A CLINICOMYCOLOGICAL STUDY OF MUCOCUTANEOUS CANDIDIASIS

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CERTIFICATE

Certified that this dissertation entitled **"A Clinicomycological study of mucocutaneous candidiasis"** is a bonafide work done by **Dr**. **M.Subhashini** Post Graduate Student in **M.D. Dermatology, Venereology and Leprology**, Madras Medical College, Chennai-600 003, during the academic year 2009-2012.This work has not previously formed the basis for the award of any degree.

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INTRODUCTION

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Candidiasis refers to a diverse group of infections caused by the yeasts of genus *Candida* which have been known for centuries. These organisms usually cause superficial infections involving the skin, nail, mucous membrane but can also produce serious systemic infections like septicemia, endocarditis and meningitis in immunosuppressed individuals.[1]

Candida species constitute a part of the normal flora of the digestive system and the female genital tract. Colonization with these organisms may occur during birth or later in life[1,2] . In healthy individuals, such colonization is asymptomatic and their overgrowth is limited by the immune system and other bacteria occupying the gastrointestinal tract and vagina .When the immune system is deranged or an alteration in the ecology occurs, there is overgrowth of these organisms producing infection.[1,2]

There are over 200 species of Candida till date and their epidemiology is constantly changing with varying clinical patterns, virulence and antifungal susceptibility.[2]

REVIEW OF LITERATURE

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HISTORY

The history of discovery and naming of Candida dates from the ancient Greeks to modern day researchers.

Around 400 BC, Hippocrates in "Of the Epidemics " described oral candidiasis, the first form of the disease as "the mouth affected with aphthous ulceration " [3,4].The first description of thrush in modern medicine were made by Rosen Von Rosenstein and Underwood in 1771.The word "thrush" derived from ancient Scandinavian or Anglo-Saxon words was used to denote candidiasis .The French used the term "*le Muguet"* which means *'lilly-of-the-valley'* to describe this condition.In 1835,Veron first described the case of oesophageal candidiasis and postulated that newborns acquire it during passage through the vagina. In 1839, initial discovery was made when Langenbeck observed a fungus in scraping of oral thrush from a patient with typhus [5,6]. The correct association of oral thrush and its mycotic pathogen was made in 1842 by Gruby who classified the microorganism as Sporotrichum species.[1]

In the subsequent years, various pathological conditions were shown to be associated with Candida. In 1842, Bennett isolated the fungus from the sputum of tuberculous patient. Following his work, Wilkinson (1849) isolated it from vaginal candidiasis while Robin (1853) isolated it from a patient with systemic infection.

The dimorphic nature of the fungus, the budding yeast form, the mycelial form and chlamydospores was noticed by Grawitz in 1877.[2] In 1886, the genus “Monilia” included certain filamentous fungi isolated from rotting fruits and leaves as defined by Saccardo. In 1890, Schmorl reported a case of disseminated candidiasis involving many organs. In the same year, Zopf named the fungus Monilia albicans from which moniliasis, the early name of Candidiasis originated. *Torulopsis glabrata* was first isolated from grapes in 1894 by Berlese and was described in humans by Anderson in 1917.[1]

In 1912, Aldo Castellani was the first to suggest the possibility of Candida species other than *Candida albicans* while describing “tea taster’s cough”. In 1923, Berkhont established the Genus Candida to accommodate “monilia” and defined it to include anascosporogenous yeast species that develop pseudohyphae. This was later accepted as the official name of the genus by the Eighth Botanical Congress held in Paris in the year 1954.[5] In 1959, the species *Candida viswanathii* was designated in honour of Dr.Viswanathan, the first director of the Vallabhbhai patel chest institute(VPCI), Delhi. In 1995, *Candida dublinensis* was described as new species by Sullivan and colleagues from Dublin, Ireland. These events in conjunction with the biological techniques, has helped in extensive research into the newer species, pathogenetic mechanisms, new concepts in diagnosis and treatment with increasing demands for newer antifungal agents with fewer side effects. In the last decade, there had been major changes in the epidemiology, clinical spectrum and fungal susceptibility.[1,2]

FUNGAL CHARECTERISTICS OF THE ORGANISM

Candida belong to the class of blastomyces under the order Cryptococcales .There are over 200 species identified of which Candida albicans has been considered as the pathogenic organism. Other non Candida species of pathogenic significance include *Candida tropicalis, Candida glabrata (previously Torulopsis glabrata), Candida kefyr (previously pseudotropicalis), Candida dublinensis, Candida krusei,Candida parapsilosis, Candida guillermondii, Candida viswanathii, Candida lusitaniae and Candida zeylanoides. Candida albicans* is an oval yeast measuring 2-6 micron x 3-9 micron in size which exhibits polymorphism producing various morphological forms such as budding yeast cells, pseudohyphae and true hyphae.[1]

GROWTH CHARACTERISTICS

Candida grows easily in Sabouraud's dextrose agar at 37^0 C at room temperature within 24-48 hrs. The morphology of the colonies and their growth in various medias like Sabouraud's dextrose agar, corn meal agar and chorme agar may vary according to the species.[1,2]

Candida albicans:

On Sabouraud's dextrose agar, the colonies are cream colored and smooth. In corn meal agar, the colonies are large with thick walled chlamydospores.[1]

Candida tropicalis:

On Sabouraud's dextrose agar, the colonies are cream colored, smooth, wrinkled with mycelial fringe. In corn meal agar, it produces blastoconidia singly or in very small groups all along the long pseudohyphae.[1]

Candida krusei:

On Sabouraud's dextrose agar, the colonies are dull, dry and wrinkled. In cornmeal agar, pseudohyphae with blastoconidia forming crossed match stick appearance are seen. Positive Urease test is specific for the species and is indicated by a purple pink or red color in Christensen's urease medium.[1]

Candida parapsilosis

On Sabouraud's dextrose agar, the colonies are cream colored, shiny and smooth. In corn meal agar, short pencil like pseudohyphae with blastocondia arranged singly along the pseudohyphae are seen[1]

Candida glabrata

The colonies on Sabouraud's dextrose agar are cream colored, smooth, soft and they produce no pseudohyphae.[1]

Candida dublinensis

Rough colonies with abundant chlamydospores are produced in Saboraud's dextrose agar. They are unable to grow at 45^0 c and in 6.5% sodium

chloride, unlike *C.albicans*. Sunflower seed husk agar can be used for the differentiation of *C.dublinensis* from *C.albicans*.[7,8,9].

EPIDEMIOLOGY OF CANDIDA SPECIES

The yeast of genus Candida have been the fourth most common primary pathogen in blood stream and seventh most common pathogen in nosocomial infection.[2] Candida infection constitutes 15% of hospital acquired illnesses, 72% of nosocomial infection and 8-15% of all nosocomial candidemia in critical care.[18,19,20]

Candidiasis can affect all age groups with differing data from various parts of the world. Neonatal superficial and systemic candidiasis have become increasingly prevalent in ICU units.[21,22] Postnatal acquisition has been attributed to increased number of invasive procedures and widespread use of broad spectrum antibiotics . Candidal infection in the elderly are attributed to poor self care, decreased salivary flow rate associated with ageing and intake of high dose of cytotoxic drugs for malignant diseases. Although superficial infections are thought to be benign, significant morbidity can occur.[21,22]

The highest proportion of *C. albicans* was found in North and Central Europe and the USA. Non-albicans species were more common in South America, Asia, and South Europe.[1,2,21] *C. glabrata* was commonly isolated in the USA and North and Central Europe; *C. parapsilosis* in South America, South Europe, and several parts of Asia; and *C. tropicalis* in South America and Asia. The relative frequency of *C. krusei* was low in all regions.[1]Most of

the *Candida spp* are isolated from the animal and other environmental sources . *Candida albicans* is considered as the major pathogen but the incidence of *non albicans* species is increasing since the last decade with the advent of newer immunosuppressives and HIV pandemic.[1,2,21]

With the exception of *Candida albicans*, which is the only endogenous yeast, all others are exogenous in origin with the sources including soil, air, water, plants, dairy products and fermenting plant products.[1,2]

In humans, *Candida spp* inhabits the gastrointestinal tract and vulvovaginal area. Colonization begins during birth directly from the birth canal sometimes during infancy or during later life. *Candida albicans* is implicated in both superficial and deep infections. *Candida parapsilosis* is found in skin, C.*kefyr* and C.*tropicalis* in the respiratory tract.[1,2]

There has been a change in the trend worldwide. There are increasing reports of *Candida tropicalis* in Indian studies in bloodstream infections. It is also the major cause of septicemia and disseminated candidiasis especially in lymphoma, leukemia and diabetes. [1,2,23]*Candida krusei* is regularly associated with some form of infant diarrhea and occasionally associated with systemic disease. It has also been reported to colonize the gastrointestinal tract, respiratory and urinary tracts of patients with granulocytopenia. Environmental isolation have been made from, skin and feces of animals and milk products.[1,2]

Candida parapsilosis is an opportunistic human pathogen which may cause both superficial cutaneous infections especially of nails and systemic disease especially endocarditis and also endopthalmitis. It specifically produces

onychomycosis which is capable of adhering and growing as biofilm on human nail surfaces. Nails also act as the reservoir of this infection.[23]. It is also a contaminant of high concentration glucose solution and prosthetic material.[1]

Candida glabrata is one of the isolates from oral cavity, denture stomatitis and vaginitis which has intrinsic resistance to fluconazole.[1]*Candida kefyr* is less common which has been isolated from vaginal, urinary, ear and gastrointestinal infections. *Candida viswanathii* has been isolated from India in clinical specimens and from the environmental sources in South Africa.[1]*Candida krusei* and *C.glabrata* fungemia is associated with previous exposure to azoles[24]

Few reports show positive correlation of candidial infection with certain blood group. Infection are increased in patients with non A group especially O blood group patients. The commonest yeast isolated is *Candida albicans* from all blood groups patients. *Candida krusei* has been found to colonise only in AB group patients. Blood group A patients show isolates of *Candida albicans* and *Candida tropicalis*. The exact mechanism for the susceptibility is not known. It is postulated that a blood group substance may play a significant role in host response to fungal infections by virtue of their cross reactivity with surface antigens on these fungal cells.[25]

PATHOGENESIS

Most infections of *Candida albicans* are endogenous and generally follows a shift in host- mycelial relationship. This shift from commensal to parasite results from a variety of influences which are as follows.

