commonly isolated organisms are Mycobacterium marinum[69] and Mycobacterium chelonae.[70]

PARASITIC INFESTATIONS

CRUSTED SCABIES

Norwegian or crusted scabies is a less common, but severe infection caused by massive infestation with Sarcoptes scabiei var. hominis. The drug induced suppression of cell mediated immunity increases the risk for acquiring the crusted scabies in transplant recipients. Crusted scabies usually manifests as crusted and hyperkeratotic plaques or nodules which commonly involves extremities. These eruptions are less pruritic, and the burrows and erythematous papules may be limited, absent or obscured by thick crust.[30]

TUMOURS

The prolonged period of immunosuppressive therapy used to preserve the allograft in renal transplant recipients plays an important role in development of cutaneous malignancies.

INCIDENCE OF TUMOURS

In the general population, the most common tumors are carcinoma of the skin, lung, prostate, female breast, colon and rectum. A markedly different pattern of tumor development is seen in organ transplant recipients. Skin and lip cancers are more frequent than in the general population, but their incidence varies with the amount of exposure to sunlight.[33]

Certain malignancies that are rare in the general population occur relatively common in organ transplant recipients. There is a 400 fold to 500 fold increase in the incidence of kaposi's sarcoma in renal transplant recipients compared with controls of the same ethnic origin.[72]

Skin tumors occurs in relatively younger group of people whose average age at the time of transplantation was 40 years. The sex ratio of male to female patient is 2:1. In contrast with other known oncogenic stimuli in humans which often take 15 to 20 years

or more before they cause clinical lesions, cancers presented in a relatively short time after transplantation.[71]

ETIOLOGY OF TUMORS

Depressed immunity results in impairment of body's ability to cope with cancers caused by various carcinogens such as sunlight and oncogenic viruses. Infection with potentially oncogenic viruses are common in immunosuppressd patients. Epstein-barr virus infection may contribute to the development of non-hodgkins lymphomas.[64] Papilloma virus infections may be involved in carcinoma of cervix, vulva, perineum and skin.[31] Human herpes virus 8 may contribute to the development of kaposi's sarcoma.[73]

BASAL AND SQUAMOUS CELL CARCINOMA

Basal cell carcinomas outnumber squamous cell carcinomas in the general population, but the opposite is true in the transplant recipients in whom squamous cell carcinoma outnumber basal cell carcinoma by 2:1.[33] In the general population, these types of skin cancer occur mostly in people in their 60s and 70s, but the average age of affected transplant patients is 30 years younger.[33]

SQUAMOUS CELL CARCINOMA (SCC)

Squamous cell carcinoma arises from atypical keratinocytes of the epidermis. It occurs most commonly in sun exposed areas and is usually associated with precursor lesions like actinic keratoses, Bowen's disease (SCC in situ), viral warts and/or keratoacanthomas. The risk of SCC is 60 to 100 times greater than in the general population.[74]

The pathogenesis is multifactorial, with cumulative sun exposure as most important factor. Also infection with human papillomavirus (HPV, particularly oncogenic HPV 5 and 8 strains) plays an important role in the development of SCC, with HPV being detected in 65 to 90% of SCC of transplant recipients.[68] Other risk factors are fair skin, age, the level of immunosuppression, duration of pretransplantion dialysis, ionizing radiation, chronic inflamed skin (like scars or chronic ulcers) and possibly smoking.[72]

SCC is more aggressive in transplant recipients than in the general population, resulting in higher risk of local recurrence (14% of patients), regional and distant metastasis (6-9% of patients) and mortality.[71]

BASAL CELL CARCINOMA (BCC)

Basal cell carcinoma arises from the basal layer of the epidermis and its appendages. It occurs on sun-exposed skin, most commonly on the face or head (up to 70%). Common sites are eyelid margins, nose folds, lips and around and behind the ears.[74]

The incidence of BCC is increased by a factor 10 to 16 in transplant recipients, compared to the general population. Intense intermittent sun exposure is important in the pathogenesis of BCC, in contrast with SCC where the cumulative sun exposure plays an important role.[72]

MELIGNANT MELANOMA

Malignant melanomas arise from melanocytes. To detect a malignant melanoma, new or changing pigmented lesions should be examined with special attention for A. assymmetry; B. border irregularity; C. color variation/dark black color; D. diameter more than 6 mm; and E, evolution or change.[75]

Malignant melanomas are classified into lentigo malignant melanomas (arising on sun-exposed skin of older individuals), superficial spreading malignant melanomas (most common, occurring in 70%, especially in Caucasian people), nodular

malignant melanomas, acral lentiginous melanomas (arising on palms, soles and nail beds, commonly in more darkly pigmented persons) and malignant melanomas on mucous membranes.[75]

The risk of developing melanoma is 3.6 times greater in renal transplant recipients than in the general population.[72] Risk factors for the development of post transplant malignant melanomas are the presence of atypical nevi, history of blistering sunburns, immunosuppression, fair skin, a personal or family history of malignant melanomas, older age at the time of transplantation and the use of depleting anti-lymphocyte antibodies.[72]

KAPOSI'S SARCOMA (KS)

Kaposi's sarcoma is a vascular neoplasm, characterized by reddish-brown or purple-blue plaques or nodules on cutaneous or mucosal surfaces, including the skin, lungs, gastrointestinal tract and lymphoid tissue. KS has been associated with the reactivation of latent human herpes virus 8 (HHV-8) infection or donor-to-recipient transfer of HHV-8 infected progenitor cells.[32]

Kaposi's sarcoma makes up 62% of post-transplant malignancies in comparision with its incidence in the general population where it constitutes only 0.02% to 0.07% of all

cancers.[72] Sixty percent had non visceral kaposi's sarcoma confined to the skin, conjunctiva, oropharyngeal mucosa and 40% had visceral disease affecting mainly the GIT and lungs.[73]

The increased incidence of kaposi's sarcoma in renal transplant recipients may be attributed to their genetic background along with immunosuppression and concomittent viral infection.[32]

NON – HODGKINS LYMPHOMA

Lymphoma account for 3% to 4% of tumors in the community but constitute 14% of all tumors in transplant patients. The majority (97%) of lymphoma were non-hodgkin's lymphoma, whereas hodgkin's lymphoma is the most common lymphoma seen in the same age group of general population.[71]

Post transplant non-hodgkins lymphomas differ from their counterpart in the general population in several aspects. The extranodal involvement occurs 24% to 48% of patients with non-hodgkin's lymphoma, whereas it is present in 73% of transplant patients with non-hodgkin's lymphoma. In the general population about 1% of non-hodgkin's lymphoma affect the brain parenchyma, whereas in organ transplant patients 32% involves the CNS usually brain parenchyma.[78]

MISCELLANEOUS DISORDERS

SEBORRHEIC KERATOSIS

These are benign warty growths with various morphological patterns commonly seen in immunocompetent individuals with increasing age and may also observed in renal transplant recipients, but the incidence is unclear. However, there could be a confusion with dysplastic lesions and a possible association with non-melanoma skin cancer may be present.[99]

SKIN TAGS

Skin tags are pedunculated benign lesions that vary in size and commonly seen along with seborrheic keratosis. Euvrard and colleagues reported multiple minute skin tags on the neck and axillary folds of 5.5% paediatric transplant population.[100]

SOLAR KERATOSIS

Solar keratosis may appear 2 to 6 months after transplantation. The lesions clinically present as localized adherent thickening of skin with yellowish hue on sun exposed regions. In transplant recipients, solar keratosis occurs as multiple lesions which tend to recur after conservative treatment and rapidly evolve into squamous cell carcinoma but in immunocompetent persons it

has low malignant potential and prolonged latency to develop squamous cell carcinoma.[85]

POROKERATOSIS

This is an unusual condition but its variant disseminated superficial actinic porokeratosis (DSAP) has been repeatedly described in transplant patients and other immunosuppresssed individuals.[76] DSAP clinically manifests as multiple small irregularly shaped thread like ring lesions with more predilection for lower limbs.[77]

DRUG EFFECTS

Patients who are immunosuppressed for long term prevention of allograft rejection or who are receiving prolonged therapy with cytotoxic or immunosuppressive agents are subjected to many pharmacological complications. The types and prevalence of certain infections, malignancies and drug side effects may depend on the specific immunosuppressive regimen used.[83]

CORTICOSTEROIDS

Corticosteroid in combination with cyclosporine or cytotoxic agent are used in most immunosuppressive protocols. Steroid related cutaneous side effects are almost always present to some

degree during the first few months after transplantation but become less prominent as maintenance dosages are tapered to lower levels.[4]

Specific cutaneous manifestations that have been described in kidney transplant recipients include skin fragility with ecchymoses and purpura (Batemans purpura), violaceous striae may be prominent especially in the axillae and groins.[36] Steroid acne commonly occurs on the trunk and extremities as small follicular papules and pustules usually at the same stage of development without comedones.[91] Severe form of acne like deep seated inflammatory nodulocystic lesions have also been reported. The androgen mediated stimulation of pilosebaceous unit is the postulated theory for the development of steroid acne and hirsutism in patients who were treated with corticosteroid.[92]

The perioral dermatitis is observed in transplant recipients receiving systemic steroids which clinically presents as redness and papulopustules around the mouth and nose.[93] Other side effect of steroids include, cushingoid facies, telangiectases, abnormal fat distribution (Buffalo hump), acanthosis nigricans, atrophy, impaired wound healing, generalized xerosis, keratosis pilaris and alopecia of the scalp.[35]

AZATHIOPRINE

Azathioprine is a purine analogue derived from mercaptopurine that is widely used as a immunosuppressive agent. The mechanism of action in immunosuppression is complex and involves non specific suppression of humoral immune responses and delayed hypersensitivity. Azathioprine is indicated as an adjuvant for the prevention of graft rejection after renal transplantation.[83]

Primary cutaneous complications attributable to azathioprine are exceedingly rare. There are no reported incidences of hypersensitivity. Azathioprine is thought to be co-oncogenic in the development of cutaneous and systemic malignancies. They act by enhancing the tumorogenic effects of other carcinogen.[74]

In renal transplant recipients, azathioprine along with an added effect of undue exposure to ultraviolet light increases the risk of developing kaposi's sarcoma. In immunosuppressed patients the lesion of kaposi's sarcoma appear from three months to four years after the onset of therapy. Discontinuation of immunosuppressive agents particularly azathioprine results in regression of tumour in some but not all patients.[73]

CYCLOSPORINE

This lipophilic cyclic polypeptide with II aminoacids is derived from the fungus Tolypocladium inflatum gams. This drug selectively inhibits T lymphocyte proliferation by inhibiting cyclophillin-calcineurin complex with a major effect on helper T cells and may favour graft acceptance by expansion of antigen specific suppressor T cells. The use of cyclosporine has markedly improved the graft survival and commonly used in renal transplant patients.[37]

Thirty to seventy percent of the patients receiving cyclosporine suffer from hypertrichosis characterized by thick and pigmented hair appearing over the trunk, back, shoulder, arms, neck, forehead, helices and malar region.[36]

Acne, folliculitis, sebaceous hyperplasia, epidermal cysts and keratosis pilaris have been reported in 10 to 20% of patients treated with cyclosporine.[35,82] Although some lesions may occur with corticosteroid administration, cyclosporine appears to have a profound effect on the pilosebaceous unit. This may be due to the fact that the drug is highly lipophilic resulting in accumulation in fat and sebaceous glands.[37]

Gum hyperplasia occurs in about one third of transplant patients treated with cyclosporine.[88] This complication generally occurs after 3 or months of treatment and can be worsened by the concomitant administration of calcium channel blockers or phenytoin.[82] Skin hyperpigmentation and bullous or vegetative lesions have also been reported in cyclosporine treated patients.[88]

TACROLIMUS (FK 506)

Tacrolimus is also an calcineurin inhibitor which acts primarily by inhibiting proliferation of T helper cells. In contrast to cyclosporine, the mucocutaneous side effects such as gingival hypertrophy and hirsutism are less commonly observed in Tacrolimus.[89] The other adverse effects includes pruritus, vesiculo bullous lesions, alopecia, nephrotoxicity and metabolic effects.[90]

MYCOPHENOLATE MOFETIL (MMF)

MMF derived from penicillium species and it affects the de novo pathway of purine synthesis by inhibiting inosine monophosphate dehydrogenase enzyme.

It has less incidence of cutaneous side effects when compared with azathioprine but there is an increased susceptibility to herpes simplex and zoster and cytomegalovirus infections.[86,87]

AIM OF THE STUDY

1. To study the prevalence of cutaneous diseases in Renal Transplant Recipients
2. To study the various dermatosis in Renal Transplant Recipients
3. To study the incidence and types of cutaneous infections in Renal Transplant Recipients
4. To study the cutaneous side effects of immunosuppressive drugs in Renal Transplant Recipients
5. To correlate the duration of the immunosuppressive therapy that predisposed to various dermatosis in Renal Transplant Recipients

MATERIALS AND METHODS

This study spanned a course of one year from December 2012 to November 2012. During this period, 80 renal transplant recipients on systemic immunosuppressive therapy attending the Department of Nephrology and Dermatology were screened.

The detailed history of each patient was noted with reference to age and sex, symptomatology and duration of skin manifestations, dose and duration of immunosuppressive agents, date of transplantation and family history of similar lesions.

The patients were examined thoroughly for all cutaneous manifestations. The duration of the cutaneous lesions, the size and extent of involvement were noted. In patients with dermatophytosis the morphology of lesion with reference to presence of inflammation, well defined or illdefined margin and central clearance were recorded. Those patients in whom the infection lasted for more than one year inspite of adequate treatment were classified as cases of chronic dermatophytosis.

All the patients were subjected to routine hematologic investigations like complete haemogram, standard biochemical

investigations like blood sugar, blood urea, serum creatinine, serum electrolytes, calcium and phosphate levels. Detailed urine examination was carried out in all of them. Screening for HIV was also done in all the renal transplant recipients.

Mycological investigations in cases of fungal infections included microscopic examination of skin scales, mucosal scraping, pus and touch smear from skin biopsy were done after adding 10% Potassium hydroxide (KOH) solution. Nail scraping material was examined under light microscopy after adding 40% KOH in suspected cases of onchyomycosis.

Gram stain and Ziehl Nielson stain were done in all suspected cases of cutaneous infection. Tzanck smear was done in vesiculo-bullous skin lesions. In willing patients, skin biopsy was done and the specimens were stained with haemotoxylin and eosin (H&E) and in required cases special stains like Periodic-acid Schiff (PAS) Gomori's methenamine silver (GMS) were used to confirm the diagnosis.

Appropriate treatment was given for all the renal transplant patients presented with cutaneous lesions.

OBSERVATIONS AND RESULTS

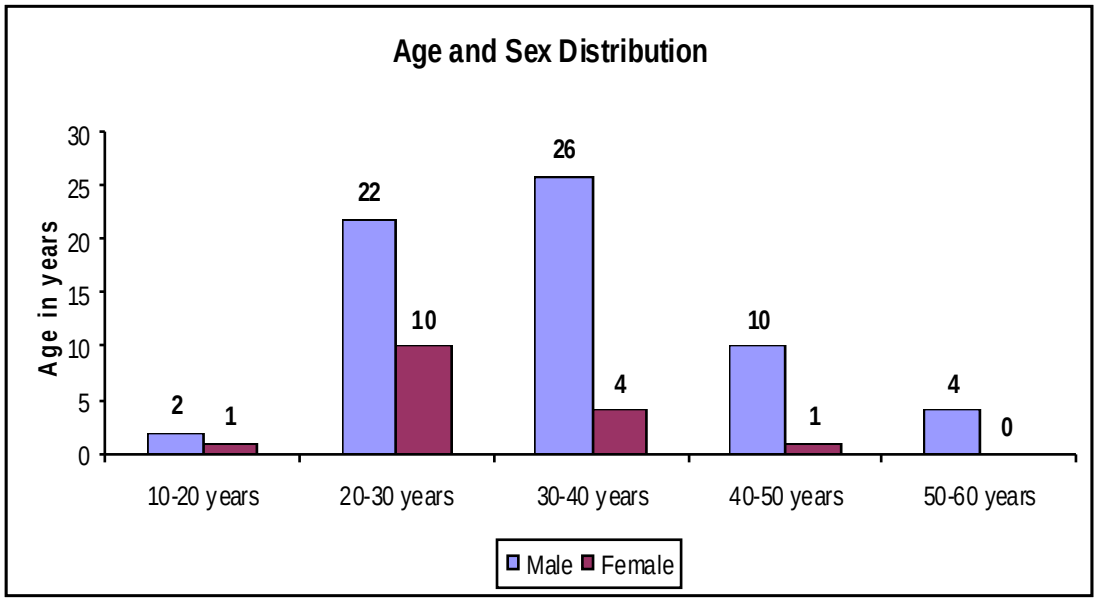
The total number of renal transplant recipients screened were 80, of whom 64 (80%) were males and 16 (20%) were females with the male to female ratio of 4:1.

The age of these patients ranged from 16 years to 55 years with an average of 33.2 years. The age of the youngest male patient in this study was 16 years, while the youngest female was 18 years. Oldest male was 55 years , where as the oldest female in this study was 42 years.

TABLE 1: AGE AND SEX DISTRIBUTION OF THE PATIENTS IN THE STUDY GROUP

Age group years	Sex distribution		Total numbers	percentage
	Male	Female		
10 – 20	02	01	03	3.75%
20 – 30	22	10	32	40%
30 – 40	26	04	30	37.50%
40 – 50	10	01	11	13.75%
50 – 60	04	-	04	5%
Total	**64**	**16**	**80**	**100%**

In the age group of 20 to 30 years, the maximum number of patients presented with cutaneous manifestations were 32 (40%). The maximum number of male patients in the age group of 30 to 40 years were 26 (40.6%) and maximum number of female patients were 10 (62.5%) in the age group of 20 to 30years.

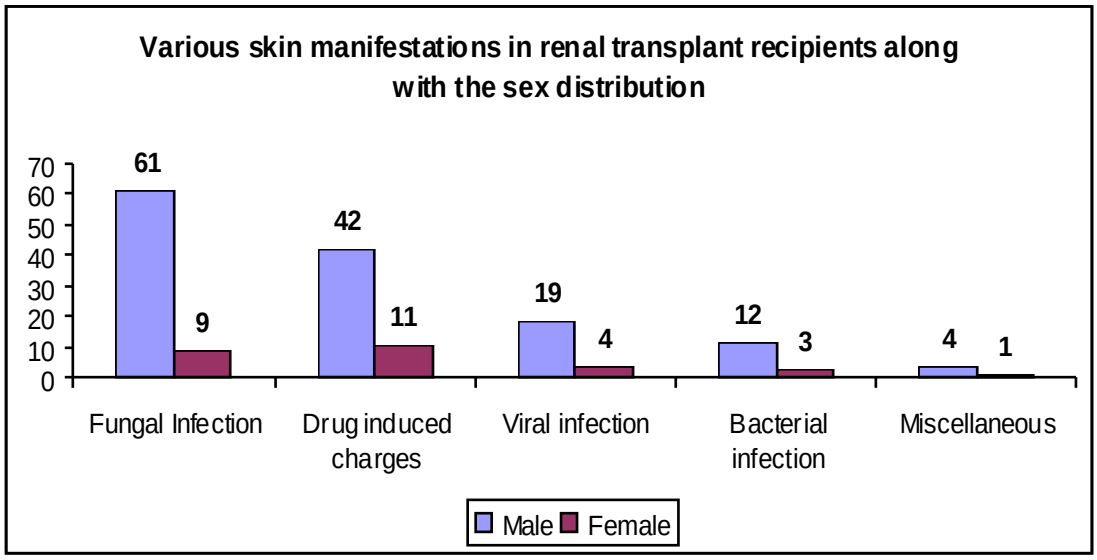


PREVALENCE OF SKIN MANIFESTATIONS IN RENAL TRANSPLANT RECIPIENTS

In this study, out of the 80 renal transplant recipients screened for skin manifestations, 70 patients (87.5%) presented with fungal infection. This was followed by drug induced changes in 53 patients (66.25%), viral infections in 23 patients (28.75%) and bacterial infections in 15 patients (18.75%). Miscellaneous cutaneous lesions were encountered in 5 patients (6.25%).