Microbial factors

a)Adherence: The ability of the yeast forms to adhere to the underlying epithelium is important for tissue invasion. It is dependent on many factors like presence of other microorganisms that may compete for cellular binding sites, nutrients like glucose, hormones like estrogen and presence of IgA . Cell surface hydrophobicity is important for adherence. Germ tube formation increases the cell surface hydrophobicity. Initial adherence is dependent on unidentified receptors, adhesins related to fibronectin , mannoprotein and other proteins.*Candida albicans* has the maximum adherence capacity followed by *Candida tropicalis and Candida parapsilosis*.[2,10]

b) Enzymes : There are about fourteen hydrolytic enzymes of which few are important for pathogenesis like, proteases, lipases, esterases, phosphatases and phospholipases. Secretion of serine aspartyl proteinases and serine proteinases facilitates the hyphal invasion especially in disseminated candidiasis.[2]

c)Invasion: Germ tube formation potentiates invasion by production of various enzymes. Proteinases are known to break down peptide bonds, of which aspartate proteinases are collagenolytic. Phospholipases enhance

invasion, of which carboxyl phospholipases are proteolytic to keratinocytes. These cause cell damage, swelling, erythema, desquamation, exfoliation and development of an acute inflammatory reaction. Secreted aspartate transaminases break down immunoglobulins and are important for skin and mucous membrane infection. Increased virulence of *C.tropicalis* isolates was observed when given orally to compromised mice, which parallels clinical observations in immunocompromised patients. Some studies have shown that *C. tropicalis* is even more invasive than *C.albicans* in the human intestine, particularly in oncology patients. Secreted aspartyl proteinase 5 and 9 (SAP5 and SAP9) activity occurs in all Candida species, in the following order: *C.albicans>C.tropicalis>Candida kefyr>Candida krusei.*[10]

The aspartic proteinases secreted by *C.tropicalis* have also been demonstrated on the surface of the fungal cell walls before invading macrophages and tissues during disseminated infections. Some *nonalbicans* species that were previously thought to be SAP negative were infact proteolytic. The purified tropiase from *C. tropicalis* (a novel acid proteinase) demonstrated the ability to increase capillary permeability and haemorrhagic activity. *C.albicans* and *C.tropicalis* produced marked levels of prostaglandins, while *C.glabrata* produced a very low level. Clinical and experimental observations suggest that morbidity and mortality rates are higher due to *C. tropicalis* infection than due to *C. albicans* infection. These findings support the hypothesis that there must be some additional *C.tropicalis* secretory products that are probably more pronounced in a T-cell-deficient host. Such

secretory products from *C.tropicalis* could be intensely cytotoxic or there could be synergistic interactions with the host cells that culminate in the deaths of immunocompromised patients. Recent studies on three specific key virulence factors such as proteinase, phospholipase and biofilm formation suggest that the detection of hydrolytic enzymes and the ability of Candida yeasts to form biofilm may be useful indicators of possible haematogenous infection. Such findings may support clinicians in the management of patients who have a high risk of haematogenous Candida infections.

d) Candida Antigens: The antigenic structure of Candida are primarily for the identification of Candida species. They are broadly classified into cell wall antigens and cytoplasmic antigens. The cell wall of candida is composed of glucan polymers which are in abundance and mannans. Mannoproteins are the major antigenic determinants. The cell wall is not antigenically consistent as they are bound to change according to the growth characteristics.. The alpha-D-mannan of the cell wall of *Candida spp* is an important constituent of its structure as it acts as a major antigen. The mannan usually has a (1 -6)-linked main backbone with side chains containing (1-2) or (1-3) linkages.[2]Certain antigens are also known to be derived from the cytoplasmic components.

e)Phenotypic switching: The ability of the organism to switch to different morphological forms such as unicellular budding yeast to filamentous pseudohyphae and true hyphae assists the fungus in evading the host defence and also contributes to the virulence of the organism. This is analogous to phase variation in bacteria.

f)Others: The glycoprotein extracts of Candida cell wall are analogous to bacterial endotoxins which are lethal and can cause anaphylactic shock . The ability to bind complement receptors may also contribute for the virulence. A wide variety of other factors like temperature above 35^0C, low oxygen tension, liquid media, non sulphur containing aminoacids, a polysaccharide carbon source, serum and a pH of 7.5 may also contribute for the pathogenesis.[10,,11,12]

HOST FACTORS[13]

a)Endogenous factors : Age plays an important role in newborn particularly premature and also in the elderly. Low birthweight infants are highly susceptible to systemic candidiasis. Severe cachexia and debilitating diseases like diabetes mellitus and malignancy are prone for candidiasis. Endocrine disorders like hypoparathyroidism, adrenal insufficiency and Cushing's disease favour candida infection. Immunodeficiency states like Acquired immunodeficiency states, Severe combined immunodeficiency disorder, Myeloperoxidase deficiency, Chediack Highasi syndrome, Hyperimmuno globulinemia E syndrome, Chronic granulomatous diseases, DiGeorge syndrome and Nezelof syndrome may increase the incidence of superficial and systemic candidiasis[12,13]

b)Exogenous factors : The various predisposing factors for candida infection are trauma, local occlusion, moisture, dentures and obesity. Nutritional deficiencies like Avitaminosis, iron deficiency and generalized malnutrition,

iatrogenic factors like indwelling catheters, exposure to X-ray irradiation, administration of glucocorticoids, immunosupressives, antibiotics, oral contraceptives, colchicine, and phenylbutazone are also considered as important factors that make the patient susceptible to the infection[13]

Immunology of candidal infection:

Most of the clinical manifestations are due to the deficiency or dysfunction of the innate and the adaptive immune systems. Both innate and humoral immune system work cooperatively to provide an effective defence against the invading yeasts.[13]

Innate immune system

The normal innate immune system against Candida include intact skin and mucosa and nonspecific humoral factors. The first line of defence that protects against the mucocutaneous form of the disease is the unbreached skin. The risk factors that increase the susceptibility of the disease by compromising the skin integrity includes maceration, trauma to the skin and mucosa and excess of carbohydrates on the surfaces. Additional nonspecific features include iron binding proteins transferrin and lactoferrin[13,14].

The second line of defence after penetration of the fungus include the phagocytic cells and the candidicidal activity of the polymorphonuclear cells. These processes include myeloperoxidase and superoxide or cationic proteins.[12,13,14]

Cell mediated immunity(CMI):

This plays an important role in host defence against Candida infections.Patients with defective cell mediated immunity develop only mucocutaneous disease whereas dysfunction of neutrophils leads to systemic involvement.[14,,15]

Candida infection of epithelial cells (EC) results in a series of events like increase in matrix metalloproteinases, which plays a role in remodeling of the epithelium, modulation of barrier function, upregulation of antimicrobial peptides, beta defensins and IL-37 which have anticandidicidal activity, playing a significant role in combating infection and invasion.[15] Phagocytic cells engulf the yeast and destroy it by respiratory burst and cytokine release. The antigen presenting cells process the candida antigens and migrate to the lymph nodes to present them to the naïve T cells in the lymph nodes which are then activated and differentiate into Th1 and Th17 effector cells. On reaching the effector site, Th1 cells release cytokines that orchestrate containment of infection to the mucosal surfaces and prevent dissemination.Th17 effector cells release IL 17 and IL 23 which have a complementary role in induction of T cell responses to infection. IL 23 is essential for the polarization of Th17 cells and IL 17 is required for the production of inferon gamma which is essential for Th1 response.[14,15,16]

Neutrophils are the predominant cell type which prevents deep seated infections[1]

HUMORAL IMMUNITY

Although patients with immunoglobulin deficiency are not particularly suscepitible humoral immunity does play a role in protection against candidal infection. The high levels of IgA found in infected subjects doesnot prevent colonization . Hence, there is no role for the use of immunoglobuins as a treatment modality.[16]

IgG and IgM are increased in deep seated infections except in immunosuppressed individuals who are unable to mount an immune response. Anti IgE antibodies are found in patients with allergy. Skin inoculation of the antigen results in flare like erythema at the site of inoculation immediately after the test.[15,16]

Recent studies have shown strong evidence of a persistent immunity resulting from a primary infection mediated by antibodies of definite specificity. The nonsecretors of lewis blood group are particularly susceptible to Candida infection.[16]

CLINICAL SPECTRUM OF CANDIDIASIS

The clinical spectrum of candidiasis is extremely varied, ranging from acute, subacute, chronic and episodic.[2] Involvement may be localized to skin and mucosa or it may be systemic as in septicemia, endocarditis and meningitis. The pathologic response evoked is diverse and vary from irritation and inflammation to chronic and acute granulomatous response.[2,16]

Oral candidiasis

Oral candidiasis is the most common type of candida infection in clinical practice.The development of infection depends on the epithelial barrier function, salivary flow rate, dentures, poor oral hygiene, antimicrobial constituents of saliva, presence of normal microbial flora and local immunity. Patients with decreased salivary flow rates as in conditions like Sjogren's syndrome and prolonged antimicrobial therapy that alters the microbial flora makes the patient vulnerable. Saliva is rich in Antimicrobial peptides, defensins and histatins which are protective. Defects in dectins 1&2, the NOD like receptor, pyrin domain containing 3 inflammosome and caspase recruitment domain family member 9 cause defective activation of Th17 cells and IL 23 increasing the likelihood of oropharyngeal candidiasis.[1]The various clinical patterns are as follows:

- **Acute pseudomembranous candidiasis** otherwise called as oral thrush is characterized by sharply defined patch of creamy, crumbly, curd like white pseudomembrane which when removed leaves an erythematous base.[26]

- **Acute erythematous candidiasis** is also as called acute atrophic oral candidiasis or antibiotic sore throat characterized by marked soreness and denuded atrophic erythematous mucous membrane, particularly on the dorsum of tongue. It is especially commonin patients on prolonged antibiotic therapy.[26]

- **Chronic pseudomembranous candidiasis** is similar to acute pseudomembranous type but it is persistent principally occuring in immunocompromised persons.[26]

- **Chronic erythematous candidiasis** which is also called as denture sore mouth occurs in persons with orthodontic appliances and is confined to the upper denture bearing areas, the palate and gums characterized by shiny atrophic epithelium with marked erythema.[26]

- **Chronic plaque candidiasis** is also called as hyperplastic candidiasis and is characterized by persistent, firm, irregular white plaques in the mouth on the cheek or the tongue which is not easily removed . Most of the patients are men over the age of 30 years. No predisposing factors are found. This condition has to be differentiated from oral leukoplakia which is a premalignant condition. Although the affected areas may undergo malignant change, it may eventually clear with appropriate anticandida therapy.[26]

- **Chronic nodular candidiasis** is a rare form which presents with cobbled appearance of the tongue, most often found in association with chronic mucocutaneous candidiasis.[26,27]

- **Angular cheilitis (Angular stomatitis; Perleche)** is characterized by soreness of the angle of the mouth extending outwards in the folds of the facial skin which is due to mechanical factors like

increased depth of the fold, malocclusion, malnutrition, due to persistent lip licking and increased salivation[26,28]

- **Median rhomboid glossitis** is a variant of chronic plaque like candidiasis with diamond shaped area on the dorsum of tongue with loss of papilla. This has been noted in denture wearers. Candida grows well in the midline of the tongue and this area of the tongue comes in contact with the palate during swallowing and at rest. "Kissing lesion" on the palate is also noted. Patients with this infection should be investigated for AIDS. It is also proposed that impaired blood supply on the dorsum of the tongue might cause median rhomboid glossitis and loss of filiform papillae.[29,30]

CANDIDIASIS OF GENITAL MUCOUS MEMBRANE

Vulvovaginal candidiasis (Vulvovaginal thrush)

Vulvovaginal candidiasis is the most common cause of vaginal infection in the tropics and second only to bacterial vaginosis in developing nations. About 75% of the women will have atleast one episode in lifetime while 40-50% have recurrences.[31] In 20% of women, colonization of Candida is asymptomatic and 4% suffer recurrences. It is 20 times more common than balanoposthitis.[32,33]

The general predisposing factors include maceration of the skin which is associated with the use of tight, vinyl cycling pants and non cotton, tight clothing in the tropics the incidence increases with the usage of vaginal

sponges and IUCDs.[34] The short term risk factors include use of broad spectrum antibiotics.[35]Hormonal factors like hormone replacement therapy and high dose estrogen therapy may predispose to VVC. Oestrogen is associated with cyclical candidiasis. Progesterone contraceptives and lactation may be protective. In post menopausal women there may be underlying factors like uncontrolled diabetes, immunosuppression from HIV, broad spectrum antibiotic therapy, douching or the use of perfumed, feminine hygiene products. [36,37]

The clinical spectrum of disease can be classified as uncomplicated or infrequent VVC and complicated VVC. Uncomplicated and sporadic disease usually occurs in nonimmunocompromised individuals with no predisposing factors including pregnancy. These patients have only mild to moderate symptoms and is usually caused by Candida albicans. Complicated VVC include recurrent severe VVC with uncontrolled diabetes, debilitation, pregnancy and immunosuppression and is caused by noncandida albicans species.[38]

The patients present with redness, swelling, pruritus with edematous vulva and adherent white discharge at the introitus and vestibular region. There may be satellite pustules around the labia and redness and involvement of the perianal area. Women with post thrush vestibulitis have tender areas around the hymenal ring particularly between 3 and 9 o clock position. There may be involvement of the periurethral area and infection of the urinary tract.[36,37,38]

Few patients have recurrent vulvovaginal candidiasis (RVVC) with 4 or more episodes of symptomatic disease per year (atleast one episode confirmed by culture). The predisposing factors are antibiotics, pregnancy, hormone replacement therapy, oestrogens, diabetes mellitus and tight clothing in tropics.[38,39] Some studies show association of atopy with RVVC with a high incidence of family history of allergies in these patients. There was also association with skin test positivity to inhalant allergens and to Candida albicans.[40,41]

Candida balanoposthitis

This is the most common cause of balanitis. There is no significant difference in the carriage rates between circumcised and uncircumcised men. Only a few develop symptoms like burning and itching in the penis with small pustules or papules in the penis which break to leave behind superficial erosions with collarette of scales and curdy accumulation under the prepuce. In circumcised men there may be glazed appearance of the glans with a scaly edge. Candida balanitis is most frequently confused with irritant balanitis, circinate balanitis, contact dermatitis and plasma cell balanitis.[42,44,]

Candidal Intertrigo (flexural candidiasis)

Inflammation of two opposing skin surfaces is termed intertrigo. Intertriginous lesions can occur in the groin, webspaces of fingers and toes and also in submammary region. The classical features are erythema which spreads beyond the contact area with fringed irregular edge and subcorneal pustules

rupturing to give tiny erosions and satellite pustules. Other predisposing factors are obesity, hot humid climate and prolonged use of occlusive foot wear. Erosio interdigitalis blastomycetica is a form of candidiasis seen as an oval area of macerated skin on the web extending to the sides of fingers mostly involving the third web space between the middle and ring finger. Usually at the center of the lesion, there are one or more fissures with raw red bases. As the condition progresses the macerated skin peels off leaving a painful denuded area surrounded by a collar of overhanging white epidermis. In the feet, the clinical picture is similar but for the fact that white sodden epidermis which is thick does not peel off freely with the involvement of fourth web space.[44]

Perianal and scrotal candidiasis

This usually starts around the anal margin with nonspecific erythema, oozing and maceration with subsequent spread to the natal cleft. Satellite lesions may or may not be present .Candidial overgrowth is also enhanced on abnormal tissue such as extramammary paget's disease or psoriasis. If the tissue does not return to normal after being treated with anticandidal drugs a biopsy is warrented. Candidiasis should be excluded in unexplained erythema of scrotal skin. [45]

Napkin candidosis (Diaper candidosis)

Diaper dermatitis is the most common skin condition in infants and constitutes 20% of all dermatitis seen in that age group with no sexual predilection. The average age at onset is 9-12 months but can occur as early as

first month. Diaper dermatitis due to candidiasis is characterized by erythema of the folds with many small erythematous desquamating satellite or daughter lesions scattered along the edges of the macules. This condition has to be differentiated from seborrhoeic dermatitis, flexural psoriasis, acrodermatitis enteropathica and langerhan cell histiocytosis.[45]

Granuloma gluteale infantum

It is a rare clinical entity of unknown etiology and candidiasis is one of the contributing factors. It presents as multiple cherry red nodules in the diaper area.[46,47] The diagnosis should be considered in longstanding and unresponsive cases of diaper dermatitis. Histopathology shows nonspecific inflammatory infiltrates of neutrophils, plasma cells, histiocytes and eosinophils with an overlying epidermis with parakeratosis. There are no granulomas and hence the name is a misnomer. Granuloma gluteale adultorum is the name given to similar clinical picture seen in adults.[48,49]

CANDIDA NAIL DISEASE

The main manifestations of candidal nail infection are in the form of chronic paronychia and onychomycosis.

Candidal paronychia

Chronic paronychia due to Candida is seen mainly among individuals who immerse their hands frequently in water especially affecting the finger nails. The nail fold is red swollen with loss of cuticle and detachment of nail

from the nail plate with intact hyponychium. Thick white discharge can be expressed from the nail folds. Onchycolysis and dystrophy are also reported but massive destruction of nails is rare.[50,51] Recent studies have shown that psoriatic patients with Candida isolates from the nails have high NAPSI score.[52]

Candidal Onychomycosis

The primary cause for onychomycosis is dermatophytes while Candida species is isolated as a second line pathogen. The predisposing factors are ageing, HIV, Cushing's disease, Raynaud's phenomenon, trauma, moisture and chemicals .There are three main manifestations of candida nail infection such as distal and subungual onychomycosis, erosion of the nail plate and total dystrophy of the nails. Distal and lateral subungual onychomycosis is associated with paronychia. Erosion of the nail plate which indicates invasion of nail plate is a specific feature and is most often found in women. [53] Total dystrophy of nail is found in chronic mucocutaneous candidiasis.[54,55]

CANDIDIASIS IN SPECIAL POPULATIONS

Candida infects all age group from infancy to old age. However candida infection that need special mention are those that occur in neonates, pregnancy and HIV.