TABLE 2: VARIOUS SKIN MANIFESTATIONS IN RENAL TRANSPLANT RECIPIENTS ALONG WITH SEX DISTRIBUTION

No.	Skin manifestation	Male	Female	Total	percentage
1	Fungal infection	61	09	70	87.50%
2	Drug induced changes	42	11	53	66.25%
3	Viral infection	19	04	23	28.75%
4	Bacterial infection	12	03	15	18.75%
5	Miscellaneous	04	01	05	6.25%



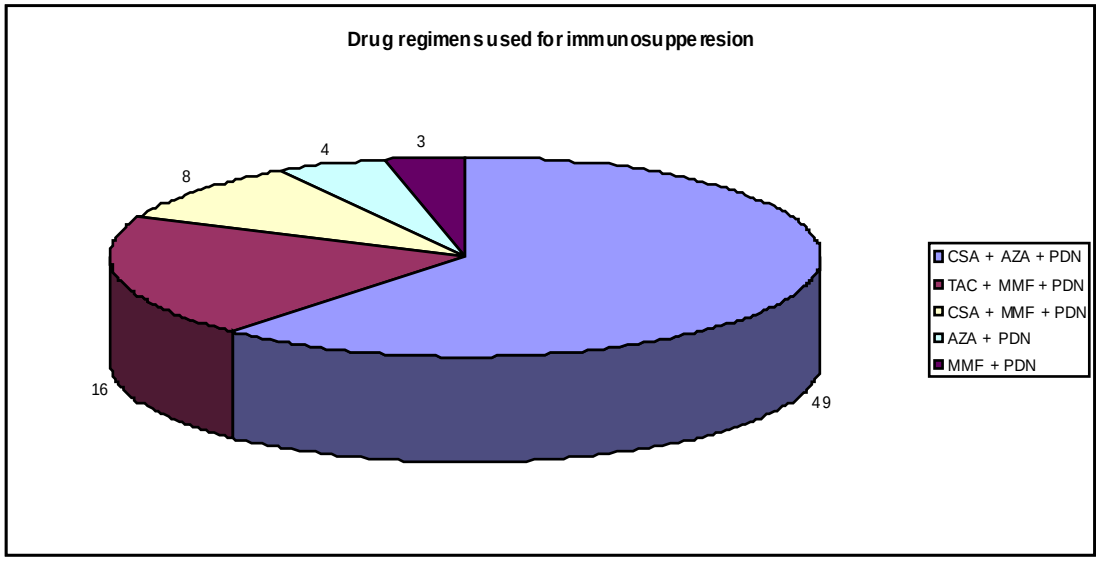
DURATION AND DRUG REGIMENS USED FOR IMMUNOSUPPRESSIVE THERAPY

The duration of immunosuppressive therapy following transplantation among the study group ranged from 2 months to 7 years. Various drug regimens has been used to induce immunsuppression to prevent graft rejection. The commonly used combination of drugs were cyclosporine(CSA), azathioprine (AZA) and prednisolone (PDN) in 49 patients (61.25%), followed by tacrolimus, mycophenolate mofetil and prednisolone combination in 16 patients (20%). In patients who were on prolonged period of immunosuppression, the maintainenace drug combination used were either prednisolone with azathioprine in 4 patients (5%) or prednisolone with mycophenolate mofetil in 3 patients (3.75%).

TABLE 3: DRUG REGIMENS USED FOR IMMUNOSUPPERESION

No.	Drug combination	No. of patients	Percentage
1	CSA + AZA + PDN	49	61.25%
2	TAC + MMF + PDN	16	20%
3	CSA + MMF + PDN	08	10%
4	AZA + PDN	04	5%
5	MMF + PDN	03	3.75%

Cyclosporine (CSA), Azathioprine (AZA), Prednisolone (PDN), Tacrolimus (TAC), Mycophenolate Mofetil (MMF), Prednisolone (PDN)

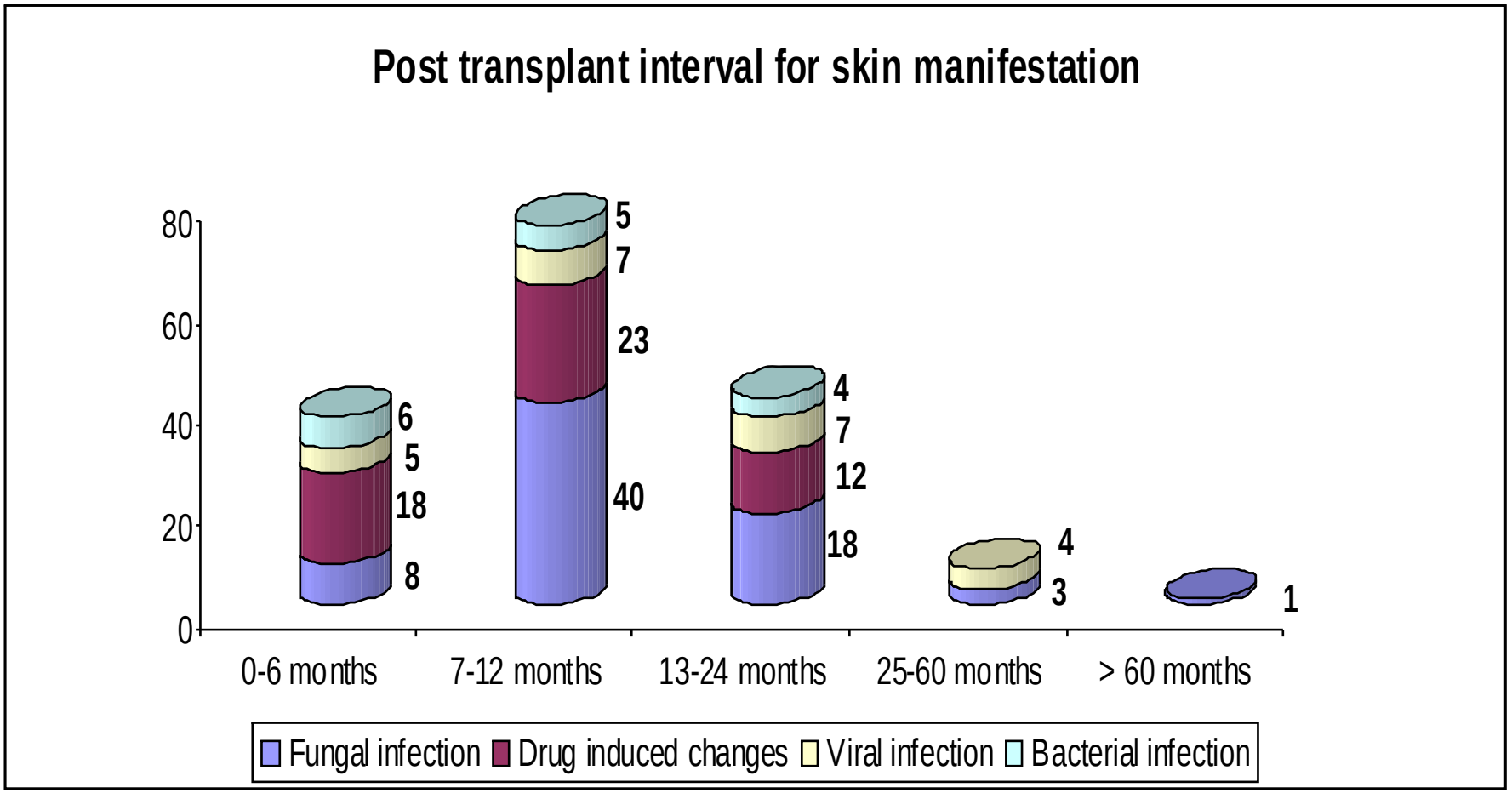


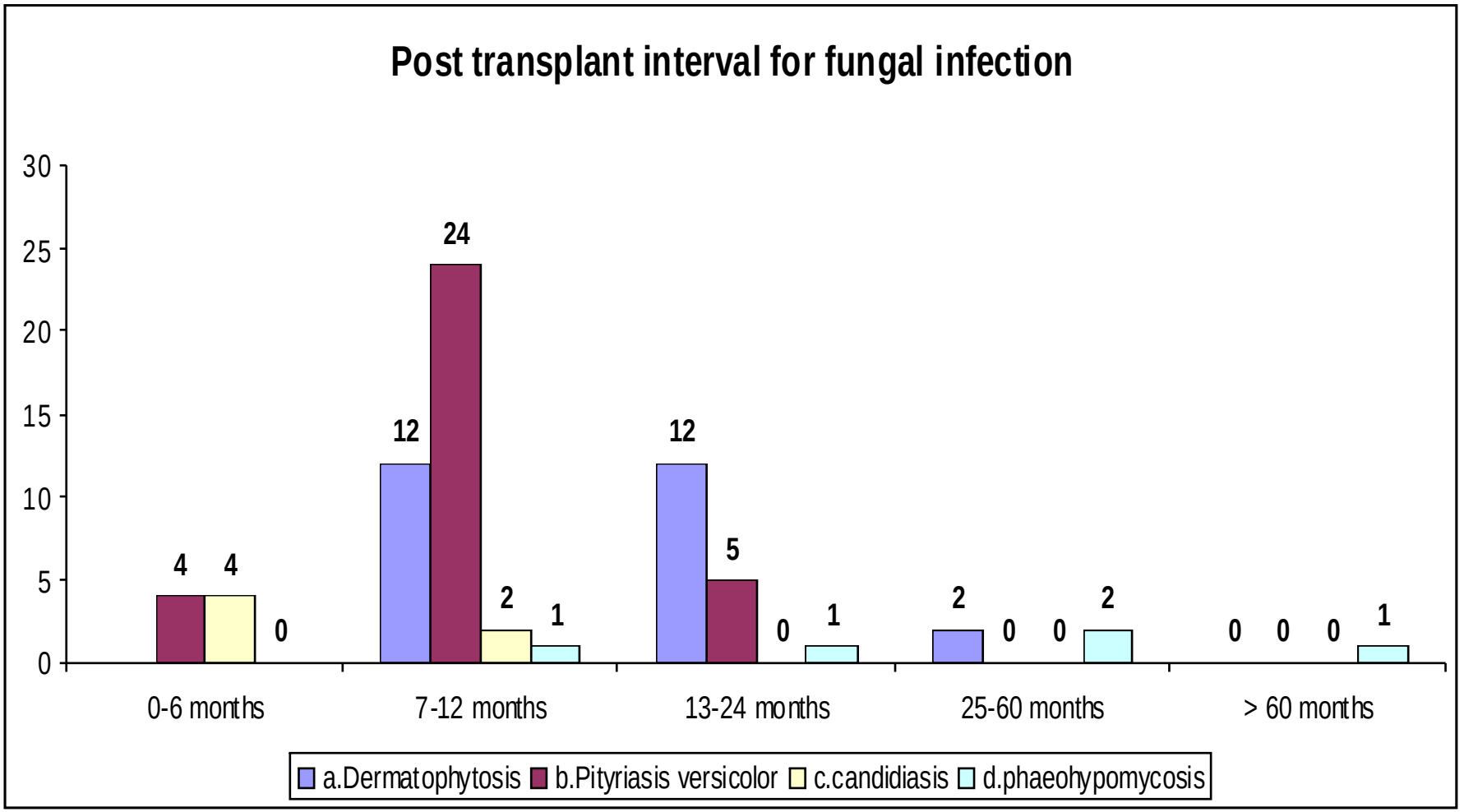
POST TRANSPLANT INTERVAL FOR SKIN MANIFESTATION

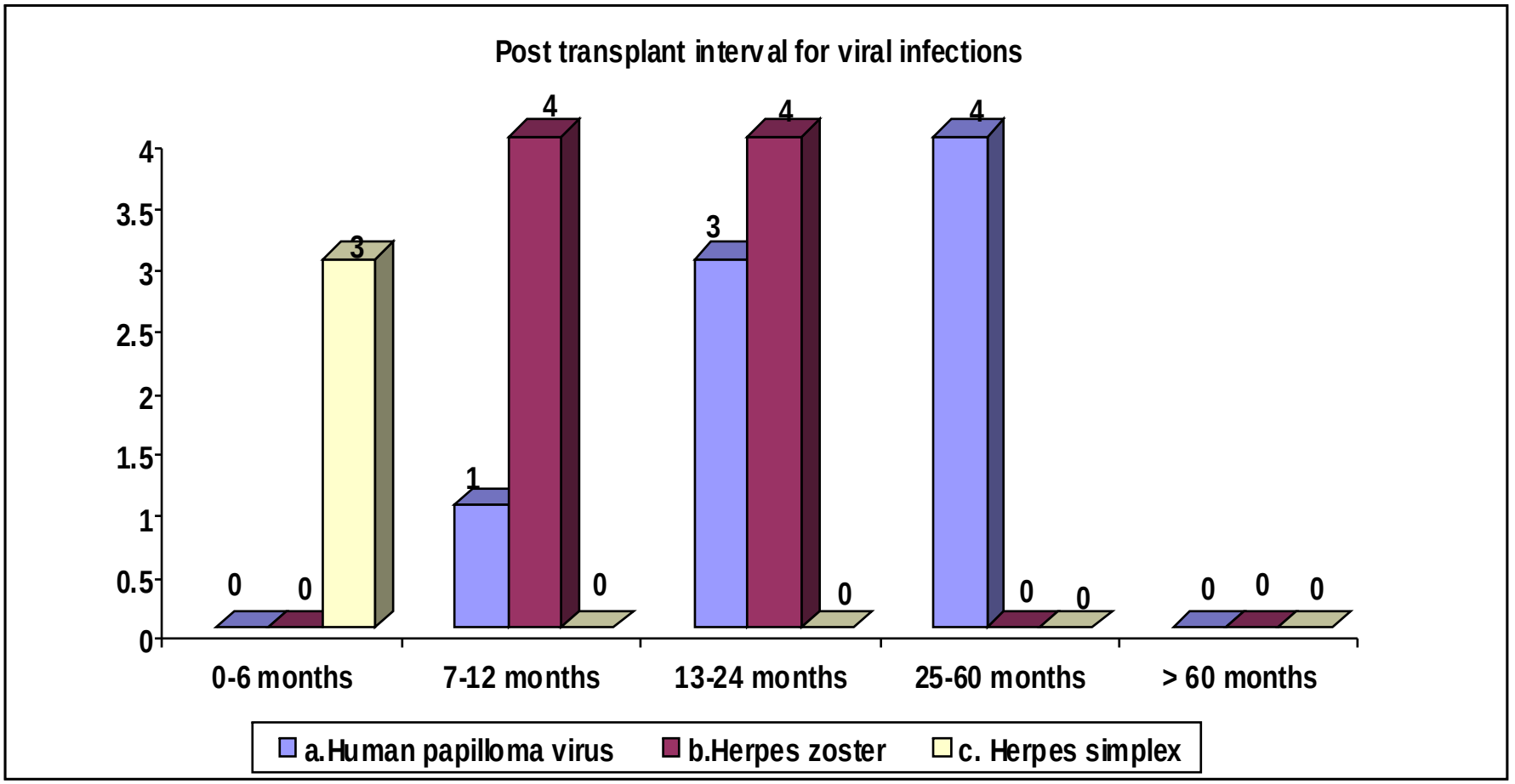
Cutaneous manifestations were seen predominantly during the initial one year of post transplant period. The most common manifestation was cutaneous infections, of which fungal infections were commonly seen and particularly during the 7 – 12 months of post transplant period. The viral infections were more commonly manifested during the 1-2 years of post transplant period. The bacterial infections were commonly seen during the initial 6 months of post transplantation. Cutaneous changes due to drugs were commonly observed during the first year of post transplantion, after which the incidence was gradually declined.

TABLE 4: POST TRANSPLANT INTERVAL FOR SKIN MANIFESTATION

S. No.	Skin manifestation	0-6 months	7-12 months	13-24 months	25-60 months	> 60 months
1	Fungal infection	08	40	18	03	01
	a.Dermatophytosis	-	12	12	02	-
	b.Pityriasis versicolor	04	24	05	-	-
	c.candidiasis	04	02	-	-	-
	d.phaeohypomycosis	-	01	01	02	01
2	Drug induced changes	18	23	12	-	-
3	Viral infection	05	07	07	04	-
	a.Human papilloma virus	-	01	03	04	-
	b.Herpes zoster	01	04	04	-	-
	c. Herpes simplex	03	-	-	-	-
4	Bacterial infection	06	05	04	-	-


Post transplant interval for skin manifestation
80
60
40
20
0
6
5
18
8
5
7
23
40
4
7
12
18
4
3
1
0-6 months
7-12 months
13-24 months
25-60 months
> 60 months
Fungal infection
Drug induced changes
Viral infection
Bacterial infection


Post transplant interval for fungal infection
30
25
20
15
10
5
0
4
4
0
12
24
2
1
12
5
0
1
2
0
0
2
0
0
0
1
0-6 months
7-12 months
13-24 months
25-60 months
> 60 months
a.Dermatophytosis
b.Pityriasis versicolor
c.candidiasis
d.phaeohypomycosis

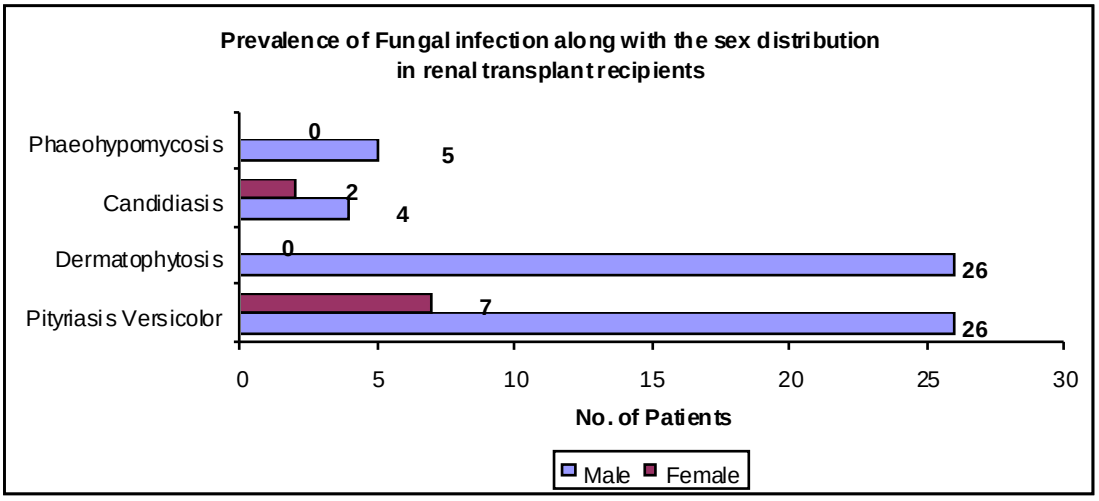

Post transplant interval for viral infections
4
3.5
3
2.5
2
1.5
1
0.5
0
0
0
3
1
4
0
3
4
0
4
0
0
0
0
0
0-6 months
7-12 months
13-24 months
25-60 months
> 60 months
a.Human papilloma virus
b.Herpes zoster
c. Herpes simplex

FUNGAL INFECTION IN RENAL TRANSPLANT RECIPIENTS

Out of 80 patients studied, fungal infections were seen in 70 patients giving an incidence of 87.5%. Of them 61 were male (88.4%) and 9 were females (11.5%). Their age ranged from 16 years to 55 years with an average of 24.5 years . Among the fungal infections pityriasis versicolor lesions were commonly encountered in 33 patients (47.14%), followed by dermatophytosis in 26 paients (37.14%), candidiasis in 6 patients (8.5%) and phaeohypomycosis in 5 patients (7.1%).