CANDIDA IN PEDIATRIC AGE GROUP

Congenital candidiasis

Congenital candidiasis is a rare entity and around 70 cases have been reported in the past forty years. This was first reported by Sonnenschein in 1960. It is considered to be an ascending infection through the mother's birth canal. The proposed risk factors are maternal age, parity, vaginal candidiasis in mother, prolonged rupture of membranes, amniocentesis, chorioamnionitis, foreign bodies like suture materials and IUCD in the uterus. It presents at or immediately after birth but can occur as late as 6 days of life characterized by erythematous macules, papules, vesicules and pustules initially over the face and chest. Oral thrush is absent. Amniotic fluid may be turbid. Few neonates show dissemination to the lungs with high mortality. In particular premature infants have widespread burn like dermatitis and increased chance of dissemination. The risk factors for systemic dissemination are birth weight <1500gm, extensive instrumentation during labour and broad spectrum antibiotics. The presence of burn like dermatitis, respiratory distress, altered liver enzymes, signs of sepsis and positive blood, urine or CSF culture strongly indicates systemic dissemination. KOH preparation of the scraping from skin specimens reveals budding yeasts and pseudohyphae.[56,57]

Neonatal candidiasis may present few days later usually acquired from vaginal infection of the mother. Amniotic fluid is clear. There is no systemic dissemination and the prognosis is good.[58].

Chronic mucocutaneous candidiasis

This is characterized by persistent candidal infection of the skin, nails and mucosa starting in infancy or early childhood and not responding to conventional treatment .[59]

The clinical features include persistent oral thrush, cutaneous candidiasis with chronic intertriginous lesions, gross hyperkeratosis and deep dermal nodules or small macules and nail changes like paronychia, nail plate thickening with total dystrophy. There may also be seborrheic dermatitis, alopecia areata and vitiligo. They are also predisposed to other infections like human papilloma virus and dermatophytosis.[60] There are different types as follows

- **Autosomal recessive CMC** usually starts in first decade with persistent oral and nail infection with no endocrine defects. They tend to improve with age.[61]

- **Autosomal dominant CMC :**These patients are severely affected than autosomal recessive type with other infections such as dermatophytosis .[61]

- **Idiopathic CMC** patients are severely affected with candida granuloma oesophageal involvement , bronchiectasis and pulmonary bullae. Candida granuloma refers to sheets of hyperkeratosis caused by candida infection on the skin and scalp. The massive

hyperkeratosis is due to defective neutrophils to destroy the organisms[61,62].

- **CMC associated with endocrinopathy:** Mutations in autoimmune regulator gene is found in the patients .Mutations in autoimmune regulator gene has been proposed. In APECED syndrome (autoimmune polyendocrinopathy, candidiasis and ectodermal defects) is attributed to defect in AIRE (autoimmune regulator) gene that is classically expressed in thymic cells, monocytes, macrophages and dendritic cells.[63] The condition is seen in early childhood and the Candida infection may preceed the endocrine abnormalities by 10 years**.** The main endocrine abnormalities reported are hypoparathyroidism, hypoadrenalism and rarely hypothyroidism. Other abnormalities include vitiligo, pernicious anemia and ovarian failure.

- **Late onset CMC** in adults may progress to develop thymoma and SLE in later life.[64]

Various immunological abnormalities like defective phagocytosis and defect in delayed hypersensitivity are reported. Candida endocrinopathy patients have shown raised levels of neutralizing antibodies to interferon alpha.[65]

Candidiasis in pregnancy

Several hormonal changes during pregnancy can predispose to candidiasis. Candida infection of the genital tract is also associated with the risk of chorioaminionitis, preterm labour and congenital candidiasis. The vaginal inflammatory status not only depends on the gestational age but also on the microbial flora . Infections like candidiasis may rise the proinflammatory cytokines and prostaglandin synthesis predisposing to preterm delivery. Therefore it is important to treat vaginal candidal infection promptly.[66]

CANDIDIASIS AND HIV

Candidiasis is the most common opportunistic infection among the HIV patients. Oral candidiasis accounts for the majority of the infections. Pseudomembranous and erythematous type are specifically supposed to be markers of immunosuppression as indicated by the CD4 count less than 200 cells/cu.mm.[67] Therefore these oral manifestations may be used as an alternative to CD4 counts with good sensitivity, better specificity and positive predictive value in field based settings in developing countries.[68] Amongst the different patterns pseudomembranous candidiasis has the highest specificity. The presence of oral candidiasis can be used as a parameter to initiate ART and as a guide for progression of disease**.** Patients with oral lesions with other features of AIDS have a poorer survival rate than those without. Colonization rates were higher in IV drug abusers **.** Despite some studies showing recurrent vulvovaginal candidiasis in HIV patients, the concept of persistent infection in these patients is less convincing.[69.70]

SYSTEMIC CANDIDIASIS

Systemic candidiasis is a fatal condition often occurring in hospitalized immunosuppressed patients. The predisposing factors are hematological malignancies, neutropenia, prolonged antibiotic therapy, central venous catheter, ablative radiotherapy, cytotoxic drugs and environmental contamination. The infection mostly arises from the patients own GI tract. The characteristic clinical features include fever, papular or nodular rash with an erythematous halo and a pale center. The other skin lesions rarely reported are ecthyma gangrenosum, nodular vasculitis like lesions, necrotic eschar, diffuse burn like dermatitis. The presence of triad of fever, papular rash and extreme myalgia is a clue for systemic candidiasis [71,72]. Other organs affected are kidneys, retina and heart valves. Candida microabscesses can occur in the spleen and lung often called hepatosplenic candidiasis occur due to candida microabscesses in the spleen and liver.[73]

Skin biopsy may show small aggregates of hyphae and spores in the dermis often located at the site of vascular damage. Focal dermal necrosis, hemorrhage and perivascular lymphocytic infilteration can be seen. Disseminated infection may show leukocytoclastic vasculitis.[74] Trans epidermal elimination of Candida spores has been reported.. As systemic candidiasis has high mortality , prompt diagnosis and treatment is mandatory.

Candida esophagitis

Candida species are the most common agents of fungal esophagitis. While this is usually caused by *C. albicans*, other species such as C. *tropicalis*, *C. krusei* and *C. stellatoidea* have also been involved. Risk factors for *Candida* esophagitis have been documented in several series.[77,78] These include pharmacological suppression of gastric acid production , use of antibiotics, previous vagotomy, functional or mechanical esophageal abnormalities, and endocrine diseases such as diabetes mellitus, hypothyroidism and hypoparathyroidism. Malnutrition, alcoholism, advanced age, and therapy with corticosteroids, either systemic or inhaled, have also been implicated.[79,80] The blood vessels below the esophageal membranes of the AIDS patients are eroded by *Candida albicans* and thus become so fragile that they bleed easily.[80]

OCULAR CANDIDIASIS

Candida species can affect both the outer and inner eye. Infection may originate from hematogenous dissemination or from direct fungal introduction, the former, generally resulting in inner eye infection and the latter in clinical manifestations of the outer parts of the eye. Both the categories of eye involvement is caused by *C.albicans* and some other Candida species, such as *C.parapsilosis, C.krusei* and *C.glabrata.*

Outer eye involvement include conjunctivitis, keratitis, blepharitis or lacrimal canaliculitis. Such infections are associated with trauma, surgery, injury and use of contact lenses, use of corticosteroid or other antibacterial

treatment. Endopthalmitis is due to hematogenous spread of fungal infection. The infection is characterized by the presence of typical white cotton like lesions, which are important diagnostic criterion for disseminated infection.

LABORATORY DIAGNOSIS OF CANDIDAL INFECTION[81,82]

Direct examination

Clinical specimens from diseased skin can be collected by scraping the affected area, materials from nails or in some instances by the use of swabs. Specimens are subjected to wet mount examination with 10% KOH.. Gram's staining, Parker's ink, lactophenol cotton blue enables easier demonstration of fungal elements. The flurochromes like calcoflour white which has an affinity for chitin and glucan aids the demonstration of fungus with a fluroscent microscope . Direct KOH examination of the specimens reveal the presence of budding yeasts and pseudohyphae. *Candida glabrata* does not produce hyphae or pseudohyphae in clinical specimens.[84,85]

CULTURE

Isolation of the organism

The routine medium used for the isolation of fungi from the mucocutaneous specimens is Sabouraud's dextrose agar (SDA) supplemented with antibiotics like chloramphenicol suppress the overgrowth of bacteria. Candida from mucocutaneous samples are easily isolated in culture. Cultures can be incubated at 28^0 C or at 37^0 C and Candida colonies will be grown with in 2-3 days.

Identification and speciation

The identification of Candida and its species is dependent on

- Macroscopic and microscopic morphology
- Physiological and biochemical characteristics
- Serology for antigenic identification of *Candida spp*
- Serotypes of the species

The macroscopic morphology of Candida species in SDA is smooth, creamy yeasty colonies and is basically the same for all species but colonies of *C.krusei* appears dry. On chromogenic agar, *C.albicans*, *C.krusei* and *C.tropicalis* appear light green, pink and blue respectively.