TABLE 5: PREVALENCE OF FUNGAL INFECTION ALONG WITH SEX DISTRIBUTION IN RENAL TRANSPLANT RECIPIENTS

No.	Fungal infection	Male	Female	Total	Percentage
1	Dermatophytosis	26	07	33	47.14%
2	Pityriasis versicolor	26	00	26	37.14%
3	Candidiasis	04	02	06	8.5%
4	Phaeohypomycosis	05	00	05	7.1%



PITYRIASIS VERSICOLOR

Out of 70 patients with fungal infection, pityriasis versicolor lesions were seen in 33 patients with the incidence of 47.14%. Of these 26 (78.7%) were males and 7 (21.21%) were females. The age of these patients ranged from 16 years to 46 years with an average of 29.48 years. Pityriasis versicolor lesions were commonly observed during the 7 to 12 months of post transplant period.

The commonest morphologic type of pityriasis versicolor noted in this study was achromic type (87.8%) distributed in usual sites like chest and upper back. The extent of involvement ranged from 3% to 70% of body surface area with an average of 17.1%. The patient with 70% area involvement was a 24 year old male who was on cyclosporine, azathioprine and prednisolone for a period of 15 months.

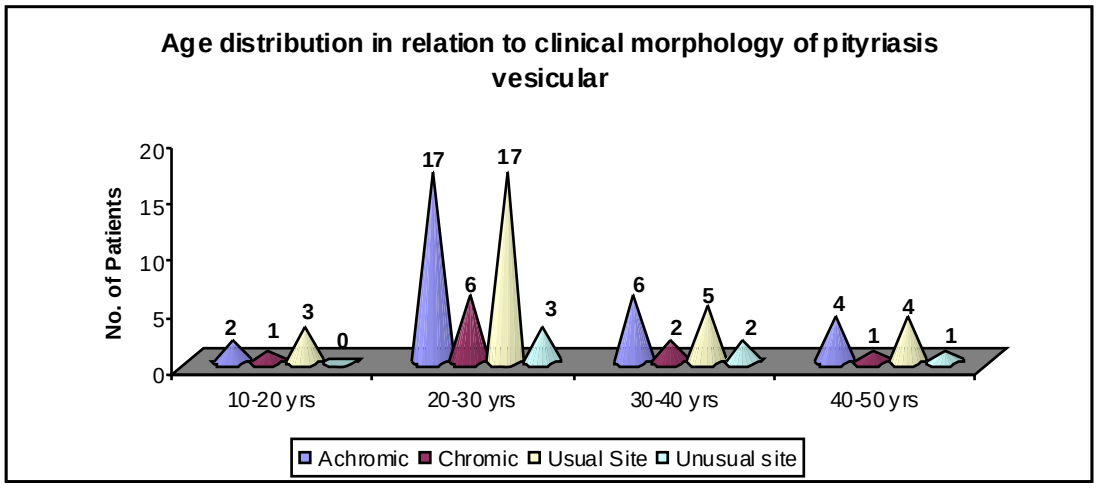
TABLE 6: AGE DISTRIBUTION IN RELATION TO CLINICAL MORPHOLOGY OF PITYRIASIS VERSICOLOR

No.	Clinical morphology	Age group (in years)				Total	Percentage
		10-20	20-30	30-40	40-50		
1	Achromic	2	17	6	4	29	87.87%
2	Chromic	1	6	2	1	10	30.30%
3	Usual site	3	17	5	4	29	87.87%
4	Unusual site	0	3	2	1	6	18.18%

Usual site: Face, chest and upper back. Unusual site: forearm and thigh.

Out of 33 patients with pityriasis versicolor lesions, 13 patients had associated dermatophytosis, two patients had herpes labialis, one post-transplant diabetic patient had candidial intertrigo groin and one patient had verruca vulgaris.

Microscopic examination of the scales in 10% in KOH showed short, angulated, aseptate hyphae with group of spores and blastospores in all the 33 patients.



DERMATOPHYTOSIS

Among the 70 renal transplant recipients with fungal infection, dermatophytosis was observed in 26 (37.14%) patients. All of them were males.

Among the various clinical types of dermatophytosis, tinea cruris was the commonest type (76.9%) followed by tinea corporis (69.2%), tinea glutealis (46.1%), tinea manuum (26.9%), tinea faciei (19.2%), tinea pedis (15.3%) and tinea unguium (15.3%).

TABLE 7: AGE INCIDENCE IN RELATION TO CLINICAL TYPES OF DERMATOPHYTOSIS

No.	Clinical types	20-30yrs	30-40yrs	40-50yrs	Total	Percentage
1	Tinea cruris	7	10	3	20	76.9%
2	Tinea corporis	6	9	3	18	69.2%
3	Tinea faciei	2	2	1	5	19.2%
4	Tinea barbae	1	1	0	2	7.6%
5	Tinea manuum	2	3	2	7	26.9%
6	Tinea glutealis	2	8	2	12	46.1%
7	Tinea pedis	1	2	1	4	15.3%
8	Tinea unguium	1	3	0	4	15.3%

Dermatophytosis was most commonly seen in the age group of 30-40 years. It was commonly seen 7 months after the transplantation and out of 26 patients with dermatophytosis, 24 patients (92.3%) were developed lesions the within 24 months of transplantation. The occurrence of dermatophytosis in relation with age was between 23 to 46 years and the mean age was about 32 years.

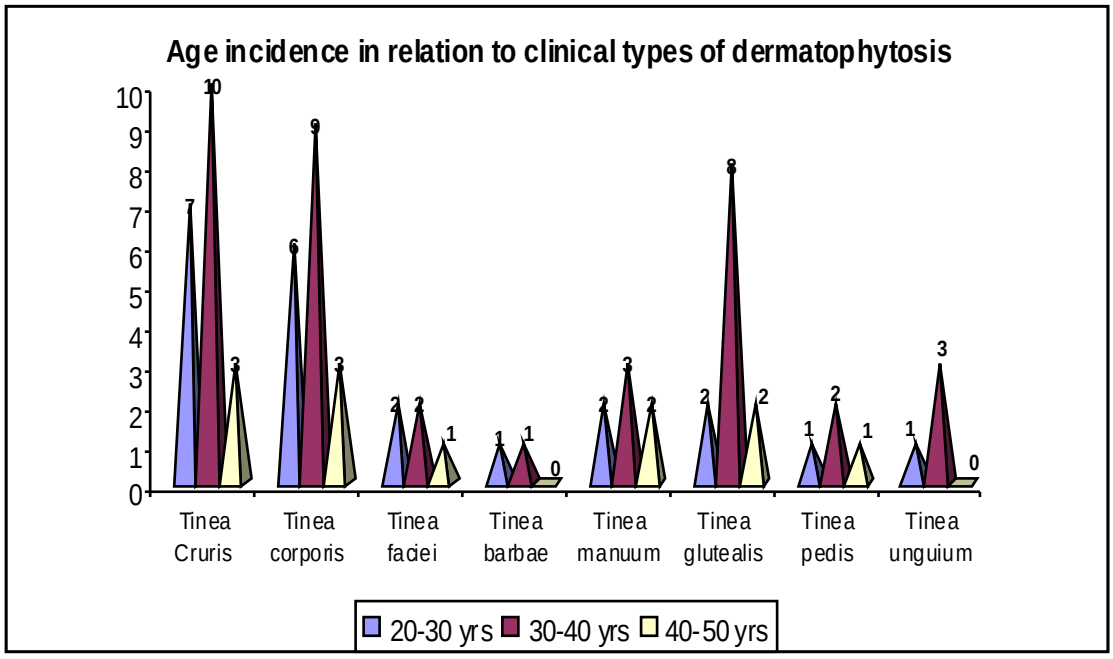


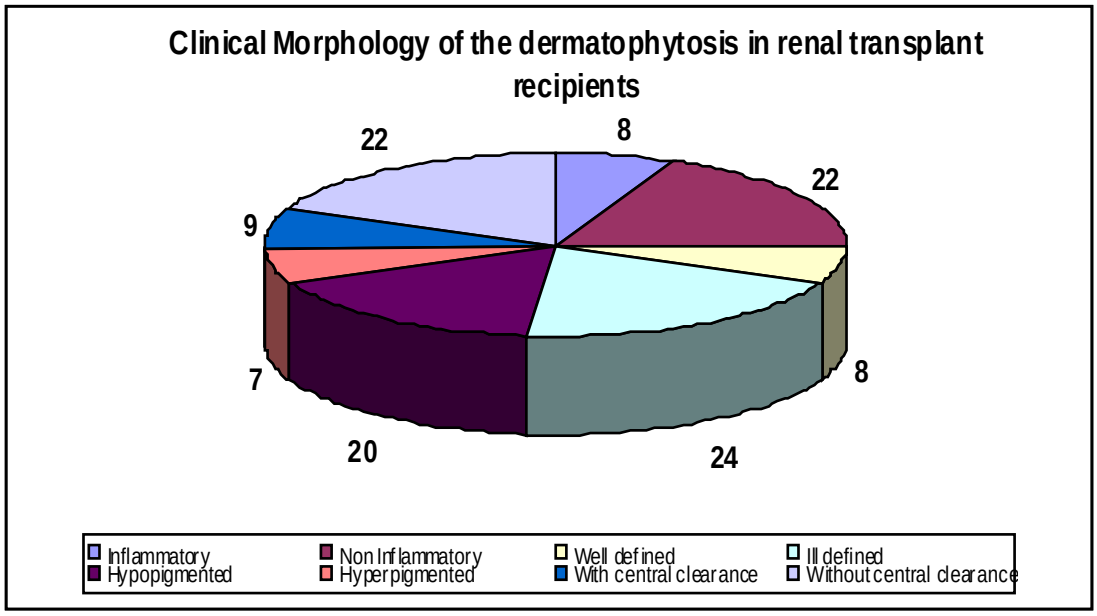
TABLE 8: CLINICAL MORPHOLOGY OF THE DERMATOPHYTOSIS IN RENAL TRANSPLANT RECIPIENTS

No.	Morphology of the lesion	Total	Percentage
1	Inflammatory	8	30.7%
2	Non - inflammatory	22	80.7%
3	Well - defined	8	30.7%
4	Ill – defined	24	92.3%
5	Hypopigmented	20	76.9%
6	Hyperpigmented	7	26.9%
7	With central clearance	9	34.6%
8	Without central clearance	22	80.7%

The commonest morphology in dermatophyte infection observed was non-inflammatory type (80.7%), in majority of patients with ill-defined margins (92.3%), of which most of the lesions showed hypopigmentation (76.9%) and absence of central clearance (80.7%). Well-defined inflammatory lesions were about 30.7%, of which 26.9% lesions showed hyperpigmentation. Out of 26 patients with dermatophytosis 11 (42.3%) patients had chronic dermatophytosis.

Among the 26 patients with dermatophytosis, 13 patients had coexistent pityriasis versicolor lesions.

The scales were obtained by gently scraping the lesions and then examined under light microscopy after adding 10% KOH which revealed hyaline, long, branching septate hyphae with arthrospores in all the 26 patients.



TINEA UNGUIUM IN RENAL TRANSPLANT PATIENTS

Out of 26 patients with dermatophytosis in this study, tinea unguium was observed in 4 patients giving an incidence of 15.38%. The duration of post transplant interval before the development of tinea unguium ranged from 12 months to 18 months. The involvement of finger nails were commonly observed in 3 patients (75%) when compared to toe nails involvement in 1 patient (25%). In all the four patients, distal and lateral subungual onychomycosis type were observed.

The subungual keratin in 40% KOH was examined under light microscopy which revealed hyaline, long, branching septate hyphae with arthrospores in all the four patients.

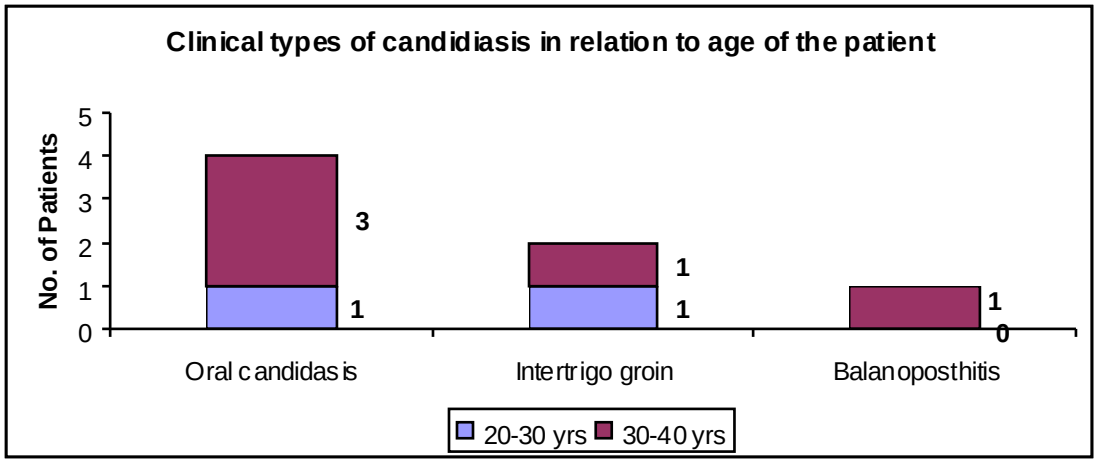
PREVALENCE OF CANDIDIASIS IN RENAL TRANSPLANT RECIPIENTS

Among the 70 patients with mycotic infection, six patients (8.5%) in toto had candidiasis, of whom four were males (66.6%) and 2 (33.3%) were females. Their age ranged from 24 years to 38 years with the mean of 31.8 years. Candidiasis was commonly observed during initial 6 months of post transplant period.

TABLE 9: CLINICAL TYPES OF CANDIDIASIS IN RELATION TO AGE OF THE PATIENT

No.	Clinical types	Age in years		Total	Percentage
		20-30	30-40		
1	Oral candidiasis	1	3	4	66.6%
2	Intertrigo groin	1	1	2	33.3%
3	Balanoposthitis	0	1	1	16.6%

Oral candidiasis were asymptomatic in all the 4 patients (66.6%), but two patients with intertrigo groin 2 (33.3%) and one patient (16.6%) with balanoposthitis had symptoms of itching and burning sensation. Of the six patients with candidiasis, 3 patients had diabetes mellitus and one patient had pityriasis versicolor. The microscopic examination of greyish white material from mucosa after adding 10% KOH showed budding yeast cells with pseudohyphae in all the six patients.



PHAEOHYPOMYCOSIS

Phaeohypomycosis was noted in 5 male patients (7.1%) and no females were affected. Age group ranged from 16 years to 52 years with the mean of 36.6 years. Four patients were developed the lesion one year after the transplantation and one patient developed 10 months after the transplantation. Vaious clinical presentations like subcutaneous cysts, abscesses, ulceroproliferative growth and carbuncle like lesion were observed among the five patients.

The seropurulent material obtained from the lesions by aspiration or touch smear of biopsy specimen in 10% KOH was seen under light microscopy which revealed pigmented septate moniliform hyphae. Skin biopsy showed suppurative fungal granuloma in the dermis and subcutaneous tissue in haemotoxylin and eosin stained section. Special staining with Periodic-acid Schiff (PAS) and Gomori's methenamine silver (GMS) showed moniliform fungal elements which confirmed the diagnosis of phaeohypomycosis in all the five patients.

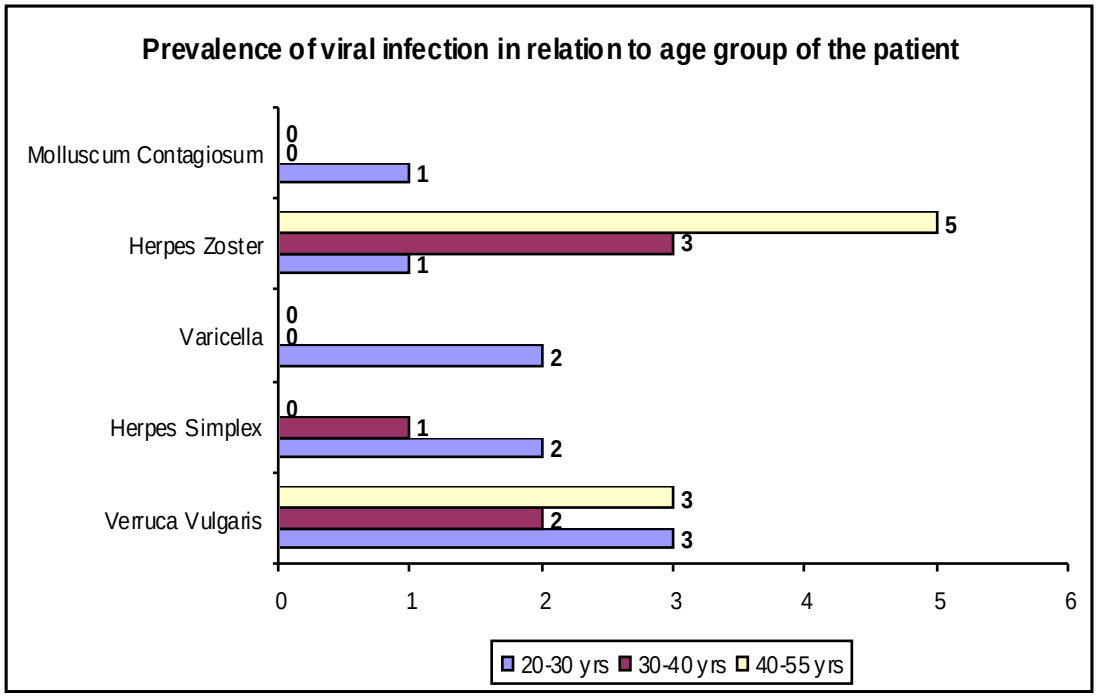
VIRAL INFECTION

The total number of patients observed to have viral infections were 23 (28.75%), of whom 19 were males (82.6%) and 4 were

females (17.3%). The age of these patients ranged from 21 years to 55 years with an average of 36.5 years. Viral infections were more commonly noted between 7 months to 24 months of post transplant period. The prevalence of various viral infections is given in table 10

TABLE 10: PREVALENCE OF VIRAL INFECTION IN RELATION TO AGE OF THE PATIENT

No.	Viral infection	Age group in years			Total	Percentage
		20-30	30-40	40-55		
1	Verruca vulgaris	3	2	3	8	34.78%
2	Herpes simplex	2	1	0	3	13.04%
3	Varicella	2	0	0	2	8.6%
4	Herpes zoster	1	3	5	9	39.13%
5	Molluscum contagiousm	1	0	0	1	4.3%



HERPES ZOSTER

Herpes zoster was the commonest viral infection noted in this study group, as it was seen in 9 renal transplant patients (39.13%), out of 23 patients with viral infections. The lesions were seen in 8 (88.8%) males and 1 (11.1%) female. Herpes zoster lesions were seen commonly during the 7 to 24 months of post transplantation period. Two patients showed multidermatomal involvement and hemorrhagic lesions. These lesions were commonly noted in thoracic dermatome in 5 patients (55.5%) followed by cervical dermatome in 3 patients (33.3%) and lumbosacral region in one patient (11.1%).

Human Papilloma Virus (HPV) Infection

HPV infection was the second commonest type of viral infection in this study. Verruca vulgaris lesions were noted in 8 patients (34.78%), out of 23 patients with viral infections and the distribution of lesions were mainly confined to the extremities. Among the 8 patients with verruca, 7 patients were (87.5%) males and 1 female patient (12.5%). These lesions were commonly observed one year after the transplantation. Out of these 8 patients, two transplant patients had associated dermatophytosis and one patient had pityriasis versicolor.

Herpes Simplex Virus (HSV) Infection

Infection with herpes simplex virus was noted in 3 (13.04%) patients, of whom 1(33.3%) was male and 2 (66.6%) were females. All the three had herpes labialis. In this study herpes labialis was commonly seen during initial 6 months of post transplant period . In one patient, lesions became ulcerated and was persisted for about one month duration and completely healed after oral acyclovir therapy.

Tzanck smear of the vesicular lesion showed multinucleated giant cells. Two patients had associated pityriasis versicolor lesions.

Chickenpox

Varicella infection was observed only in two male patients (8.6%), which were seen during the initial four months of transplantation. Among them one patient had disseminated lesions and the other patient had few discrete dew drop vesicles over the neck. The tzanck smear showed multinucleated giant cells.