Candida when grown in corn meal agar produces chlamydospores at 24-36 hrs. Chalmydospores which can be intercalary or terminal are rounded, large refractile vesicles measuring 8-12 micron arranged at the end and at the sides.

GERM TUBE TEST (Raynold Braude phenomenon)

A germ tube is defined as a filamentous extension from a yeast cell that is almost half the width and 3-4 times the length of the cell.

The principle of the test is the ability of *C.albicans or C.dublinensis* to produce blastospores when incubated in serum at 37°C for 2 hrs. It helps in the presumptive identification of *C.albicans or C.dublinensis*. A true germ tube has no constriction at the point of origin. Early pseudohyphae of *C.tropicalis*

characteristically show a constriction adjacent to the mother cell. A new monoclonal antibody specific for *C.albicans* germ tube has been described.

BIOCHEMICAL CHARACTERISATION

Candida species utilizes carbhohydrates both Oxidation (assimilation) and anaerobic means (fermentation). Various biochemical tests for assimilation and fermentation are done using glucose, maltose, dextrose, lactose and sucrose.

Sugar fermentation tests

The classic tests uses the liquid media supplemented with different carbohydrates, a color indicator to assess pH changes to measure acid formation and a tool to assess gas formation such as Durham's tube.

There are several modifications for assessment of gas production such as the use of semisolid media or a wax layer on the top of liquid medium. Production of gas and not the change of color is used as an indicator of positive fermentation.

Sugar assimilation

The ability of a particular yeast to utilize a particular carbohydrate as the sole source of carbohydrate is the basis of commercial methods for the identification of yeast. Various techniques such as classic Wickerson method, auxanographic methods and commercial kits**.**

SEROLOGICAL TESTS

The classical serology includes assays for detection of serum antibodies by various modifications of the agglutination tests. Tests aimed at detecting antibodies to candida antigens released include gel immunodiffusion (ID) or counter immunoelectrophoresis (CIE) to detect antibodies to candida cytoplasmic antigens which are standardized by their protein content. Other systems used include Enzyme linked immunosorbent assay (ELISA) or Latex agglutination (LA) test. Generally, antigen detection is used for detection of active infection .The use of combination of antigen detection and antibody detection tests are helpful in diagnosing the infection in both immunocompetent and immunosuppressed patients.

Molecular biology techniques

These techniques are based on detection of *Candida* DNA in body fluids of patients involving the use of specific DNA probes. This approach became more promising as a possible tool with the development of DNA amplification techniques, particularly PCR.

Successful use of molecular techniques for the detection of the fungal DNA in clinical specimens could possibly provide a sensitive means for early diagnosis.

THERAPY[83]

A wide variety of antifungals are effective against candidiasis. Important factors that determine the clinical response, besides the choice of antifungals include the extent and severity of the disease.

Topical antifungals

Topical antifungals for candidiasis include Gentian violet paint, terconazole, ciclopiroxolamine, nystatin and hamycin. Thrush and other mucocutaneous forms are treated with topical antifungals. Clotrimazole is available as cream, lotion, powder, spray and troche. Clotrimazole vaginal tablets are used for vaginal candidiasis. Other imidazole topical antifungals are butoconazole, micanozole, tioconazole, terconazole and econazole.

Clotrimazole has little side effects and absorbed from the GI tract poorly. Ketoconazole is available as cream.

Systemic antifungals

Fluconazole is the FDA approved drug for vaginal candidiasis and is absorbed more completely than itraconazole and ketoconazole. It is also available in suspension, tablet and parentral form. Ketoconazole is absorbed when the pH<4.0 and hence may be a problem in achlorhydria patients especially in HIV infected. The side effects of ketoconazole, itraconazole, posoconazole and voriconazole are similar, more common being headache, dyspepsia, diarrhea, vomiting, hepatitis and skin rash. Voriconazole cause

reversible mild abnormal vision. Prolonged administration of azoles may require surveillance of liver enzymes to monitor for hepatotoxicity. Caspofungin and micafungin are approved for esophageal candidiasis. Adverse effects include fever, nausea, infused –vein complications and vomiting typically are mild.

Resistance to antifungals

Resistance to antifungals are due various factors like mutation colonization with inherently resistant species and patients infected with multiple strains. *Candida krusei* is inherently resistant to fluconazole. There has been increasing reports of *Candida glabrata* being resistant to fluconazole. *Candida albicans* is replaced by *Candida dublinensis* in fluconazole treated patients. Isolates of *C.dublinensis* resistant to fluconazole may however still be susceptible to voriconazole and itraconazole.

The development of resistance during short term use of fluconazole is not a problem although on an institutional level the widespread use of fluconazole may shift the range of infecting species toward more resistant species. Much research is into the resistance of the organism in the era of HIV and other immunosuppressed states.

Candidal vaccine

Fungal vaccine development has mostly used cell wall extracts, which contain polysaccharides that are generally poorly immunogenic, and protection

in animal models has been controversial. In fact, antibody mediated protection has been difficult to demonstrate because inhibitory and protective antibodies seem to be equally induced. However, the monoclonal antibody 2G8 was isolated and able to control infections caused by two fungi, *Candida* and *Cryptococcus*.

The conjugation technology that has been so successful in making immunogenic bacterial polysaccharides may be useful in the development of universal “cross-kingdom” vaccines able to protect against multiple fungal infections.

AIM AND OBJECTIVES

AIM AND OBJECTIVE OF THE STUDY

BACKGROUND

Candida is an ubiquitious organism causing superficial fungal infection that is commonly encountered in clinical practice.Yeast infections caused by *Candida* is increasingly being reported worldwide. This increased incidence of infections are attributed to immunocompromised diseases like HIV and the development of wide range of newer immunosuppresives. A change in the epidemiology, clinical spectrum and antifungal susceptibility has been observed. The prompt detection of different species of yeast infections may aid for the appropriate treatment decisions.

This study has been designed,

1. To study the age wise distribution of mucocutaneous candidiasis.
2. To study the sex wise distribution of mucocutaneous candidiasis.
3. To study the predisposing factors in individuals with mucocutaneous candidiasis.
4. To study the most common clinical features of mucocutaneous candidiasis
5. To identify the different species of candida by culture,subculture and appropriate biochemical tests in all patients with mucocutaneous candidiasis.
6. To identify the common blood group susceptible to mucocutaneous candidiasis

MATERIALS AND METHODS

MATERIALS AND METHODS

This study was conducted in Rajiv Gandhi Government General Hospital, Madras Medical college.

One hundred new patients with symptoms and signs of mucocutaneous candidiasis attending the OPD, Mycology section of The Department of Dermatology were included in the study. Culture in SDA agar, Hichrome candida agar and biochemical tests like sugar fermentation were done for all patients with positivity for *Candida* in 10% KOH examination.

INCLUSION CRITERIA

1. Patients with symptoms and signs of mucocutaneous candidiasis.
2. Patients who test positive for *Candida* in KOH examination.
3. All patients including immunosuppressed, pregnant and pediatric age group are included.

EXCLUSION CRITERIA

1. Patients with negative results in KOH examination.
2. Those who are on topical for two weeks and systemic antifungals for four weeks prior to the study.

Informed consent was obtained from all patients for their participation in this study. The skin and mucosal samples were collected and evaluated by appropriate laboratory methods.

MYCOLOGICAL EXAMINATION

Specimens from mucosal and cutaneous scrapings were examined in 10% potassium hydroxide (KOH) solution for the presence of fungal spores, hyphae and pseudohyphae.

Inoculation was done on Sabouraud's dextrose agar (SDA) with chloramphenicol (0.005mg/ml) at 37^0C and was observed everyday for the growth of candidial colonies which appeared as white or cream coloured, smooth with a yeasty odour. Hichrome media was used for species identification which was by the production of different colours and corn meal agar was used for detection of chlamydospores . Germ tube test was done by incubating the colonies with human serum at 37^0C for two hours and observed for the formation of germ tube under light microscope. Sugar fermentation using glucose, lactose, sucrose, maltose and galactose were also carried out to differentiate between the various species.

SABOURAUD'S DEXTROSE AGAR

MEDIA PREPARATION

Ingredients:

Dextrose - 2g

Peptone - 1g

Agar - 3g

Distilled water - 100ml

pH - 6.5

The ingredients were weighed accurately and then dissolved in 100 ml of distilled water. This is then heated gently till the boiling point of water so that agar dissolves completely and the solution becomes homogenous. When the media has become transparent, heating is stopped. Antibiotic chloramphenicol is added (0.005mg/ml).

The media is then dispersed in tubes and autoclaved at 121^0C for 15 minutes and the final pH is adjusted to 6.5. The sterilized media is then allowed to cool to 50^0 C and then poured into sterile test tube.

HICHROME CANDIDA AGAR

Hichrome Candida agar is recommended for rapid isolation and identification of species of *Candida*

Composition

Ingredients	Grams/Litre
Peptic digest of animal tissue	15.0
Agar	5.0
Chloramphenicol	0.5
Chromogenic mixture	11.22
Dipotassium hydrogen phosphate	1.0
Final pH	6.3+_0.2

Constitution of the media

21.36 gms of Hichrome agar is dissolved in 500ml of distilled water. It is then heated to boiling point to dissolve completely. The medium is cooled to 50^0 C and poured into sterile petri dishes.