Molluscum contagiosum

This infection was observed in only one transplant patient (4.3%). The lesions were multiple, dome shaped, skin coloured,

firm, umblicated papules with an expressible cheesy core and distributed over the thigh. Molluscum bodies were demonstrated microscopically by using leishman stain.

BACTERIAL INFECTIONS

Bacterial infections were observed in 15 (18.75%) patients, of whom 12 (80%) were males and 3 (20%) were females. The age of these patients ranged from 26 years to 43 years with an average of 34.6 years. It was observed more commonly in first year of post transplantation . In this study most common bacterial infection observed was furunculosis in 6 patients (40%), followed by impetigo in 4 patients (26.6%) and cellulitis in 1 patients (13.3%). In a 43 year old post transplant diabetic patient both furunculosis and cellulitis were observed. The gram stain of pus material showed gram positive cocci in all the cases of furunculosis, impetigo and cellulitis. Erythrasma was noted in 4 patients (26.6%) and the diagnosis was confirmed by coral-red flourescence in Wood's lamp examination.

TABLE 11: PREVALENCE OF BACTERIAL INFECTION ALONG WITH AGE DISTRIBUTION IN RENAL TRANSPLANT RECIPIENTS

No.	Bacterial infection	Age in years			Total	Percentage
		20-30	30-40	40-50		
1	Furunculosis	1	3	2	6	40%
2	Impetigo	2	1	1	4	26.6%
3	Cellulitis	0	1	1	2	13.3%
4	Erythrasma	1	2	1	4	26.6%

SKIN MANIFESTATIONS DUE TO DRUGS IN RENAL TRANSPLANT RECIPIENTS

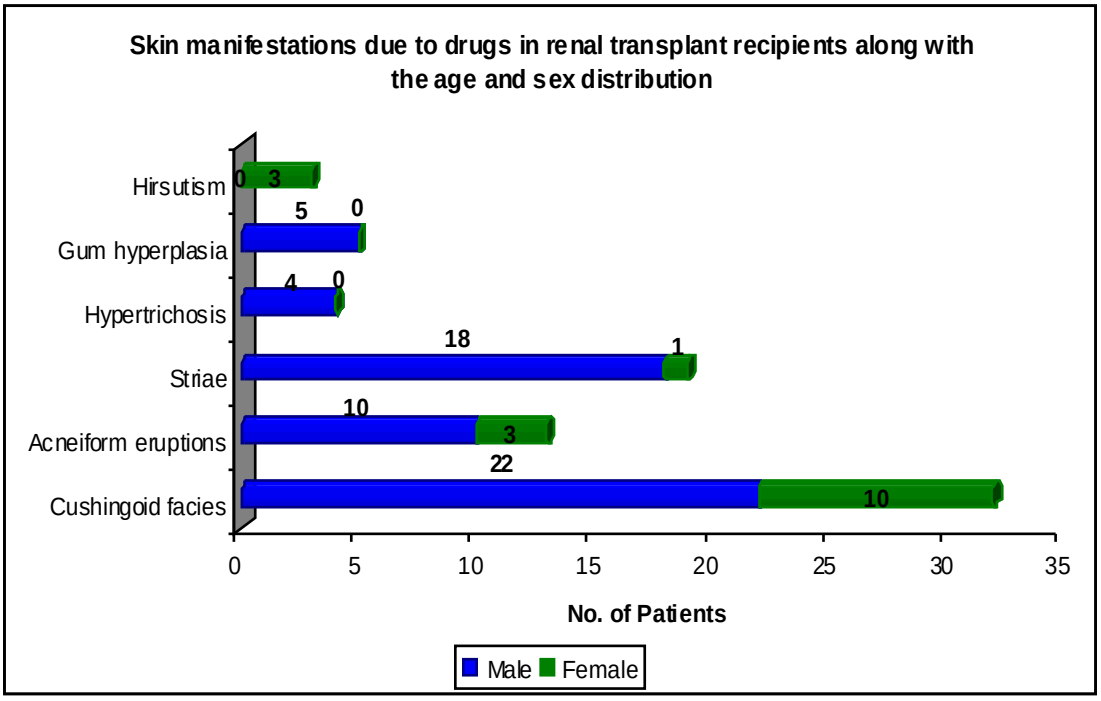
Drug induced changes were seen in 53 (66.25%) renal transplant patients, of whom 42 were males (79.2%) and 11 were females (20.7%). Their age ranged from 16 to 55 years with an average of 31.9 years. The various drug regimens used to induce immunosuppression was shown in Table 3. The commonly used regimen was combination of cyclosporine, azathioprine and prednisolone in 49 (61.25%) patients, followed by combination of

tacrolimus, mycophenolate mofetil and prednisolone in 16 (20%) transplant recipients.

The commonest side effect observed was cushingoid facies in 31 patients (60.3%), followed by striae in 19 patients (35.8%) and acneiform eruptions in 13 patients (24.5%). Hypertrichosis over the face, chest, upper arm, and back was observed in four patients (7.5%) and these patients were on cyclosporine containing drug therapy. Gum hyperplasia was noted in five male patients (9.4%), who were all had treatment with cyclosporine. Three patients (5.6%) on cyclosporine developed hirsutism.

TABLE 12: SKIN MANIFESTATIONS DUE TO DRUGS IN RENAL TRANSPLANT RECIPIENTS ALONG WITH AGE AND SEX DISTRIBUTION

No.	Skin changes	Male	Female	Total	Percentage
1	Cushingoid facies	22	10	32	60.3%
2	Acneiform eruptions	10	03	13	24.5%
3	Striae	18	01	19	35.8%
4	Hypertrichosis	04	-	040	7.5%
5	Gum hyperplasis	05	-	05	9.4%
6	Hirsutism	-	03	03	9.6%



MISCELLANEOUS DISORDERS

In this study, few miscellaneous cutaneous disorders were seen in five patients (6.25%). Keratosis pilaris was seen in one male patient who was on cyclosporine and prednisolone. Exaggerated insect bite allergy was noted in one HIV negative female patient. Fixed drug eruption was noted in one male patient and the probable drug was not known. One female patient developed lichen planus two years after the transplantation. A forty three year old male patient had classical scabies.

DISCUSSION

Renal transplant patients may present with various cutaneous lesions during the post transplant period. This study has been conducted to highlight the spectrum of skin lesions seen in renal transplant recipients in a tropical environment.

The study results shows that infections were the most common cutaneous manifestation in renal transplant recipients. Among the infections, fungal infections were the most common (87.5%), followed by viral (28.75%) and bacterial infections (18.75%). These results were similar to the study conducted in India by Leni George et al in 2010,[39] and discordant with the study conducted in Tehran by Ghaninejad et al[40], which showed that viral infections (40%) were the commonest skin infection.

In this study, among the fungal infections, pityriasis versicolor (47.14%) being the most common infection followed by dermatophytosis (37.14%) and candidiasis (8.5%). The Leni George et al[39] (36.5%), Gulec et al[42] (36.3%) and Zamanian et al[41] (24.9%) studies also showed that pityriasis versicolor was the commonest fungal infection.

The prevalence of pityriasis versicolor is higher in this study when compared to other studies like Chugh et al[43] (13.3%) and Koranda et al[36] (18%).

The pityriasis versicolor lesions were commonly noticed during the initial one year of post transplant period. The increased incidence of pityriasis versicolor in renal transplant recipients could be attributed to increased thickening of horny layer of skin, delayed desquamation of stratum corneum, overgrowth of Malassezia spp and mycelial shift due to immunosuppression and particularly with the use of systemic steroids.[79]

Dermatophytosis being the second commonest fungal infection in this study and the prevalence of dermatophytosis was about 37.14%, which was slightly lower than the study conducted by Selvi et al,[11] in which the prevalence of 42% was reported. In Leni George et al[39] study, dermatophytosis accounted for only 10% of total skin lesions which grossly differ from this study.

All patients affected by dermatophytosis were males and none of the female was affected. This could be attributed to the large number of males were screened when compared with females.

However, dermatophyte infection seems to be generally have less incidence in females as observed in various studies conducted.[11,45]

In this study group dermatophyte infection frequently seen in 7 to 24 months of post transplant period which were similar to the results of Leni George et al[39] study, states that dermatophytosis were common in patients with post transplant period more than six months. Out of 26 patients with dermatophytosis 11 patients (42.3%) had chronic dermatophytosis inspite of adequate treatment. This incidence was almost equal to the observation noticed in Selvi et alstudy.[11]

The high prevalence and chronicity of the dermatophytosis observed in these patients could be due to the constant immunosuppression induced by the immunosuppresants. In addition, increased thickening of the horny layer of the skin and delayed desquamation of stratum corneum induced by the action of systemic steroids also plays significant role in the persistence of infection.[46]

The commonest clinical type noticed in this study was tinea cruris (76.9%), followed by tinea corporis (69.2%) and tinea

glutealis (46.1%). These results were comparable with the study conducted by Selvi et al[11].

In the majority of dermatophytosis patients, the lesions were non-inflammatory with ill defined margin which was similar to the results obtained in Selvi et al study.[11] These type of clinical lesions indicate the diminished host response to dermatophyte infection.[11]

Tinea unguium was observed in 15.3% of patients and the distal and lateral subungual (DLSO) type of clinical presentation was noted in all the patients. The proximal subungual white onychomycosis (PSWO) type of tinea unguium was not seen in this study population but it was commonly noted in patients on immunosuppression.[11,15]

The incidence of candidiasis in this study population was (8.5%) and occurred commonly during the early (< 6 months) phase of post transplant period. These results were similar to the results of various studies like Ghaninejad et al,[40] Sandhune et al[47] and Formicone et al.[48]

Oral candidiasis was the commonest clinical presentation observed in this study population and pseudomembranous glossitis

was noted in all the patients. The candidial intertrigo manifested as maceration, glazed erythema and satellite pustular lesions. The diabetes mellitus may be an additional predisposing factor along with immunosuppressive treatment in 3 candidiasis patients.

The decreased incidence of candidiasis in renal transplant recipients compared to other fungal infection could be attributed to the factors like prophylactic antifungal therapy and asymtomatic nature of infection due to depressed immunity related deceased inflammatory response.[6]

In this study phaeohypomycosis was occurred in 7.1% of patients with different clinical morphological patterns like multiple cysts, abscesses, ulceroproliferative growth and carbuncle, where as in Leni George et al[39] study one patient had a phaeohypomycotic cyst. There are few case reports from India on the presence of phaeomycotic cysts in renal transplant recipients.[56-58]

Phaeohypomycosis was commonly seen in renal transplant patients with more than one year of post transplant period and prolonged immunosuppressive therapy.[21]

Herpes zoster (39.13%) was the most common viral infection observed in the study population. Leni George et al[39] study observed herpes zoster only in 7.5% patients. The immunosuppression induced reactivation of varicella-zoster virus occurred mainly between 7 to 24 months of post transplant period but according to Ghaninejad et al[40] study, the zoster lesions were commonly noted in early post transplant period (< 6 months).

Verruca vulgaris (34.78%) was the second commonest viral infection noted in this study which is almost similar to the results of the study conducted by Ghaninejad et al[40]. In renal transplant patients the occurrence of warts increased with the duration of immune suppression rather degree of immunosuppression[49] and frequently seen in patients on post transplant immunosuppressive therapy of more than one year duration.[50]

In this study the prevalence of herpes simplex infection was (13.04%) which was lower than the reported incidence of 35% in Koranda et al[36] study. Herpes simplex virus infections were substantially higher in the initial six months of post transplant period. In one patient, lesions became ulcerated and was persisted

for about one month duration and completely healed after oral acyclovir therapy.

The prevalence of bacterial infection in this study was 18.7% and commonly manifested during the first one year of post transplant period. In this study, the prevalence of bacterial infection were little high when compared to Lugo-Janer et al[46] – 11%, Chugh et al – 8.9% and Barba et al[51] – 3.5%.

The commonest cutaneous lesion caused by bacterial infection was furunculosis (40%) followed by impetigo (26.6%) and the results (48.5% and 30% respectively) were comparable with Leni George et al[39] study.

The probable reasons for decreased prevalence of bacterial infections in renal transplant individuals includes prolonged antibiotic therapy following transplantation and well preserved B lymphocyte function.[46]

Drug induced cutaneous changes were more common in the initial one year of post transplant period. This may be attributed to the high dose of immunosuppressive drugs used during the early phase of post transplantation when the risk of rejection is higher.[39]

Cushingoid facies (60.3%) were observed to be the most common drug induced skin change, which is higher than the study results of Chugh et al (27.4%) [43] and Bencini et al (32.7%).[45] Striae (35.8%) was the second common drug induced cutaneous change observed in this study, but Leni George et al study shows only 3.9%.

Acneiform eruptions (24.5%) were significantly higher in patients whose post transplant duration was less than six months and the results (24.6%) were similar to Leni George et al study[39] . These lesions were commonly observed with cyclosporine, azathioprine and prednislone combination therapy because these drugs may act separately and/or synergistically on sebaceous gland.[82]

The incidence of gum hyperplasia was found to be higher (6.25% vs 2.4%) and hypertrichosis was lower (5% vs 9.9%) when compared to Leni George et al study.[39] and these changes also commonly noted in patients treated with cyclosporine .[82]

Keratosis pilaris was noted in one male patient in this study and could be due to steroid and cyclosporine therapy.[35] In this study the drug induced changes showed a declining incidence as the transplantation interval lengthened as reported by Goldstein GD et al.[54]

In this study , cutaneous malignancies were not seen which is similar to the observation by Leni George et al study done in south India[39] and the incidence of skin malignancies in Chugh et al[43] study were only 0.6%. Various other studies conducted in European countries showed that the incidence of skin cancer among kidney transplant individuals varied from 8% at 1 year to 44% at 15 years.[78]

The cumulative effect of viral infections, prolonged immunosuppression and UV exposure has been thought to predispose renal transplant patients for the development of cutaneous malignancies.[85] The increased level of melanin[52] and the pattern of melanosmal dispersion in individuals with skin phototypes V and VI are the important factors in decreasing the occurrence of skin malignancies by providing protection from the cutaneous effects of UV radiation and hence a very low incidence of malignant skin lesions in Indian renal transplant recipients.[53]

CONCLUSION

The prevalence of skin lesions in renal transplant recipients was found to be high. Among the screened patients, most common manifestation were fungal infections, followed by drug induced cutaneous changes, viral infections and bacterial infections.

The superficial fungal infections like pityriasis versicolor, dermatophytosis and candidiasis were commonly encountered, of which pityriasis versicolor was the commonest, followed by dermatophytosis . The renal transplant recipients could be considered as a high risk group for the infection with malessezia and dermatophyte. Candidiasis was less frequently seen in kidney transplant patients.

There is an increased incidence of phaeohypomycosis in renal transplant patients on prolonged immunosuppression.

Herpes zoster and verruca vulgaris were the commonest viral infections seen in renal transplant patients. Among the bacterial infections , the commonest was furunculosis followed by impetigo.

In drug induced cutaneous changes, cushingoid facies were commonly seen, followed by striae and acneiform eruptions. Gum

hyperplasia and hypertrichosis were commonly seen in cyclosporine containing drug regimen.

The drug induced cutaneous changes were less common after one year of post transplantation.

In the initial 6 months of post transplant period commonly observed cutaneous manifestations were candidiasis, herpes labialis, chickenpox , furunculosis and acneiform eruptions.

Pityriasis versicolor lesions were frequently seen during the 7 to 12 months of post transplant period.

The dermatophytosis, herpes zoster and verruca vulgaris were commonly manifested between 7 to 24 months of post transplant period.

The anticipation of certain cutaneous lesions in the particular phase of post transplant interval and early diagnosis and treatment will improve the quality of life in renal transplant recipients.

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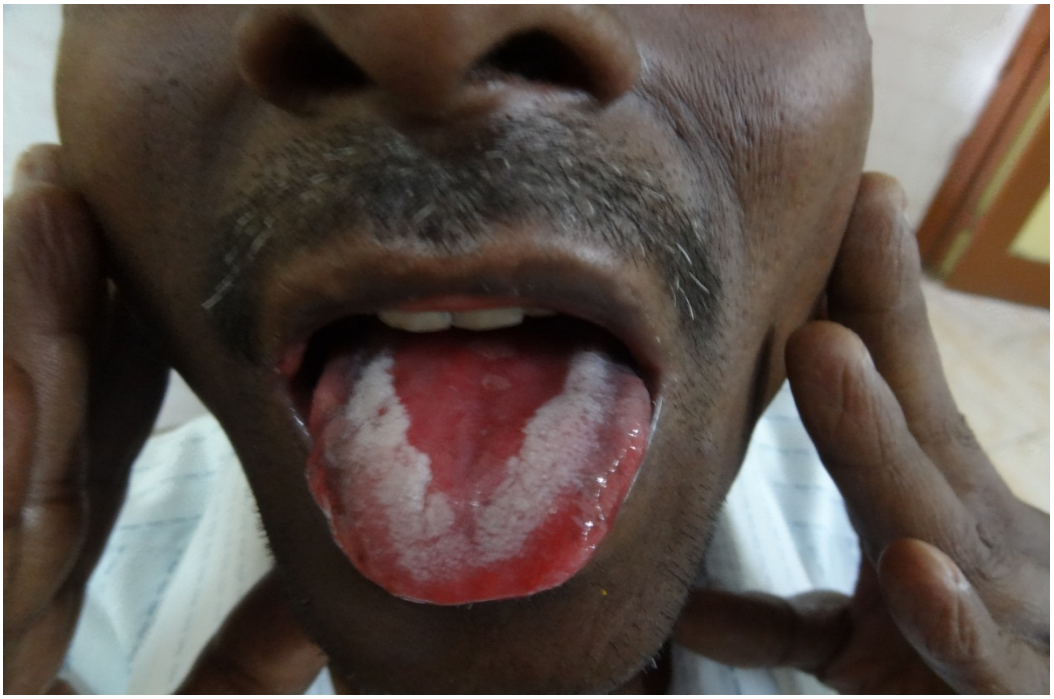
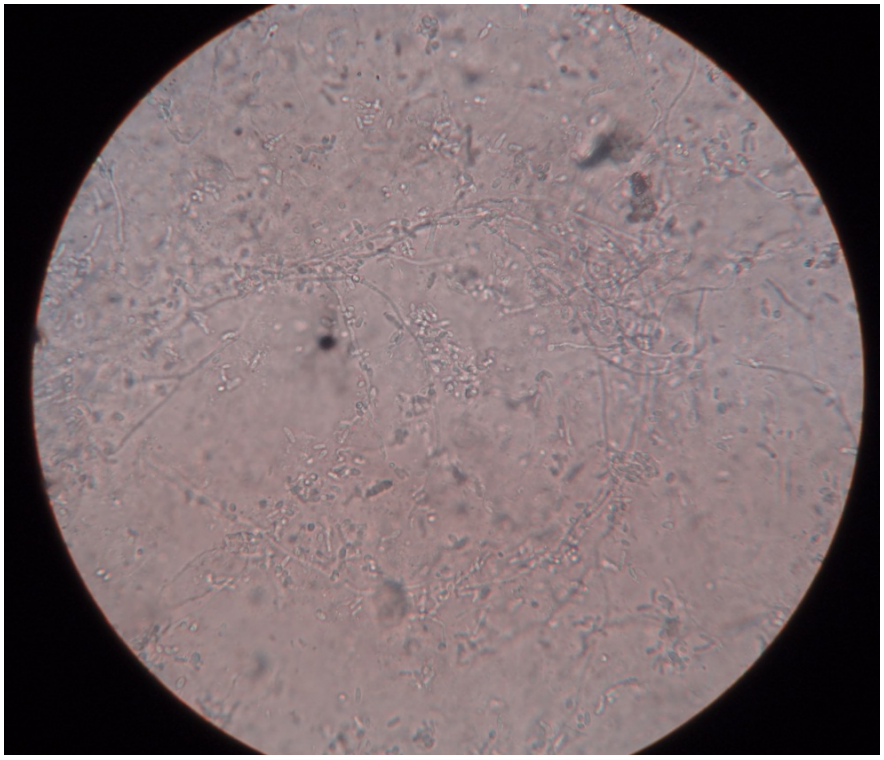
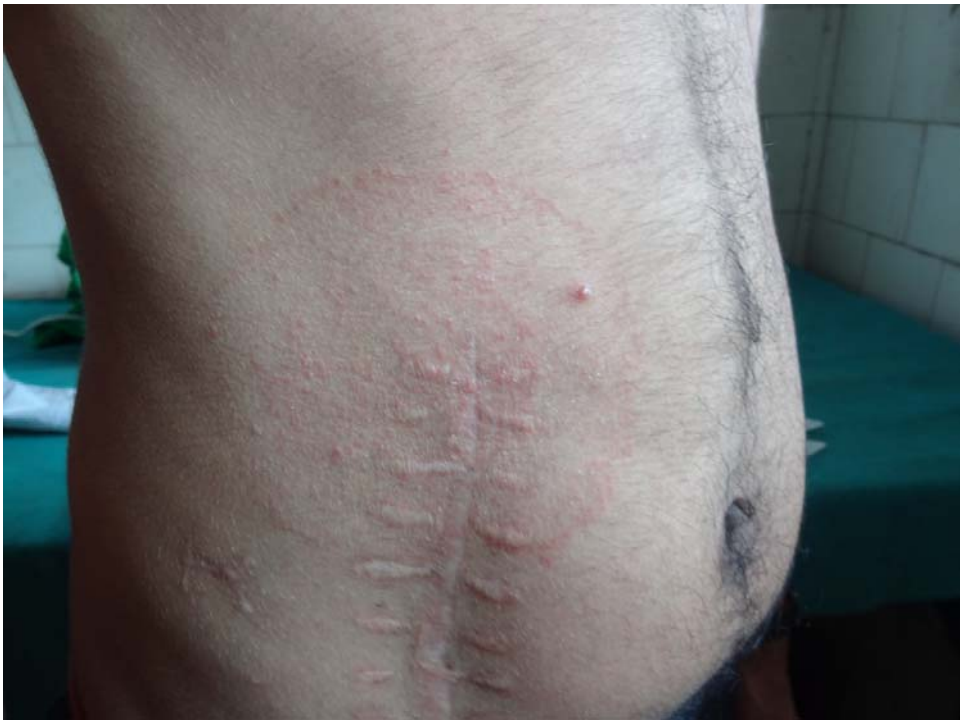


ORAL CANDIDIASIS

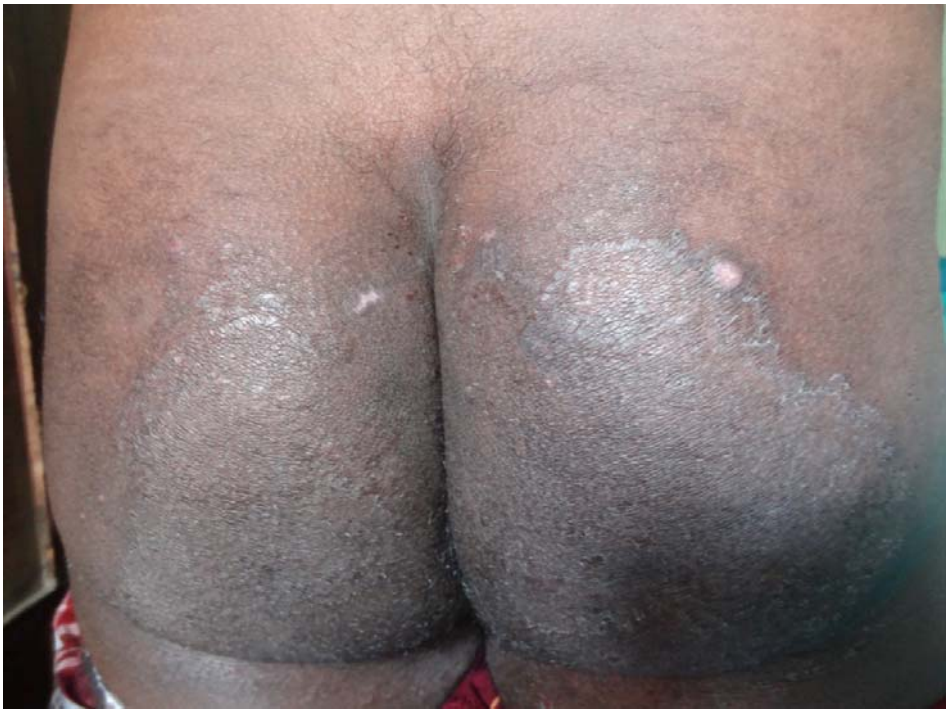


10% KOH
BUDDING YEAST CELLS WITH PSEUDOHYPHAE
CANDIDA

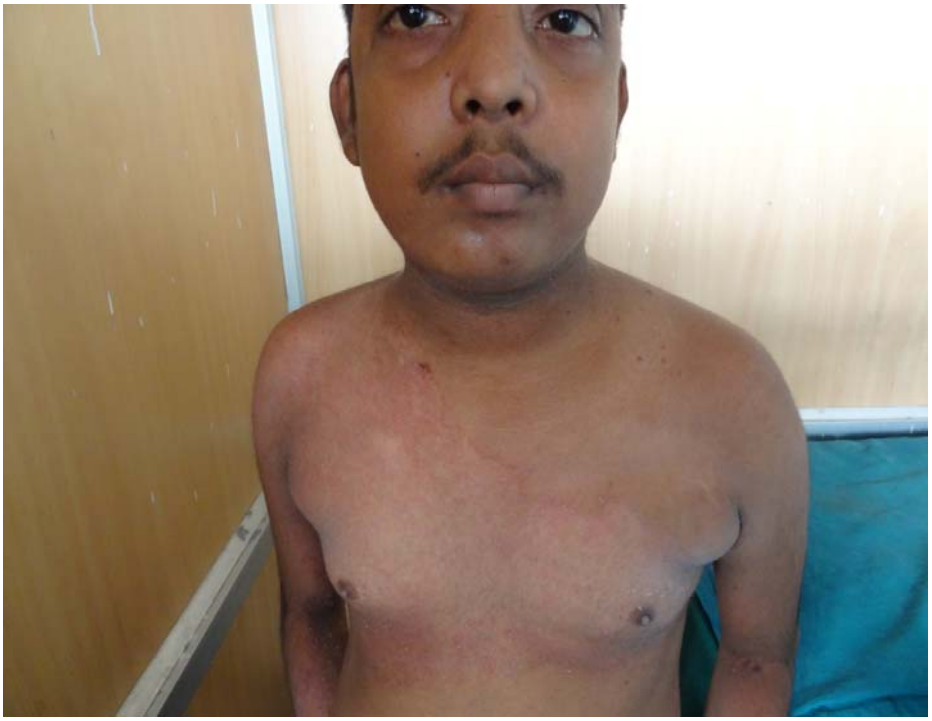
CANDIDAL BALANOPOSTHITIS



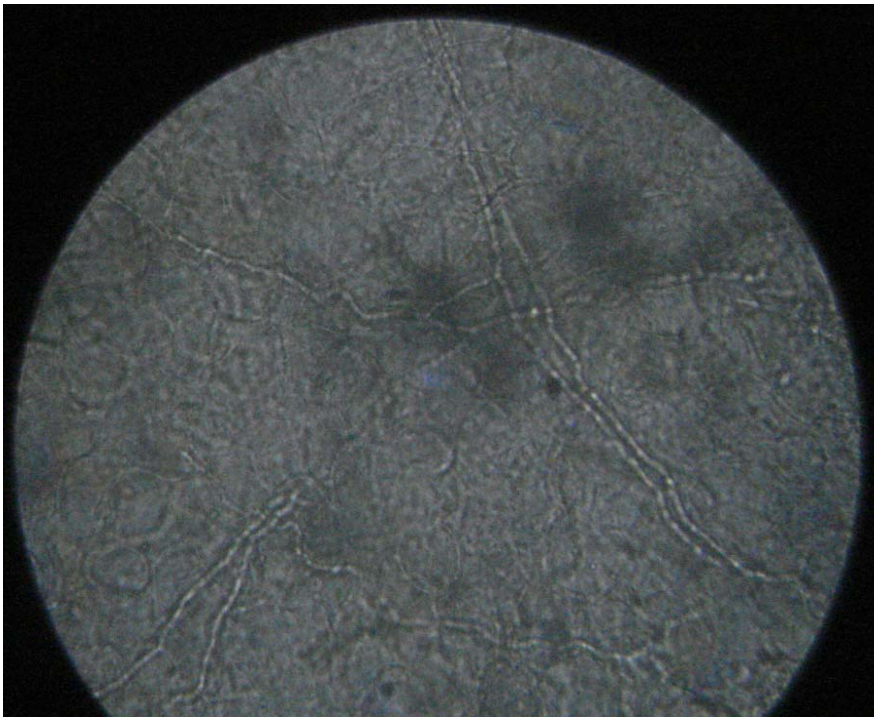
TINEA CORPORIS



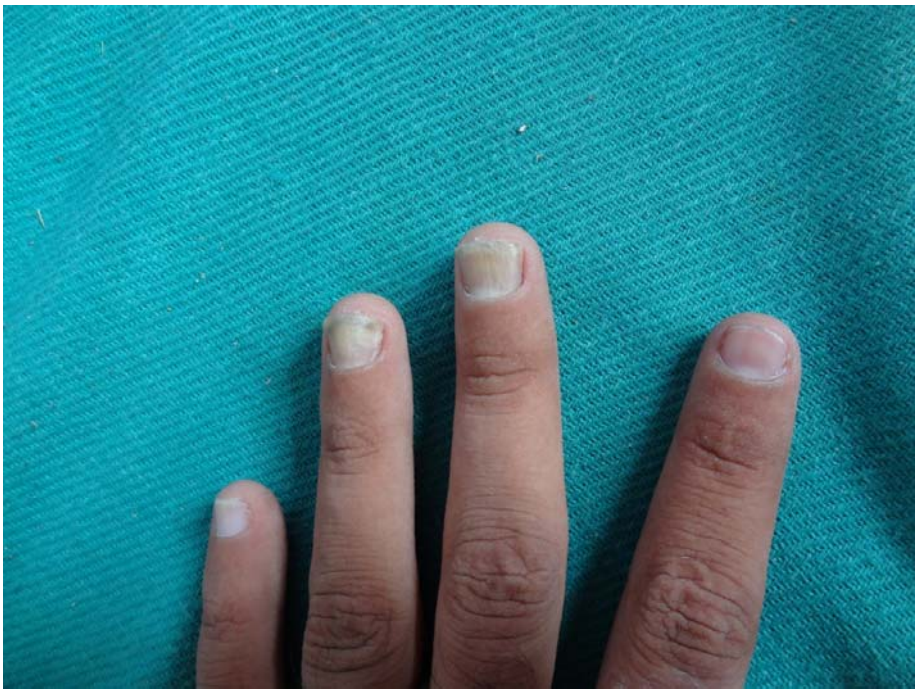
TINEA GLUTEALIS



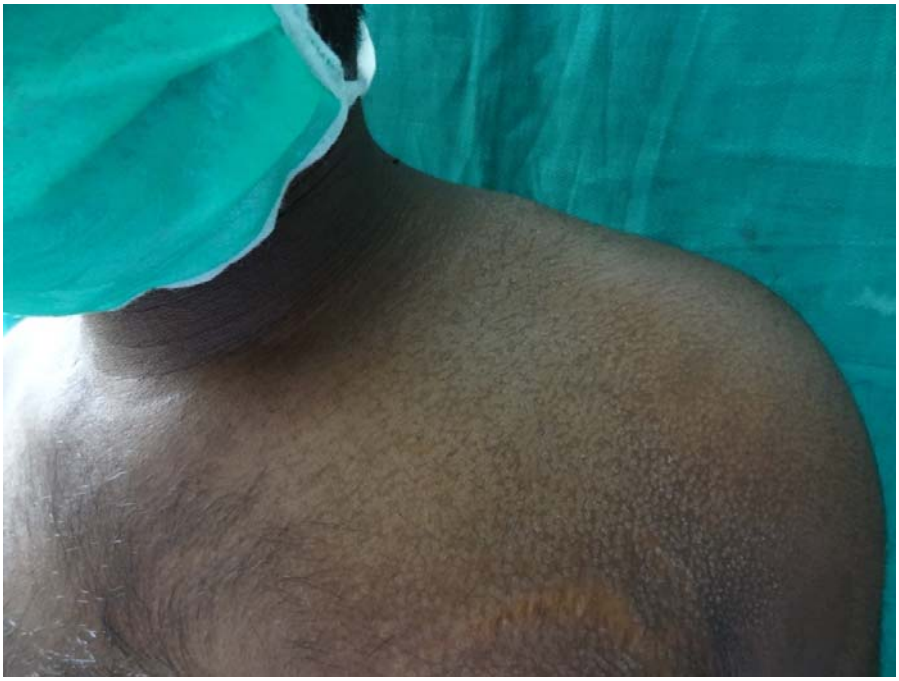
CUSHINGOID FACIES WITH TINEA CORPORIS



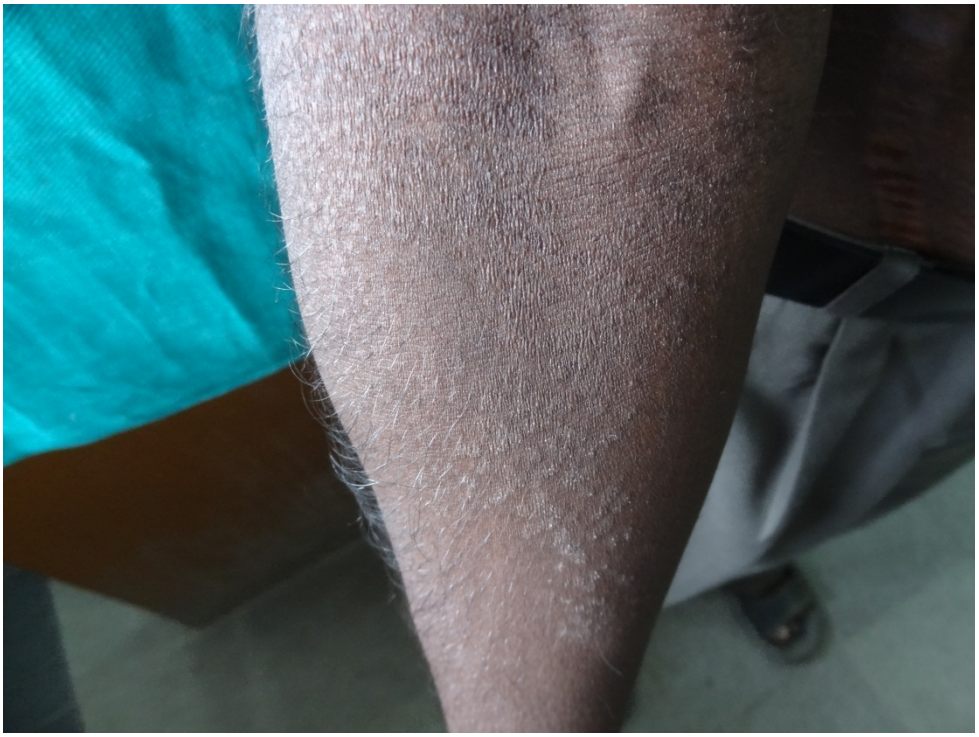
10% KOH
HYALINE BRANCHING SEPTATE HYPHAE WITH ARTHROSPORES
DERMATOPHYTE



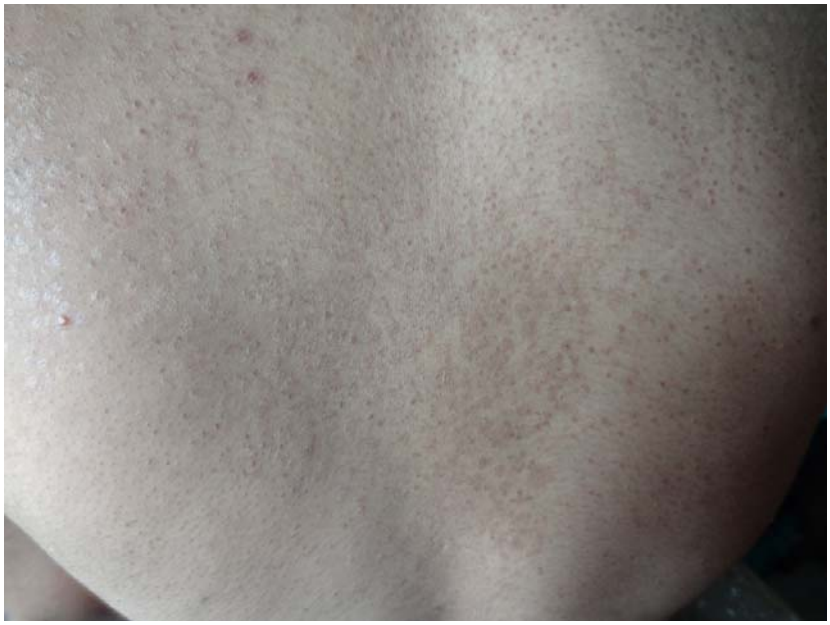
DISTAL AND LATERAL SUBUNGUAL ONYCHOMYCOSIS



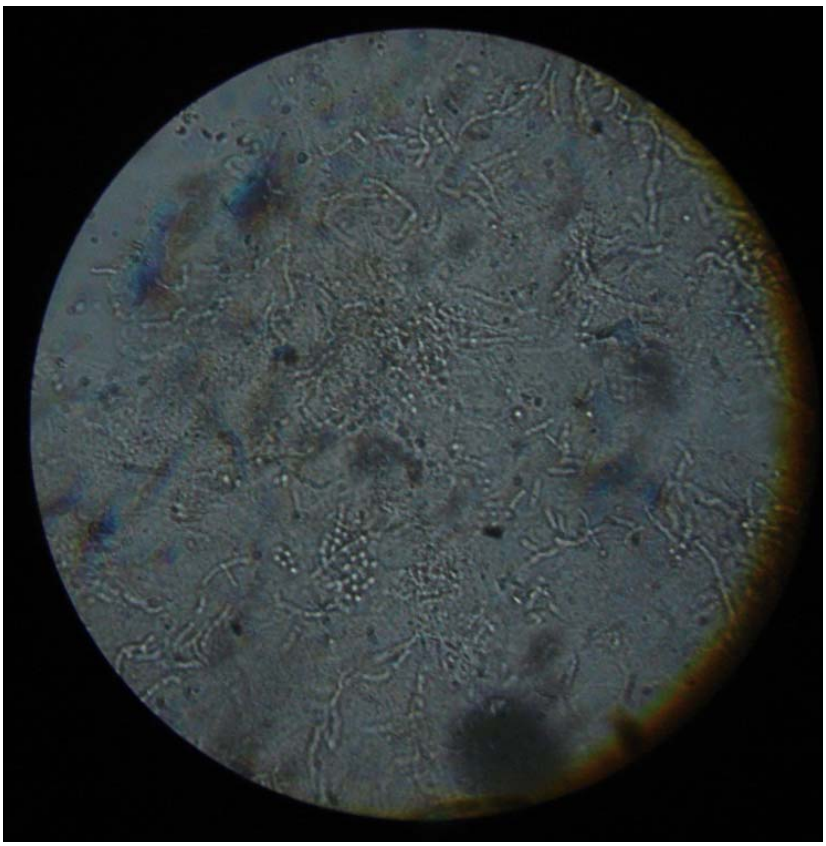
STRIAE WITH ACHROMIC PITYRIASIS VERSICOLOR