Interpretation

Candida produces an enzyme beta-N-acetyl galactosaminidase/ hexosaminidase into the growth media which helps in identification of *Candida*. Hichrome media is a selective and differential media which facilitates rapid isolation of yeasts from mixed cultures and allows differentiation on the basis of colonization and colony morphology.

Cultural response:

Organism	**Colour**
C.albicans	light green
C.tropicalis	steel blue with pink hallow
C.krusei	pink
C.parapsilosis	cream colored
C.glabrata	Purple
C.dublinensis	dark green
C.guillermondii	pale pink to purple

SUGAR FERMENTATION

The classic tests involves liquid media supplemented with different carbohydrates . Change of color from blue to yellow in the fermentation fluid is considered as the indicator of positive fermentation.

Various species are identified by their difference in fermenting ability as shown in the table below:

Species	**Dextrose**	**Maltose**	**Sucrose**	**Lactose**	**Galactose**
C. albicans	+	+	-	-	+
C.tropicalis	+ / v	-	**+/v**	-	-
C.glabrata	+	-	-	-	-
C.krusei	+	-	-	-	-
C.parapsilosis	+	-	-	-	-

v-variable results;'+' shows fermentation; '-'no fermentation

OBSERVATION AND RESULTS

OBSERVATION AND RESULTS

A total of 100 patients with features of mucocutaneous candidiasis who tested positive for *Candida* in KOH mount were selected for this study. The minimum age group affected was a one month old infant and maximum age group affected was 70 years (mean= 41.5). The maximum number of cases were found to be in the age group of 31-50.[Table no 1]

Table no 1 :Age wise distribution

Age	No of cases		Total no of cases
	Male	Female	
0-10	1	1	2
11-20	3	0	3
21-30	3	16	19
31-40	2	22	24
41-50	11	14	25
51-60	5	9	14
61-70	2	11	13
Total	27	73	100

SEX DISTRIBUTION

There was a female predominance with 73% (n=100) and males were 27% (M:F ratio 1:2.7) . Maximum number of females were in the age group of 31-40yrs and maximum number of males were in the age group of 41-50 yrs. [Table 2]

Table no.2:Sex distribution(n=100)

Males	Females
27	73

CLINICAL PATTERNS:

In this study, mucosal candidiasis was found in 82 patients and 18 patients had cutaneous candidiasis.

Oral candidiasis was detected as the most common clinical presentation in 48 patients. Of the 48 patients with oral candidiasis, 18 were males and 30 were females. It wasfound that pseudomembranous pattern of candidiasis was present in 30 patients (62.5%) followed by angular cheilitis (perleche) in 10 patients (20.8%) and acute erythematous type in 8 patients (16.7%). A single patient with multicentric reticulohistocytosis who was on prolonged steroids initially presented with acute erythematous type of oral candidiasis and subsequently developed esophageal candidiasis. Acquired immunodeficiency disorder was found in 3 patients (6.25%) of which 2 patients had pseudomembranous type and one patient had perleche.

Next to oral candidiasis, vulvovaginal candidiasis was the common clinical pattern in mucocutaneous candidiasis in 32%.Intertriginous lesions were noted in various sites like groin in of patients 13%, finger webspaces (2%), toe cleft (2%) and neck (1%). Balanoposthitis was present in 2% of patients [Table no 3&]. Recurrent vulvovaginal candidiasis were found in about 18.75% (6/32). All six patients were diabetic [Table3,4].

Table no 3: Clinical patterns n=100

Clinical presentation	M	F	Total no of cases
Oral candidiasis	18	30	48
Vulvovaginal candidiasis	-	32	32
Intertrigo groin	3	10	13
Intertrigo webspace	1	1	2
Intertrigo toe cleft	2	-	2
Balanoposthitis	2	-	2
Intertrigo neck	1	-	1

Table no 4 :Patterns of oral candidiasis n=48

Type of lesion	No of cases
Pseudomembranous candidiasis	30
Angular cheilitis	10
Acute erythematous type	8

Predisposing factors

In this study, there were 67 immunosuppressed individuals and 33 were immunocompetent. Immunosuppression was the major predisposing factor. Among the immunosuppressed, 52 patients (77.61%) had diabetes mellitus, 29 patients (43.28%) were on immunosuppressives for various conditions like pemphigus vulgaris, bullous pemphigoid, Systemic lupus erythematoses, multicentric reticulohistiocytosis, pustular psoriasis and post renal transplant state. Two of them had chronic renal failure [Table no 5]. All diabetic patients had their random blood sugar level in the range of 200-290 mg/dl. The diabetic status of 50% of patients were on steroids induced.

In oral candidiasis, the most common predisposing factor was found to be immunosuppression in 34 patients. In 20 patients (58.8%), diabetes was the predominant cause for immunosuppression followed by intake of immunosuppressive drugs like steroids and cytotoxic drugs for conditions like post renal transplant state, systemic lupus erythematosus and pustular psoriasis. Other associated dermatological diseases were mostly bullous disorders like pemphigus vulgaris in 17 patients (35.4%), systemic lupus erythematosus in 3 patients, one patient in each of pustular psoriasis multicentric reticulohistiocytosis and erythroderma. Diseases like carcinoma cheek and cholecystitis were also found in one patient each.

In vulvovaginal candidiasis, about 27 patients (84.4%) were diabetic and 5 patients (15.6%) were normal. Diabetes was found to be the common cause of immunosuppression. One patient was in her second trimester of pregnancy with gestational diabetes.

In patients with intertriginous lesions of the groin, the predisposing factors like obesity, excessive sweating, hot humid climate and poor personal hygiene were noted. Intertrigo of finger web spaces and toe cleft were due to prolonged immersion in water.

Species distribution

Of the 100 patients, 45% of isolates were found to be *C.tropicalis* followed by *Candida albicans* in 37%, *C.glabrata* in 9%, *C.krusei* in 8% and *C.parapsilosis* in 1%. *C.albicans* were isolated in the younger age group in the

first decade in two patients. *C.parapsilosis* was isolated from an elderly diabetic female. Between 31-50 yrs, *C.tropicalis* was found in 22 patients followed by *C.albicans* in 20 patients.[Table 5]

In oral candidiasis, *C. tropicalis* was the predominant organism in 20 patients (41.7%) followed by *C.albicans* in 19 (39.6%), *C.glabrata* in 6 patients (12.5%) and *C.krusei* in 3 patients (6.2%). [Table 6]

In vulvovaginal candidiasis, the predominant organism isolated was *C.tropicalis* accounting for about in 17 patients (53.1%) followed by *C.albicans* in 10 patients (31.2%), *C.glabrata* in 3 patients (9.5%) ,*C.parapsilosis* and *C.krusei* in one patient each (3.1%). *C.tropicalis* was isolated from a pregnant female with vulvovaginal candidiasis in the third trimester who also had gestational diabetes. In two cases of balanoposthitis, *C. albicans* and *C.tropicalis* were isolated.

In patients with intertrigo groin, *Candidia tropicalis* was isolated in 5 patients (38.5%) followed by *C.albicans* in 5 patients (38.5%), *C.krusei* in 3 patients (23%). In two cases of intertrigo toe cleft, *C.krusei* and *C.albicans* were isolated. In two cases with intertrigo webspace, *C.tropicalis* was isolated.

We also found that Candidiasis was predominantly found in immune compromised individuals in about 67% patients and 33% of immunocompetent individuals. Overall, 63% of isolates were *nonalbicans* species and 37% were *albicans* species. Out of the immune suppressed individuals, *C.albicans* species in 21 patients (31.3%), *C.tropicalis* in 30 patients (44.8%), *C.glabrata*

in 9 patients (13.4%), *C.krusei* in 6 patients (9%) and *C.parapsilosis* in one patient (1.5%). In non immunosuppressed, *C.albicans* was isolated in 16 patients (48.5%), *C.tropicalis* in 15 patients (45.5%), *C.krusei* in 2 patients (6%) [Table 5,6,7&8]

TABLE 5:Overall species distribution

Species	No of cases
C .tropicalis	45
C .albicans	37
C .glabrata	9
C .krusei	8
C .parapsilosis	1

TABLE 6:Clinical pattern and the species distribution

Species	OC	VVC	BP	IG	INTWS	INTTC	INTN
C.tropicalis	20	17	1	5	2	-	-
C.albicans	19	10	1	5	-	1	1
C.glabrata	6	3	-	-	-	-	-
C.krusei	3	1	-	3	-	1	-
C.parapsilosis	-	1	-	-	-	-	-
Total	48	32	2	13	2	2	-

Table-7:Species distribution between immunosuppressed and nonimmunosuppressed

Species	Immunosuppressed	Nonimmunosuppressed
C .albicans	21	16
C .tropicalis	30	15
C .glabrata	9	-
C .krusei	6	2
C.parapsilosis	1	-
Total	67	33

OC-oral candidiasis; VC-vulvovaginalcandidiasis; INT.N-intertrigoneck; INT WS-intertrigowebspace; INT TC-intertrigo toe cleft; BP-balanoposthitis.