PITYRIASIS VERSICOLOR
UNCOMMON SITE



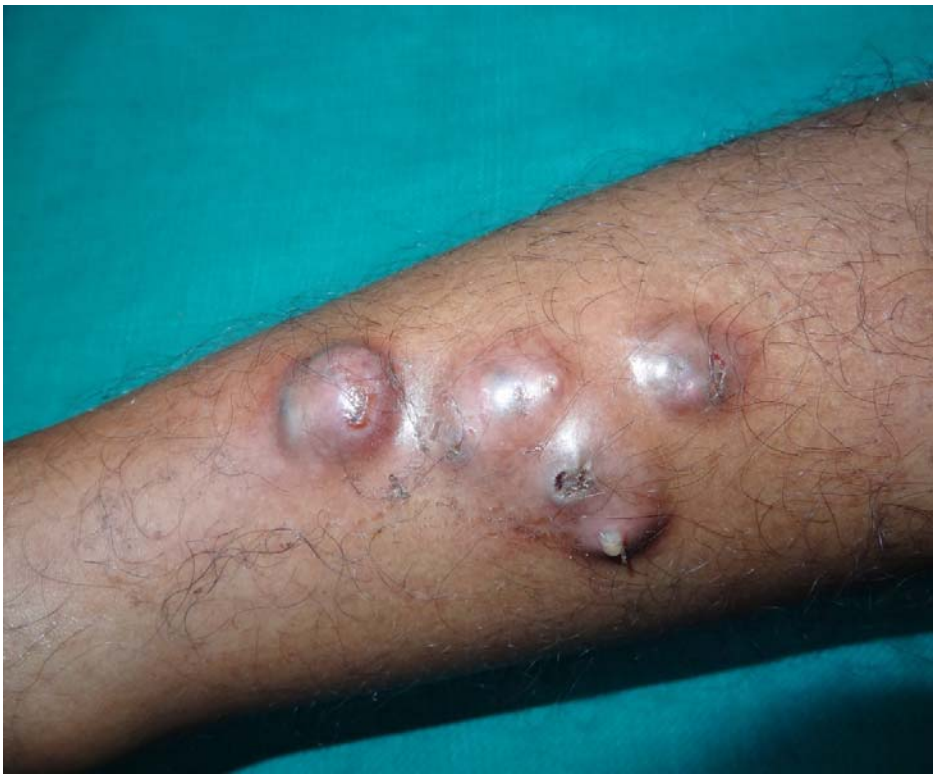
CHROMIC PITYRIASIS VERSICOLOR



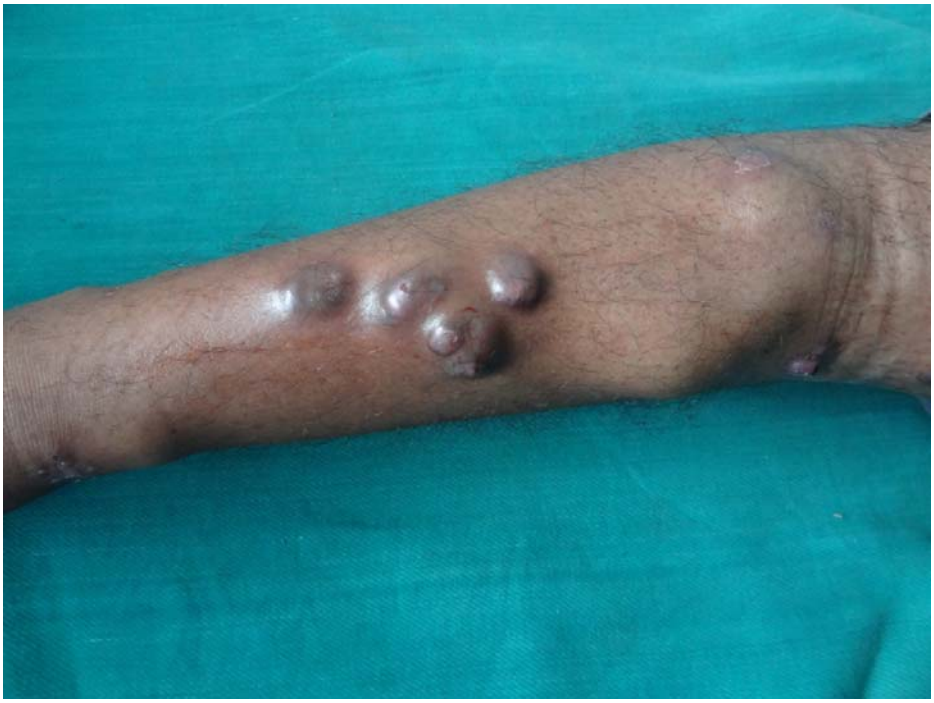
10% KOH

SHORT ANGULATED ASEPTATE HYPHAE WITH GROUP OF SPORES AND BLASTOSPORES

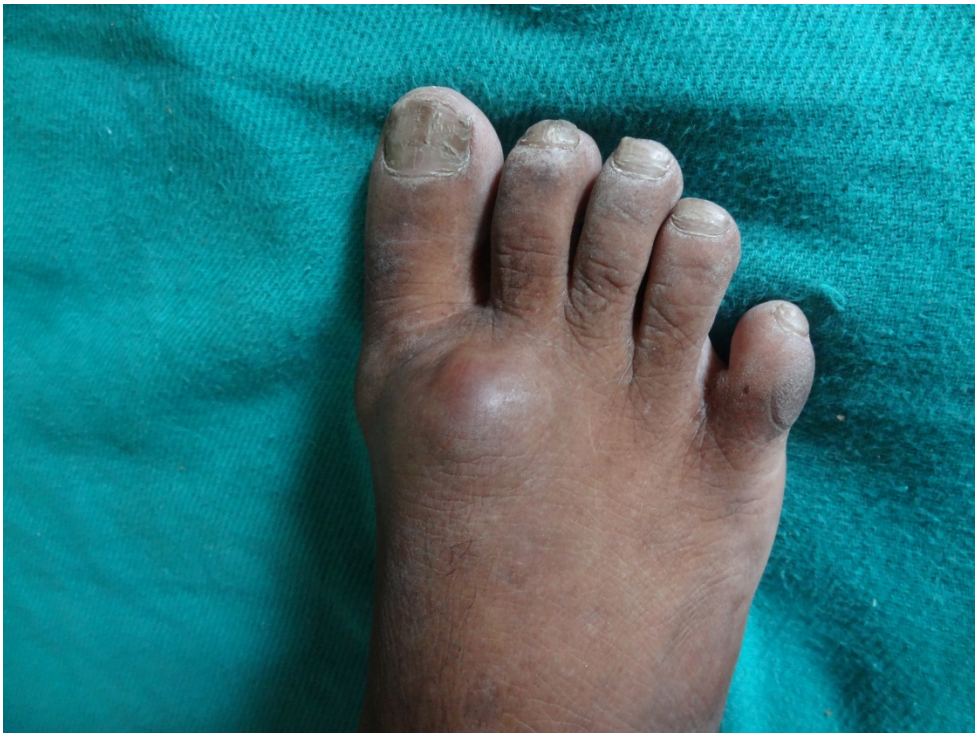
MALESSEZIA



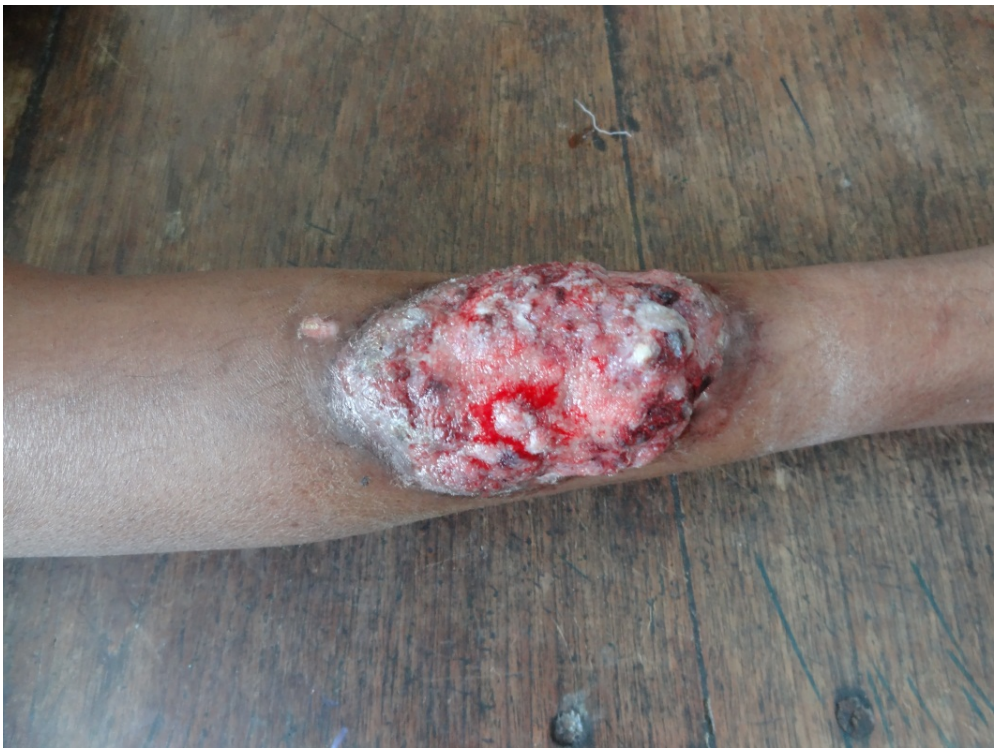
MULTIPLE ABCESS
PHAEOHYPOMYCOSIS



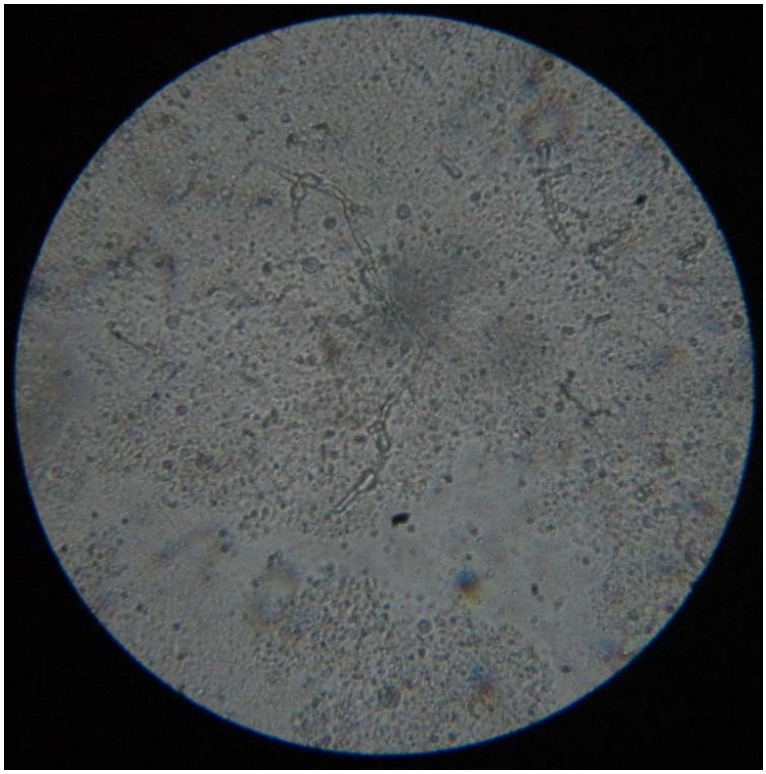
MULTIPLE ABCESS AND CYSTS
PHAEOHYPOMYCOSIS



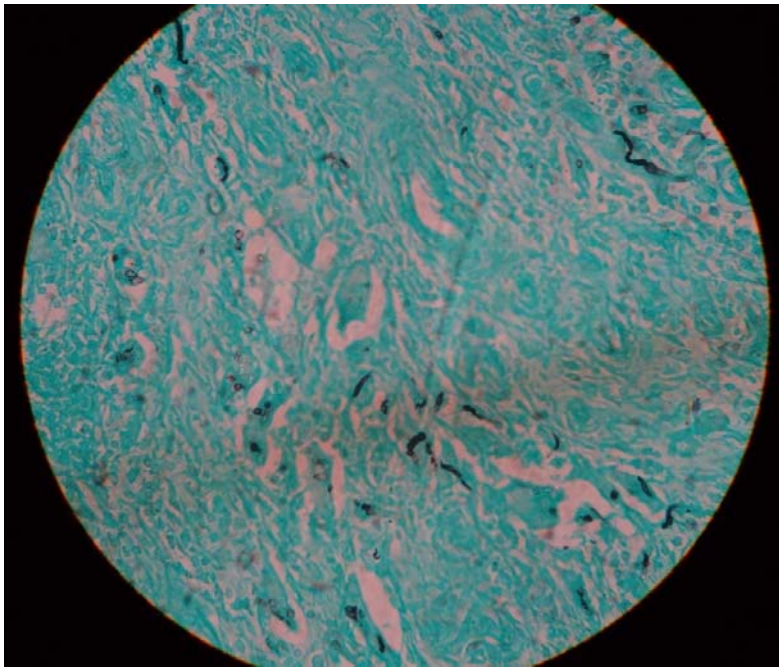
PHAEOHYPOMYCOTIC CYST



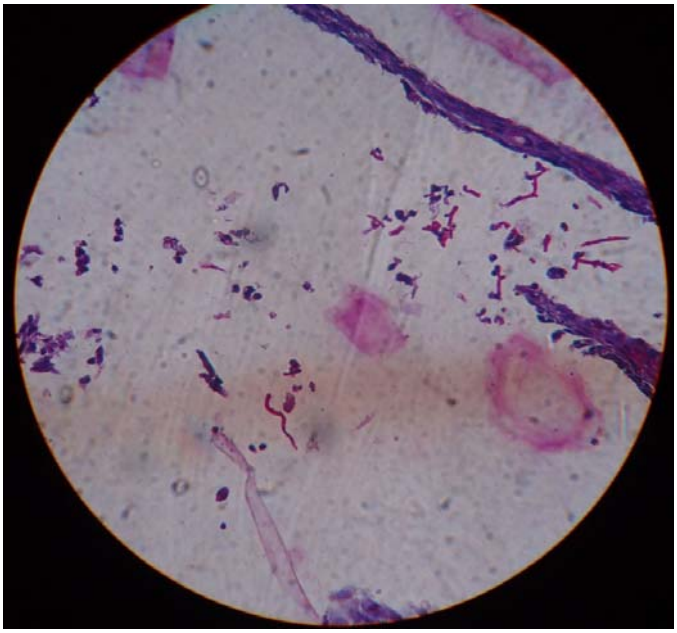
ULCEROPROLIFERATIVE GROWTH
PHAEOHYPOMYCOSIS



10% KOH
SEPTATE MONILIFORM HYPHAE
PHAEOHYPOMYCOSIS

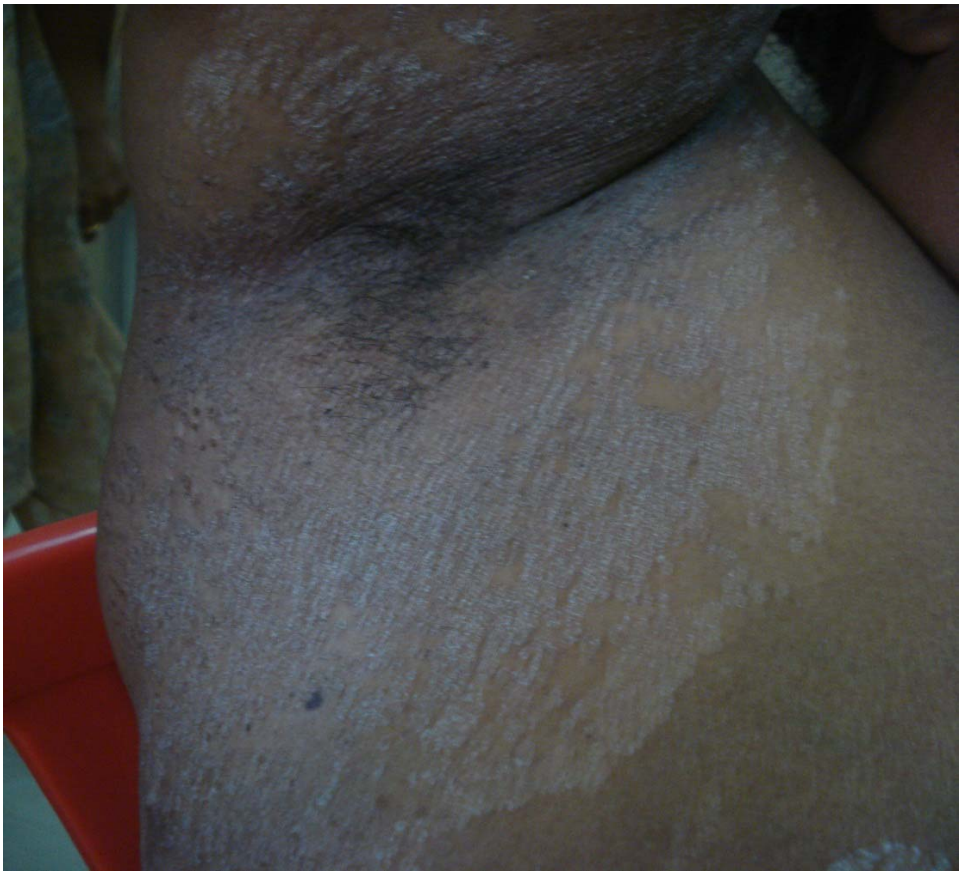


GOMORI'S METHENAMINE SILVER STAIN (GMS)
MONILIFORM FUNGAL ELEMENTS
PHAEOHYPOMYCOSIS

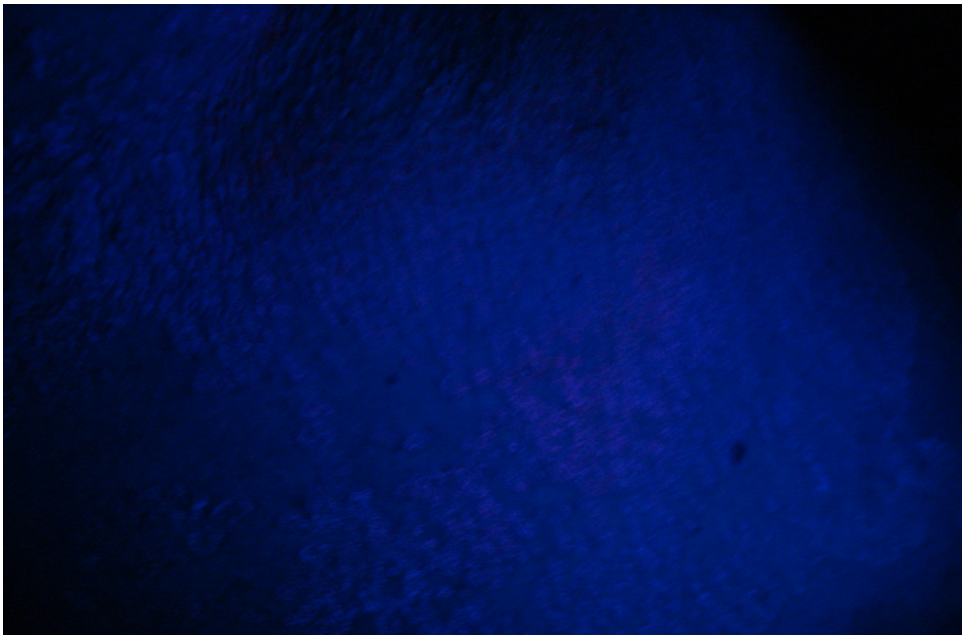


PERIODIC ACID SCHIFF STAIN (PAS)
MONILIFORM FUNGAL ELEMENTS
PHAEOHYPOMYCOSIS

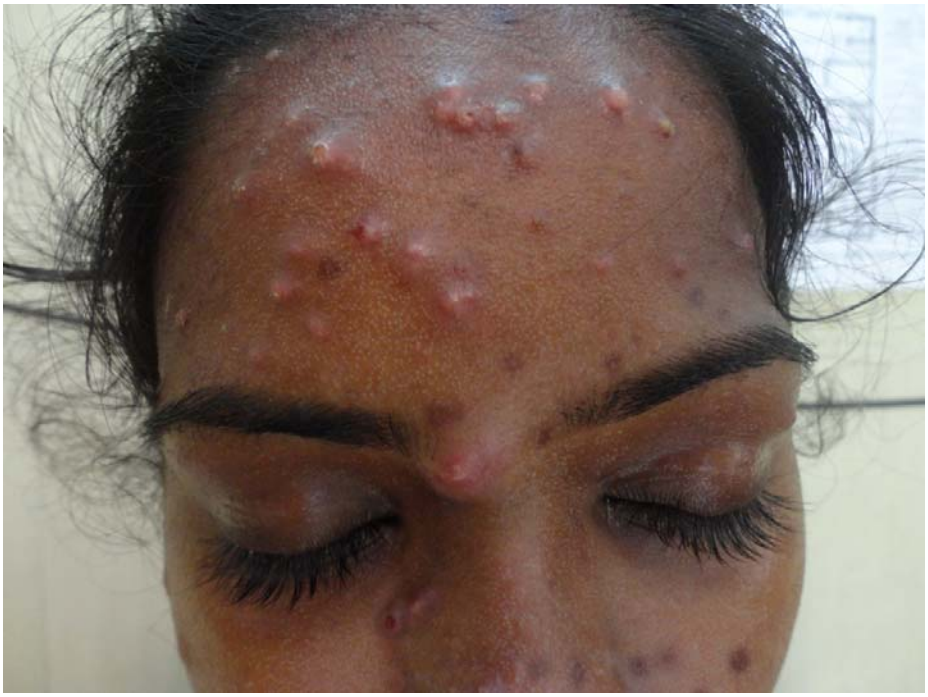
SCABIES



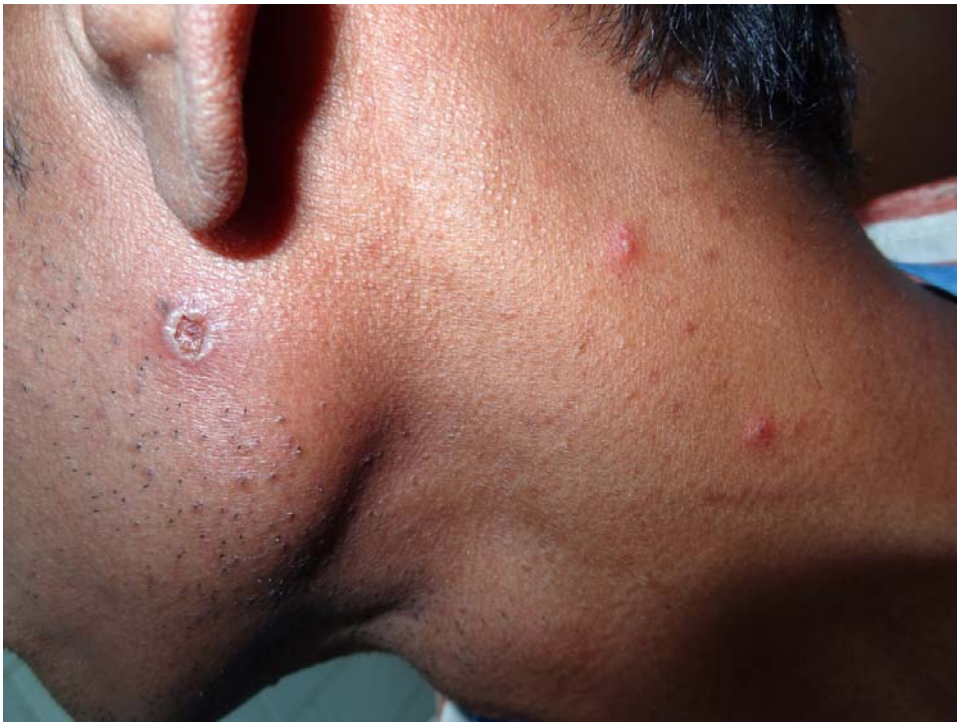
ERYTHRASMA



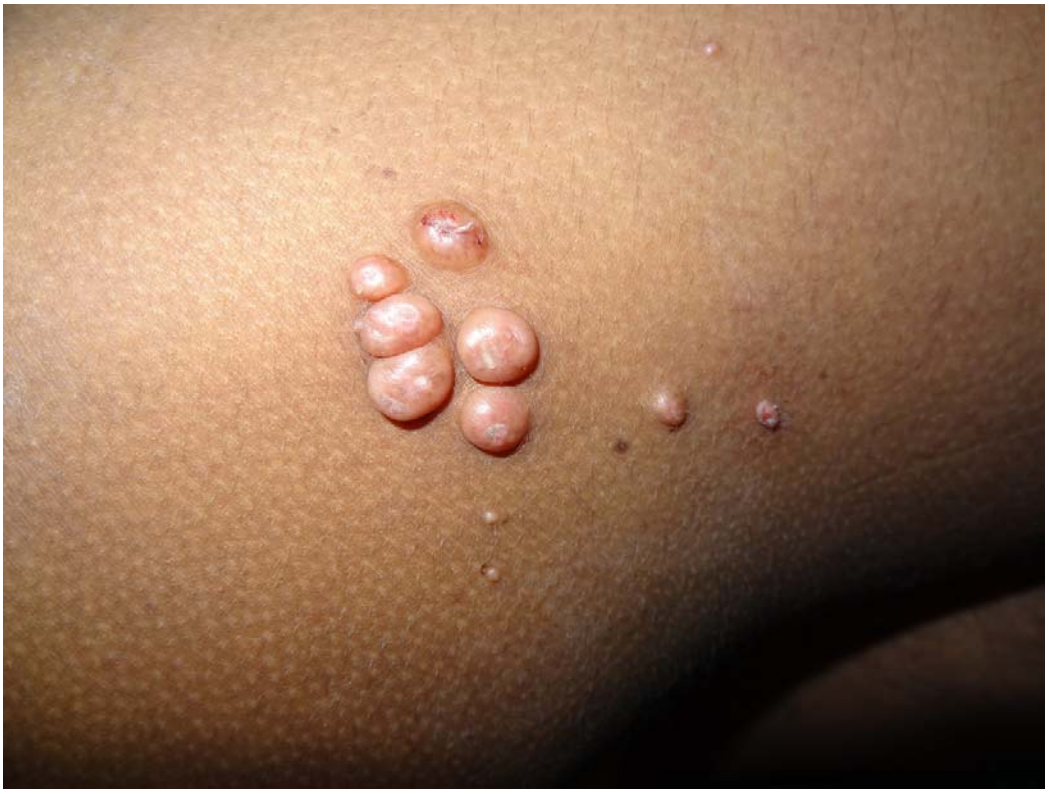
WOODS LAMP
CORAL RED FLOURESENCE
ERYTHRASMA



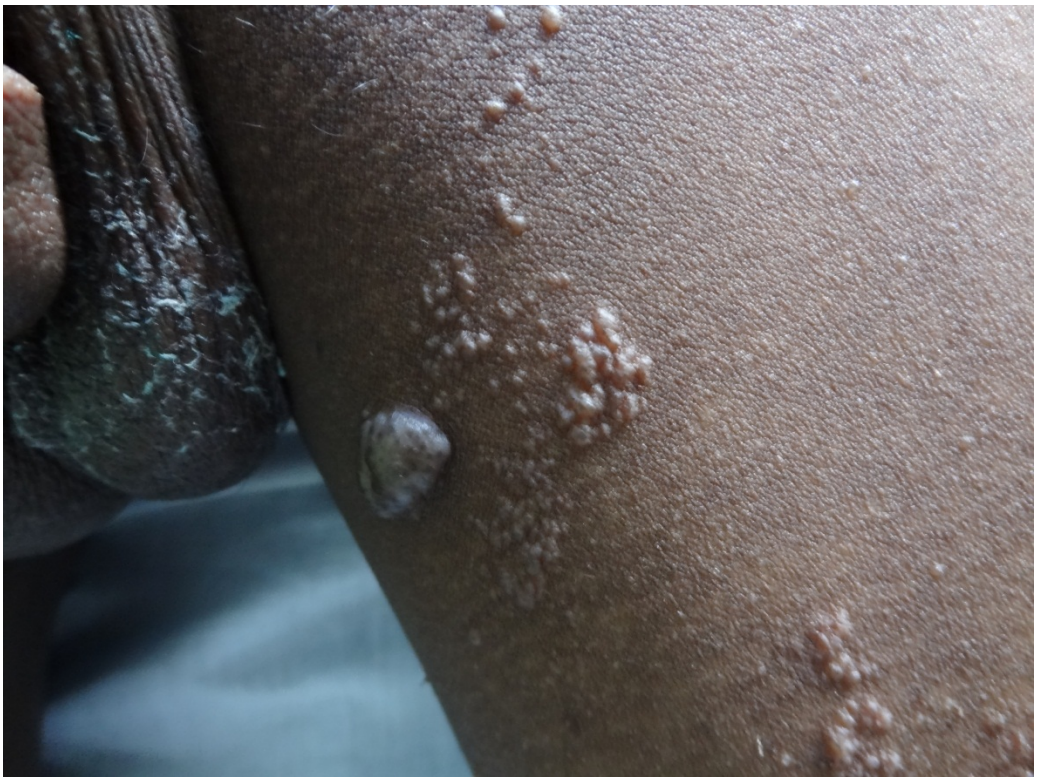
FURUNCULOSIS



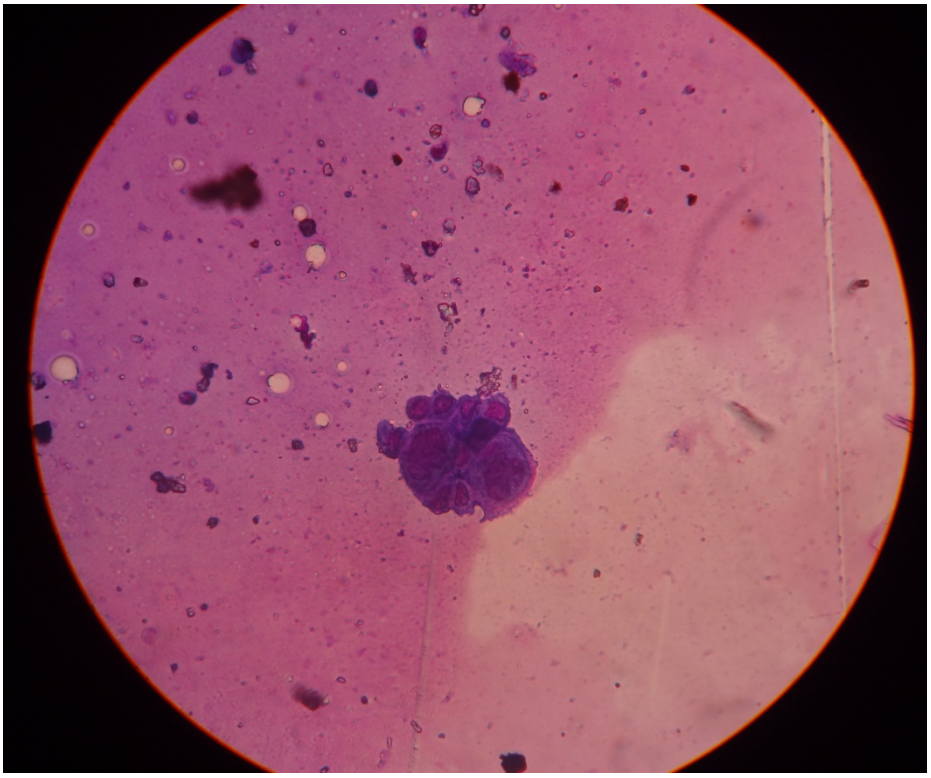
CHICKEN POX



MOLLUSCUM CONTAGIOUSM

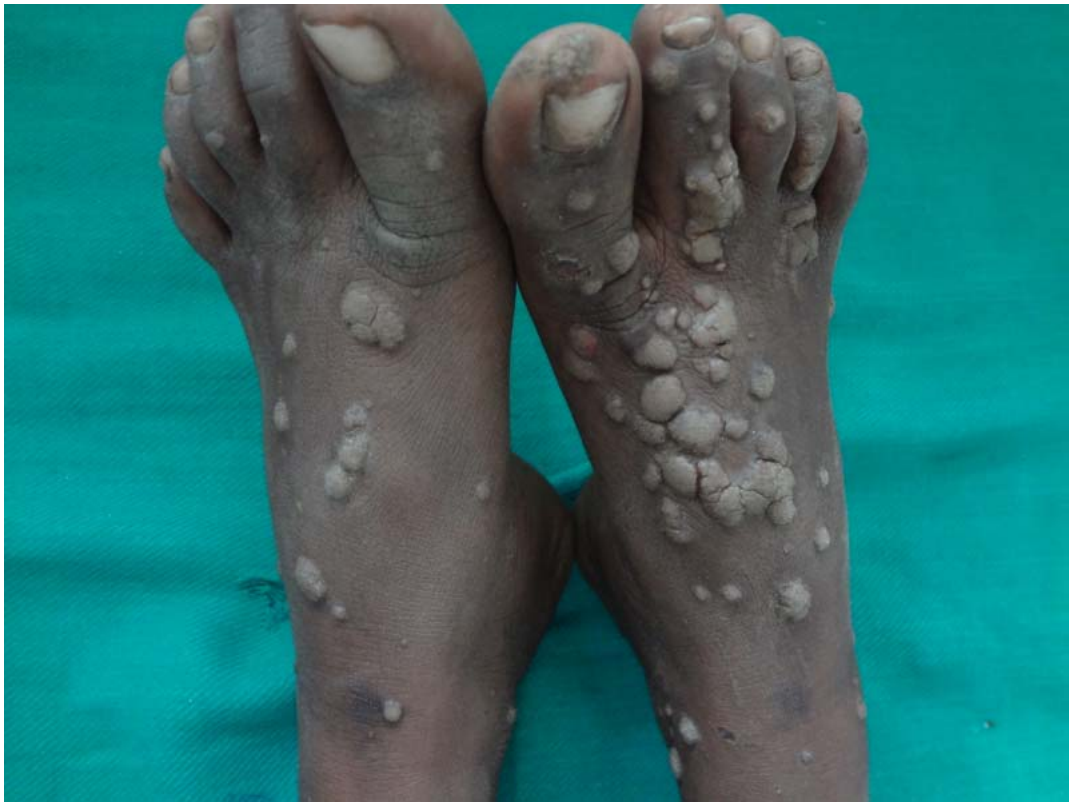


HERPES ZOSTER

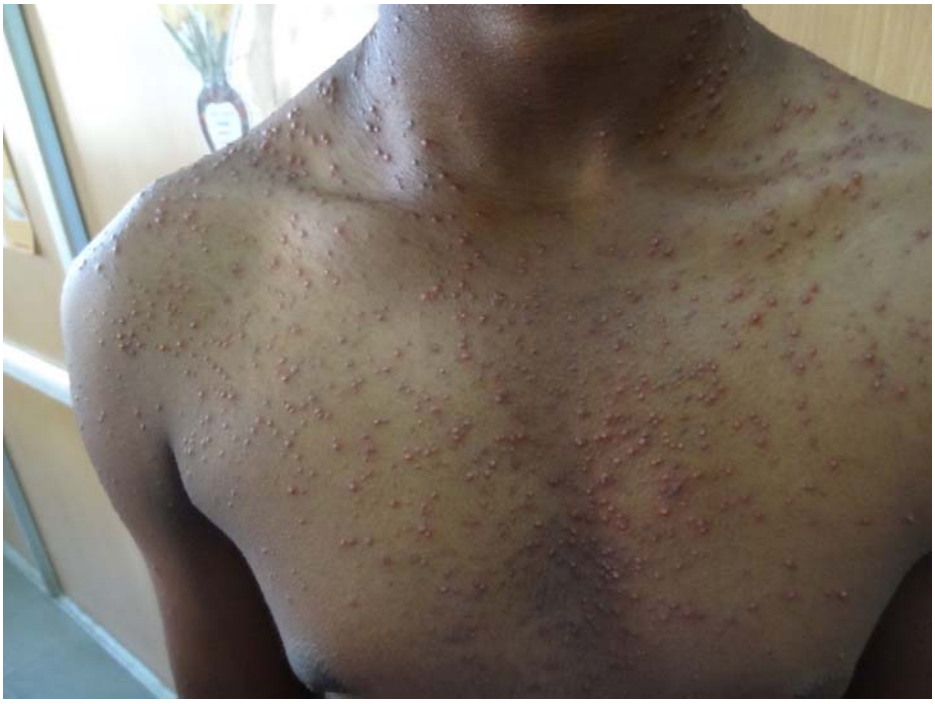


TZANCK SMEAR
MULTINUCLEATED GIANT CELL

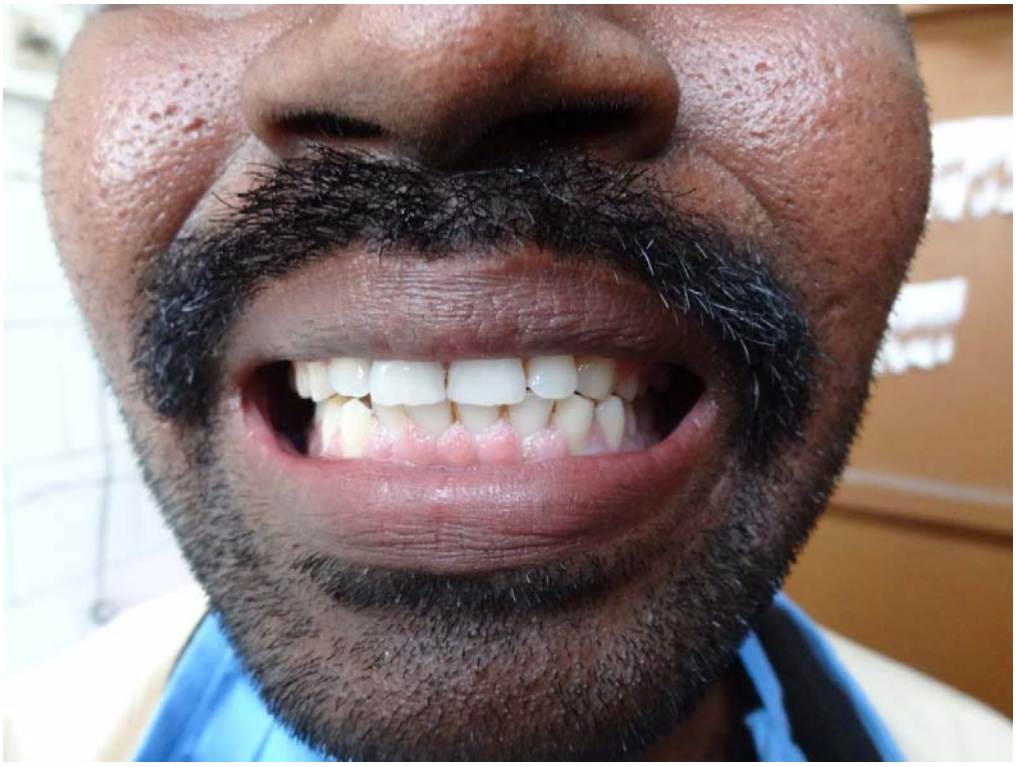
HERPES LABIALIS



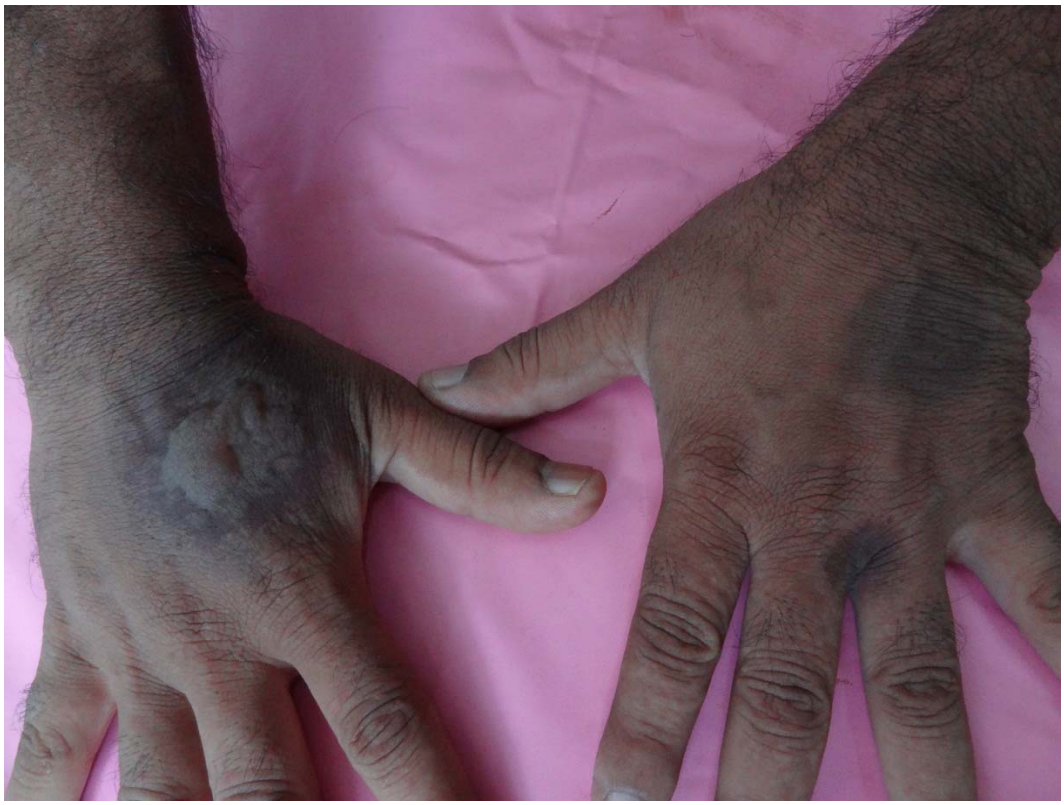
VERRUCA VULGARIS



ACNEIFORM ERUPTIONS



GUM HYPERPLASIA



FIXED DRUG ERUPTION

PROFORMA

CLINICAL STUDY OF CUTANEOUS MANIFESTATIONS IN RENAL TRANSPLANT RECIPIENTS

Name Nephrology no

Age Case no

Sex

Address

Occupation Marital status

Cause of renal failure

Renal transplantation done on

Duration of post transplantation period

Duration of immunosuppression before the development of skin lesions

Drugs

COMPLAINTS REGARDING SKIN MANIFESTATIONS

Dryness

Itching

Pigmentation

Red spots

Raised skin lesions

Fluid filled lesions

Poor wound healing

Hair changes

Nail changes

Any other changes

CLINICAL EXAMINATION

	Date of appearance	Post transplant duration
Skin changes		
Cushingoid		
Acne		
Facial erythema		
Atropy & dryskin		
Purpura		
Telangiectasia		
Hyperpigmentation		
Bullous lesions		
Icthyosis		
Palms and Soles		
Hair changes		
Nail changes		