Table-8:Species distribution among different age groups

Age	*C.albicans*	*C.tropicalis*	*C.glabrata*	*C.krusei*	*C.parapsilosis*
1-10	2	-	-	-	-
11-20	-	2	1	-	-
21-30	7	8	3	1	-
31-40	9	11	1	3	-
41-50	11	11	-	3	-
51-60	4	7	2	1	-
61-70	4	6	2	-	1

Blood group and Candidiasis

We found that ‘O’ positive individuals showed higher candidal infection in about 70% followed by ‘B’ positive blood group in 20%, ‘A’ positive in 8%, ‘O’ negative and ‘AB’ negative in 1% each. O blood group developed oral candidiasis in 32 patients (45.7%) followed by vulvovaginal candidiasis in 20 patients(28.5%), intertrigo groin in 11 patients (15.7%), balanoposthitis, intertrigo web space, intertrigo toe cleft in 2 patients each (2.9%) and intertrigo neck in1 patient (1.4%). ‘B’ group had oral candidiasis in 10 patients (50%) followed by vulvovaginal candidiasis in 8 patients (40%) and intertrigo groin in 2 patients (10%). [Table 9,10]

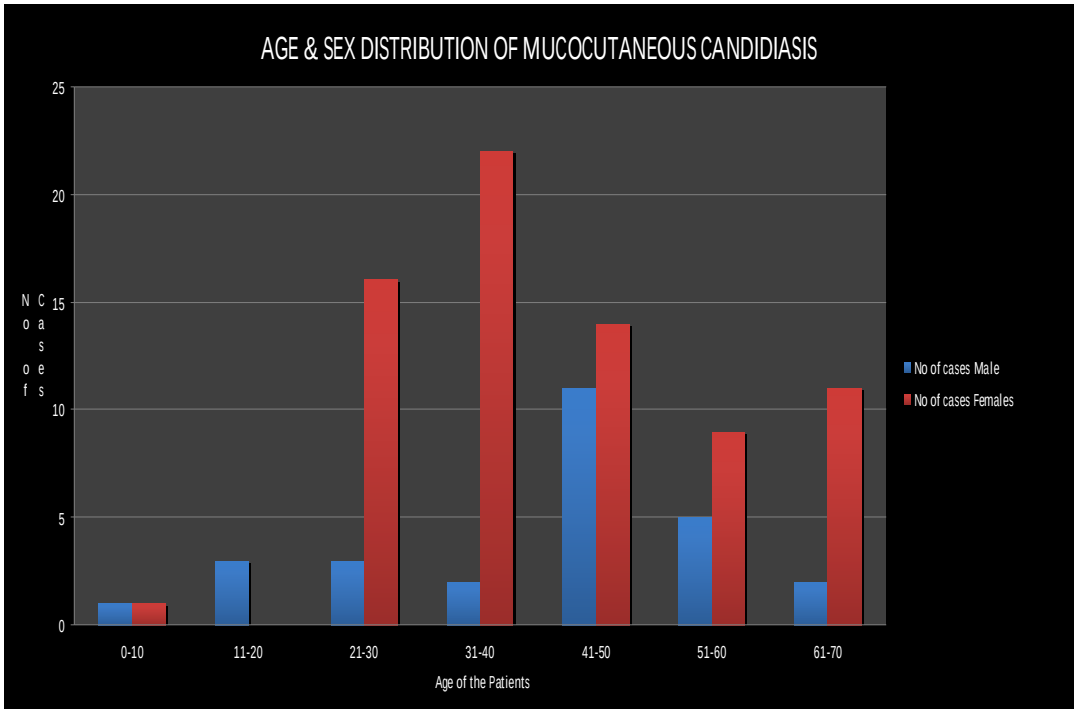
Table 9-Blood group distribution

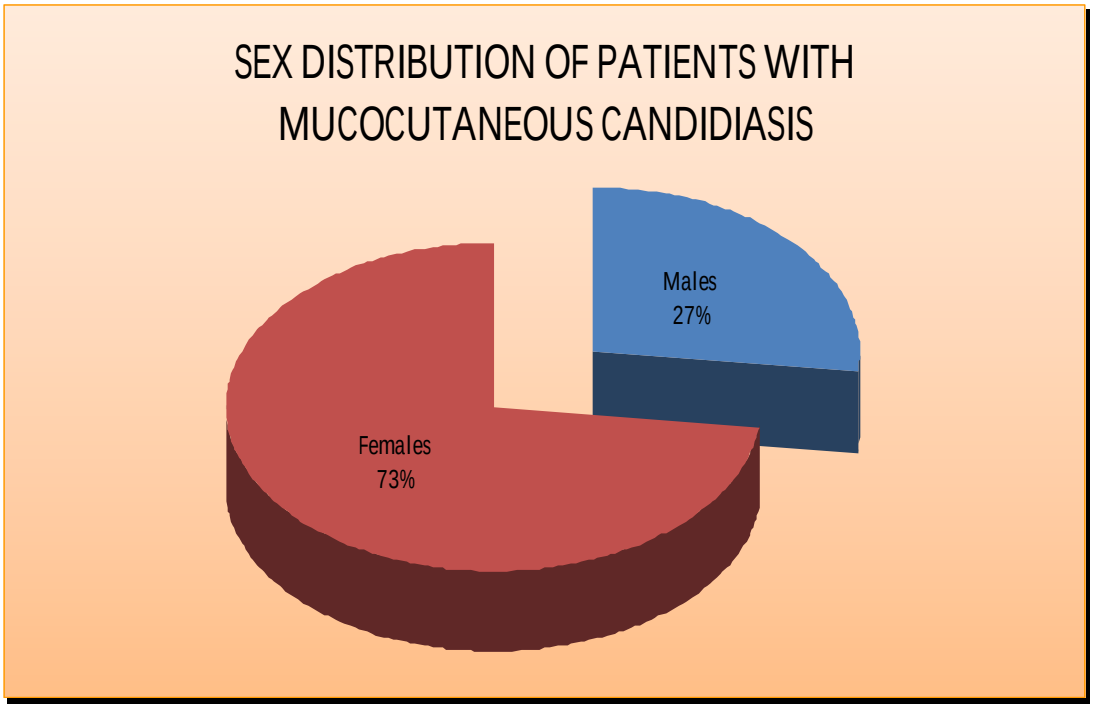
BLOOD GROUP	NO OF CASES
O+	70
B+	20
A+	8
O-	1
AB-	1

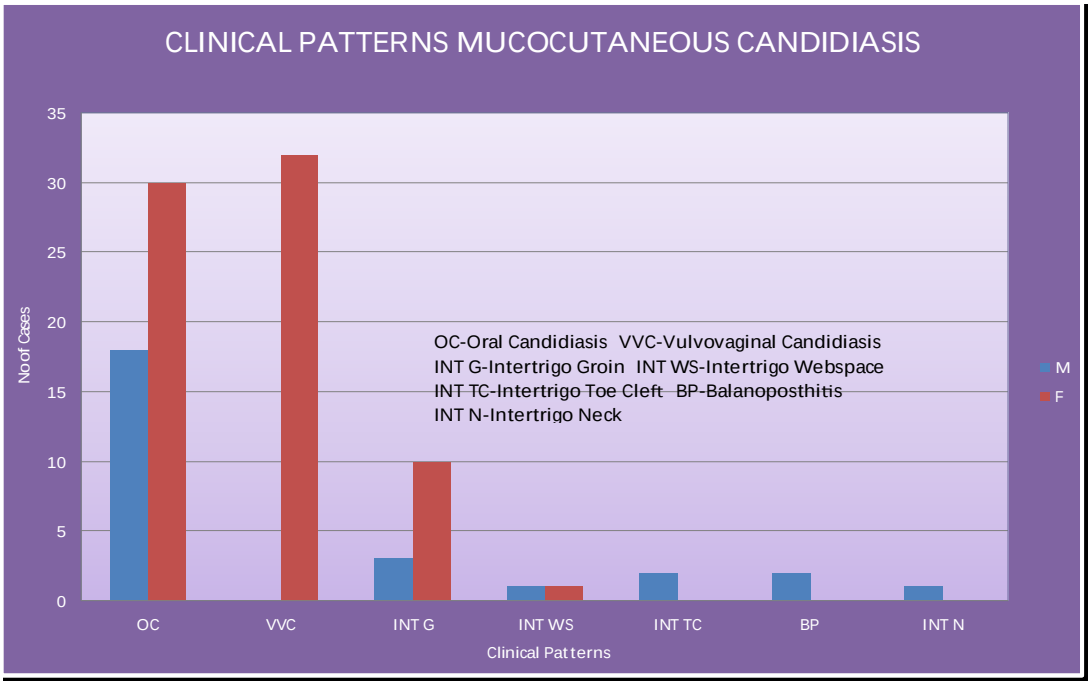
Table no 10<u>Blood group and Candidiasis</u>