INFECTION

	Date of appearance	Post transplant duration
Wart		
HSV		
Varicella		
Zoster		
MC		
Impetigo		
Furunculosis		
Cellulitis		
Erythrasma		
Scabies		

FUNGAL INFECTIONS

Dermatophytosis

Tinea capitis / T.Faciei / T.Barbae/

T.Corporis / T.Cruris / T.Manuum/

T.Pedis / T.Unguium/

Clinical morphology

Inflammatory/non inflammatory

Well defined/ill defined

Hypo or hyperpigmented/combined

With or without central clearance

DEEP DERMATOPHYTOSIS

PITYRIASIS VERSICOLOR

Chromic or Achromic

Usual or Unusual site

Surface area

CANDIDIASIS

Intertrigo/Paronychia/Onychia/

Oral Thrush/Perleche/Glossitis/

Vulvovaginitis/Balanoposthitis

OTHER MYCOSIS

ORAL MUCOSA CHANGES

Ulceration

Gum hyperplasia

Any other changes

NAIL CHANGES

Beau's lines

Mee's lines

Muehrcke's lines

Half and half nail
Terry's nail

Splinter haemorrhage

Onycholysis

HAIR CHANGES

Alopecia

Thinning of hair

Changes in colour

Hypertrichosis

Any other changes

INVESTIGATIONS

Hb% ,TC ,DC,ESR ,Platelet count

Blood sugar,urea , Sr creatinine

Liver function test

Serum electrolytes, pottasium, calcium

Urine albumin,sugar,deposits

Tzanck smear

Gram stain

AFB stain

Scraping for fungus / Mite

Nail clipping and Hair root examination

Fungal culture in SDPA/SDA

Woods lamp study

Skin biopsy

S.No	Sex	Age	PTI	Immuno suppressive Drugs					Pityriasis versicolor				Dermatophytosis							Tinea unguium			Candi-diasis			Phaeohypomycosis	Viral infection					Bacterial Infection				Drug induced Changes						Miscellaneous					
				C	A	P	M	T	A	C	US	UUS	TCR	TC	TF	TB	TM	TG	TP	DLSO	PSWO	TDO	OC	I	B		VV	HS	CP	VZ	MC	I	F	C	ERS	CF	AE	ST	HY	HI	GH	KP	LP	FDE	EI	SC
1	M	16	10 mon	Y	Y	Y			Y		Y															Y										Y			Y			Y				
2	M	17	8 mon	Y	Y	Y				Y	Y																									Y										
3	F	18	8 mon	Y		Y	Y		Y		Y																																			
4	M	21	12 mon	Y	Y	Y																								Y								Y								
5	M	22	4 mon	Y	Y	Y			Y		Y																									Y	Y									
6	M	23	10 mon	Y		Y	Y		Y		Y		Y	Y																						Y										
7	M	24	12 mon			Y	Y	Y		Y	Y			Y																																
8	M	24	15 mon			Y	Y	Y	Y	Y	Y	Y						Y																					Y							
9	M	25	12 mon	Y	Y	Y			Y	Y	Y			Y																																
10	M	25	4 mon	Y	Y	Y																							Y							Y	Y									
11	M	26	24 mon			Y	Y	Y																			Y											Y								
12	M	26	6 mon	Y	Y	Y																							Y							Y	Y									
13	M	26	6 mon			Y	Y	Y	Y	Y	Y																					Y				Y	Y									
14	M	27	18 mon	Y	Y	Y			Y	Y	Y																Y											Y								
15	M	27	10 mon	Y	Y	Y			Y		Y															Y						Y				Y	Y		Y							
16	M	27	24 mon			Y	Y	Y																																						
17	M	28	10 mon	Y	Y	Y			Y	Y	Y	Y																								Y	Y									
18	M	28	12 mon	Y		Y	Y		Y		Y		Y																										Y								
19	M	28	14 mon	Y	Y	Y			Y			Y	Y	Y	Y	Y																						Y								
20	M	29	8 mon	Y	Y	Y			Y		Y													Y												Y										
21	M	29	11 mon	Y	Y	Y			Y		Y		Y	Y			Y																													
22	M	29	12 mon	Y	Y	Y			Y		Y		Y				Y	Y		Y																				Y						
23	M	30	12 mon			Y	Y	Y					Y	Y					Y																											
24	M	30	15 mon	Y	Y	Y							Y		Y																									Y			Y				
25	M	30	18 mon	Y	Y	Y																								Y								Y								
26	F	21	6 mon	Y	Y	Y																						Y								Y									
27	F	23	6 mon	Y	Y	Y																						Y								Y									
28	F	23	10 mon			Y	Y	Y	Y		Y																									Y									
29	F	24	2 mon			Y	Y	Y																Y												Y	Y								
30	F	25	11 mon	Y	Y	Y			Y		Y																																			
31	F	26	10 mon	Y	Y	Y			Y		Y																									Y									
32	F	27	24 mon			Y	Y	Y																			Y																Y				
33	F	27	18 mon	Y	Y	Y																												Y						Y					
34	F	29	6 mon			Y	Y	Y																									Y				Y	Y								

S.No	Sex	Age	PTI	Immuno suppressive Drugs					Pityriasis versicolor				Dermatophytosis							Tinea unguium			Candi-diasis			Phaeohypomycosis	Viral infection					Bacterial Infection				Drug induced Changes						Miscellaneous					
				C	A	P	M	T	A	C	US	UUS	TCR	TC	TF	TB	TM	TG	TP	DLSO	PSWO	TDO	OC	I	B		VV	HS	CP	VZ	MC	I	F	C	ERS	CF	AE	ST	HY	HI	GH	KP	LP	FDE	EI	SC
35	F	29	10 mon	Y		Y	Y		Y		Y																									Y				Y						
36	M	31	12 mon	Y	Y	Y			Y		Y		Y	Y				Y																			Y	Y								
37	M	31	4 mon	Y	Y	Y																										Y			Y	Y									
38	M	32	6 mon	Y	Y	Y																										Y			Y										
39	M	32	6 mon	Y	Y	Y																										Y			Y										
40	M	32	4 mon			Y	Y	Y																Y		Y										Y										
41	M	34	8 mon	Y		Y	Y		Y	Y	Y																					Y				Y										
42	M	34	12 mon	Y	Y	Y			Y			Y	Y																									Y			Y						
43	M	34	8 mon	Y	Y	Y				Y	Y																	Y								Y	Y								
44	M	34	12 mon	Y	Y	Y																								Y								Y								
45	M	36	15 mon	Y	Y	Y			Y			Y		Y				Y																							Y					
46	M	36	18 mon	Y		Y	Y						Y	Y	Y				Y																					Y						
47	M	36	12 mon	Y		Y	Y						Y	Y	Y				Y																												
48	M	36	18 mon	Y	Y	Y							Y	Y		Y		Y		Y																				Y						
49	M	36	16 mon	Y	Y	Y							Y	Y			Y	Y		Y																										
50	M	37	16 mon	Y	Y	Y							Y	Y			Y	Y		Y																				Y			Y				
51	M	37	14 mon	Y	Y	Y							Y	Y			Y	Y																												
52	M	37	15 mon			Y	Y	Y					Y	Y																																
53	M	37	12 mon			Y	Y	Y					Y																								Y									
54	M	37	32 mon			Y	Y	Y																			Y																		
55	M	37	18 mon	Y	Y	Y																													Y			Y						
56	M	37	24 mon		Y	Y																													Y									
57	M	38	3 mon	Y	Y	Y																												Y		Y	Y								
58	M	38	6 mon	Y	Y	Y																								Y						Y	Y								
59	M	38	10 mon	Y	Y	Y																			Y					Y						Y									
60	M	40	30 mon		Y	Y												Y									Y																		
61	M	40	32 mon			Y	Y											Y									Y																		
62	F	32	12 mon	Y	Y	Y			Y		Y																											Y						Y		
63	F	32	10 mon	Y	Y	Y			Y		Y																									Y									
64	F	34	4 mon			Y	Y	Y																Y												Y									
65	F	34	6 mon			Y	Y	Y																Y												Y									
66	M	41	15 mon	Y	Y	Y			Y		Y		Y	Y	Y		Y	Y														Y						Y								
67	M	43	12 mon	Y	Y	Y			Y		Y		Y	Y			Y	Y															Y					Y								
68	M	43	10 mon	Y	Y	Y				Y	Y																						Y	Y											Y

S.No	Sex	Age	PTI	Immuno suppressive Drugs					Pityriasis versicolor				Dermatophytosis							Tinea unguium			Candi-diasis			Phaeohypomycosis	Viral infection					Bacterial Infection				Drug induced Changes						Miscellaneous					
				C	A	P	M	T	A	C	US	UUS	TCR	TC	TF	TB	TM	TG	TP	DLSO	PSWO	TDO	OC	I	B		VV	HS	CP	VZ	MC	I	F	C	ERS	CF	AE	ST	HY	HI	GH	KP	LP	FDE	EI	SC
69	M	44	6 mon	Y	Y	Y			Y			Y																								Y	Y									
70	M	46	6 mon	Y	Y	Y			Y		Y																									Y	Y									
71	M	46	12 mon	Y	Y	Y							Y	Y					Y								Y																			
72	M	48	12 mon	Y	Y	Y																								Y																
73	M	49	15 mon	Y		Y	Y																							Y									Y							
74	M	49	18 mon	Y	Y	Y																								Y																
75	M	50	24 mon			Y	Y																							Y																
76	F	42	12 mon	Y	Y	Y																								Y																
77	M	51	84 mon		Y	Y																				Y																			
78	M	52	48 mon		Y	Y																				Y																			
79	M	52	36 mon			Y	Y																				Y																			
80	M	55	30 mon	Y	Y	Y																					Y																			

KEY TO MASTER CHART

C.NO. - **Case Number**

PTI - **Post Transplant Interval**

IMMUNOSUPPRESSIVE DRUGS

A - **Azathioprine**

P - **Prednisolone**

C - **Cyclosporine**

T - **Tacrolimus**

M - **Mycophenolate mofetil**

DERMATOPHYTOSIS

TC - **Tinea capitis**

TF - **Tinea faciei**

TB - **Tinea barbae**

TC - **Tinea corporis**

TCR - **Tinea cruris**

TG - **Tinea glutealis**

TM - **Tinea manuum**

TP - **Tinea pedis**

TINEA UNGUIUM

DLSO - **Distal and lateral subungual onychomycosis**

PSWO - **Proximal subungual white onychomycosis**

TDO - **Total dystrophy onychomycosis**

CANDIDIASIS

OC	**-**	**Oral Candidiasis**
I	**-**	**Intertrigo**
B	**-**	**Balanophosthitis**

PITYRIASIS VERSICOLOR

C	**-**	**Chromic**
AC	**-**	**Achromic**
US	**-**	**Usual site**
UUS	**-**	**Unusual site**

VIRAL INFECTION

VV	**-**	**Verruca vulgaris**
VZ	**-**	**Varicella zoster**
HS	**-**	**Herpes simplex**
MC	**-**	**Molluscum contagiosum**
CP	**-**	**Chicken pox**

BACTERIAL INFECTION

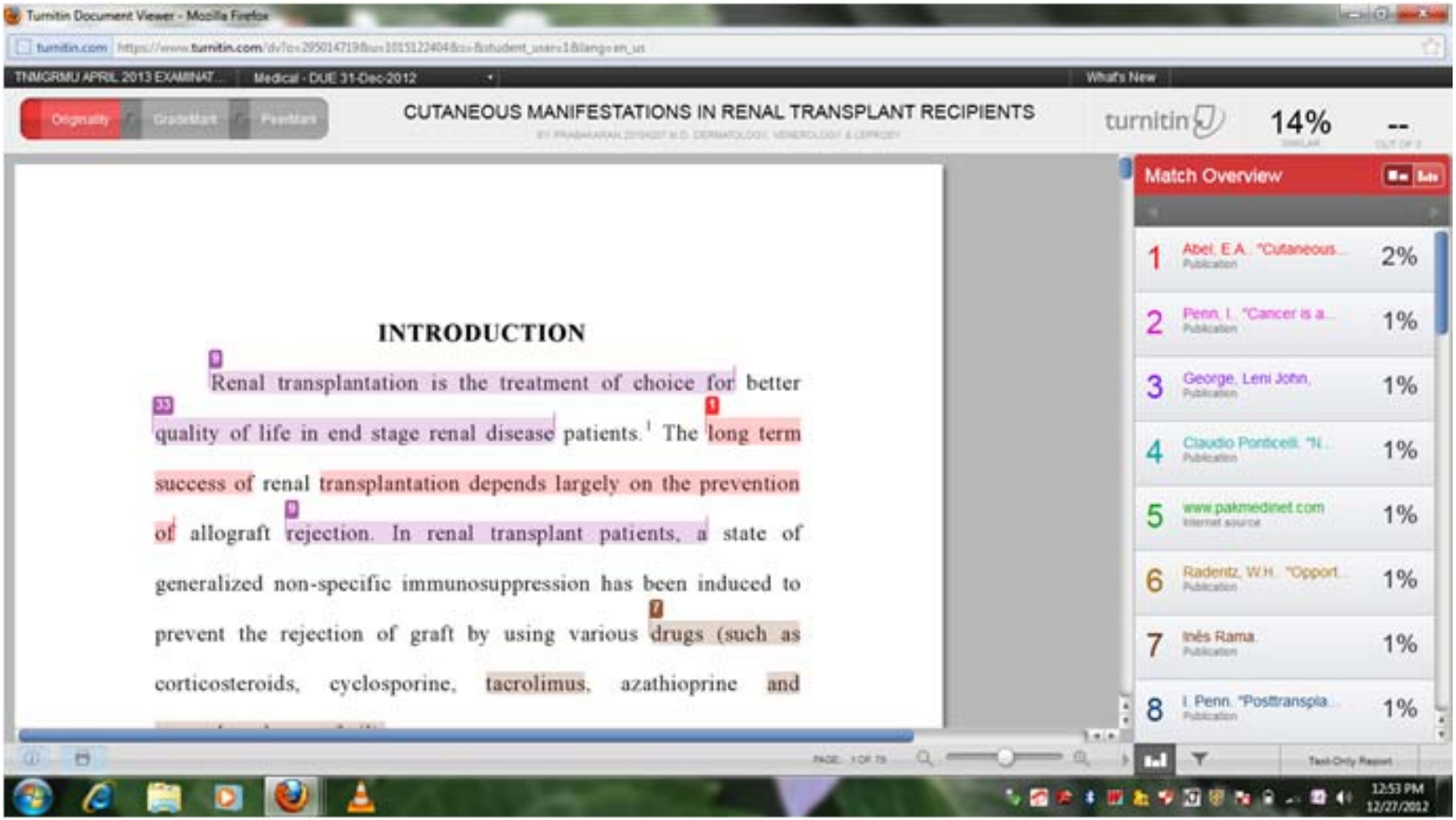
I	**-**	**Impetigo**
F	**-**	**Furuncle**
C	**-**	**Cellulitis**
ERS	**-**	**Erythrasma**

DRUG INDUCED CHANGES

CF	**-**	**Cushingoid facies**
AE	**-**	**Acneiform eruptions**
ST	**-**	**Striae**
HY	**-**	**Hypertrichosis**
HI	**-**	**Hirsutism**
GH	**-**	**Gum hypersplasia**

MISCELLANEOUS

KP	**-**	**Keratosis pilaris**
LP	**-**	**Lichen planus**
FDE	**-**	**Fixed drug eruption**
EI	**-**	**Exaggerated insect bite allergy**
SC	**-**	**Scabies**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INTRODUCTION
Renal transplantation is the treatment of choice for better quality of life in end stage renal disease patients.[1] The long term success of renal transplantation depends largely on the prevention of allograft rejection. In renal transplant patients, a state of generalized non-specific immunosuppression has been induced to prevent the rejection of graft by using various drugs (such as corticosteroids, cyclosporine, tacrolimus, azathioprine and
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INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI -3

Telephone No : 044 25305301
Fax : 044 25363970

CERTIFICATE OF APPROVAL

To
Dr. M. Prabakaran
PG in MDDVL
Madras Medical College, Chennai -3

Dear Dr. M. Prabakaran

The Institutional Ethics committee of Madras Medical College, reviewed and discussed your application for approval of the proposal entitled " Cutaneous manifestations in renal transplant recipients " No. 29012012.

The following members of Ethics Committee were present in the meeting held on 27.01.2012 conducted at Madras Medical College, Chennai -3.

1.	Prof. S.K. Rajan. MD	-- Chairperson
2	Prof. Pregna B. Dolia MD Vice Principal, Madras Medical College, Chennai -3 (Director , Institute of Biochemistry, MMC, Ch-3)	-- Member Secretary
3.	Prof. B. Kalaiselvi. MD Prof of Pharmacology ,MMC, Ch-3	-- Member
4.	Prof. Shruti Kamal MS Prof of Surgery, Madras Medical College , Ch-3	-- Member
5.	Thiru. S. Govindsamy. BA BL	-- Lawyer

We approve the proposal to be conducted in its presented form.

Sd/ Chairman & Other Members

The Institutional Ethics Committee expects to be informed about the progress of the study, and SAE occurring in the course of the study, any changes in the protocol and patients information / informed consent and asks to be provided a copy of the final report.

Member Secretary, Ethics Committee