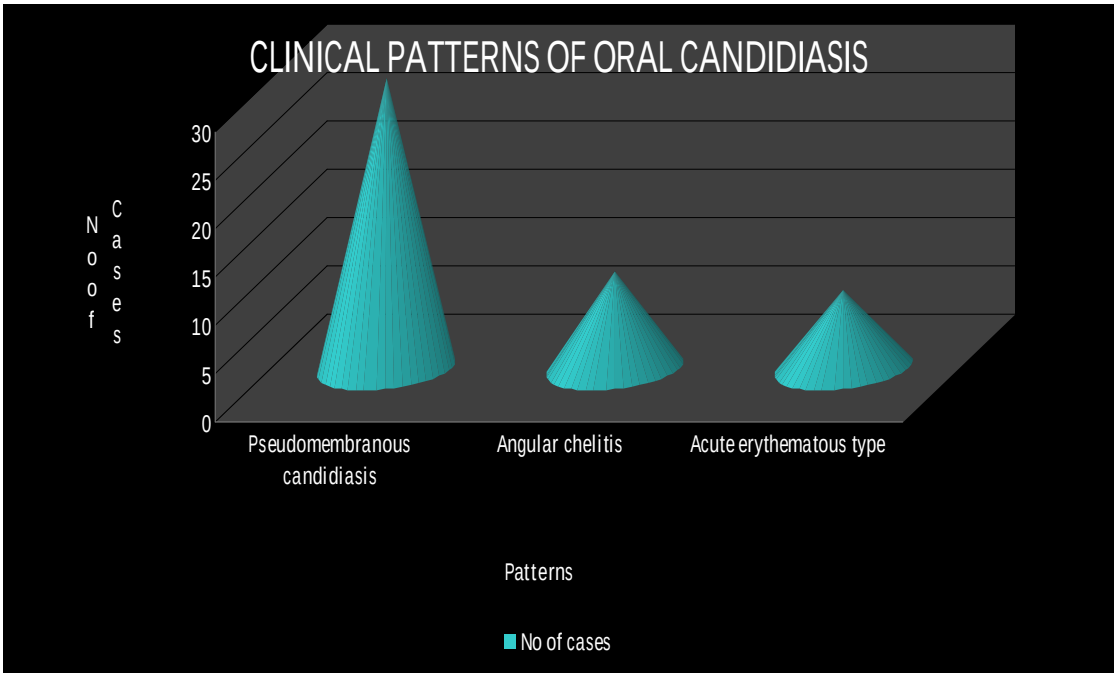
Clinical type	O+	B+	A+	AB-	O-
OC	32	10	5	-	1
VVC	20	8	3	1	-
INT G	11	2	-	-	-
INT WS	2	-	-	-	-
INT TC	2	-	-	-	-
BP	2	-	-	-	-
INT N	1	-	-	-	-

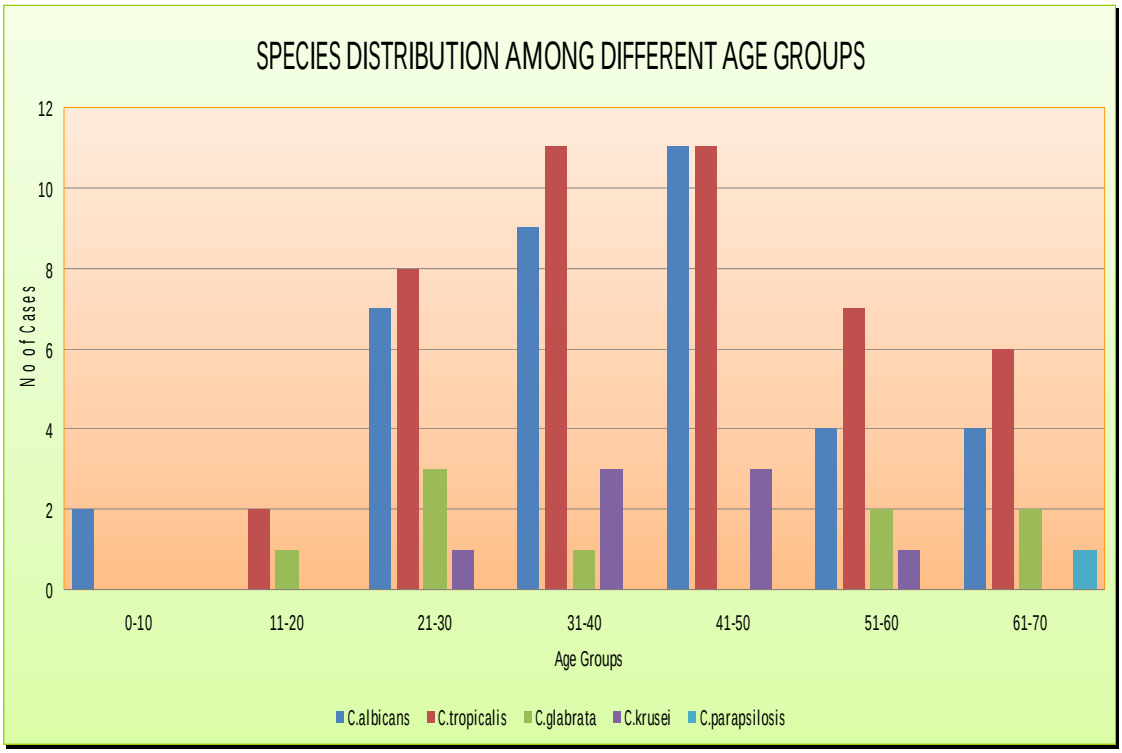
OC-oral candidiasis; VVC-vulvovaginal candidiasis;INT.N-intertrigo neck; INT WS-intertrigo webspace; INT TC-intertrigo toe cleft; BP-balanoposthitis

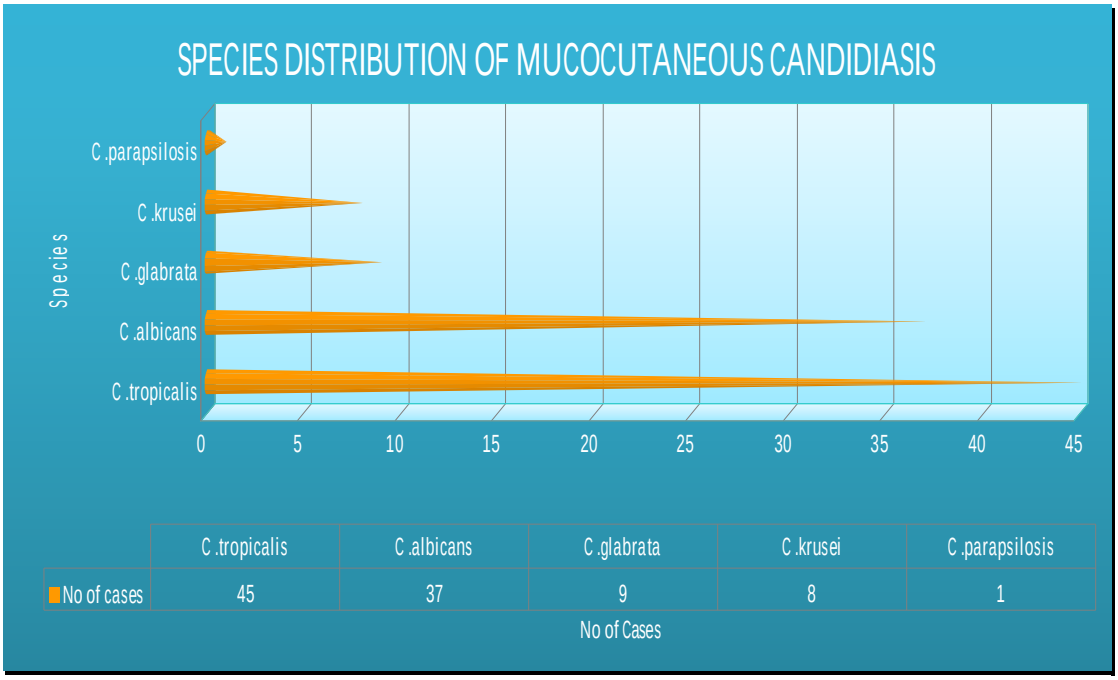

AGE & SEX DISTRIBUTION OF MUCOCUTANEOUS CANDIDIASIS
No of Cases
25
20
15
10
5
0
0-10
11-20
21-30
31-40
41-50
51-60
61-70
Age of the Patients
No of cases Male
No of cases Females

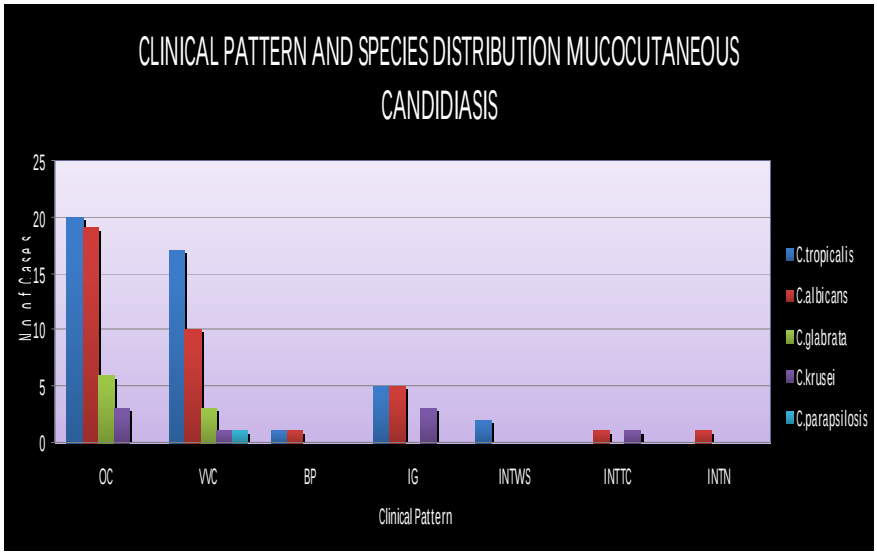

SEX DISTRIBUTION OF PATIENTS WITH MUCOCUTANEOUS CANDIDIASIS
Males
27%
Females
73%

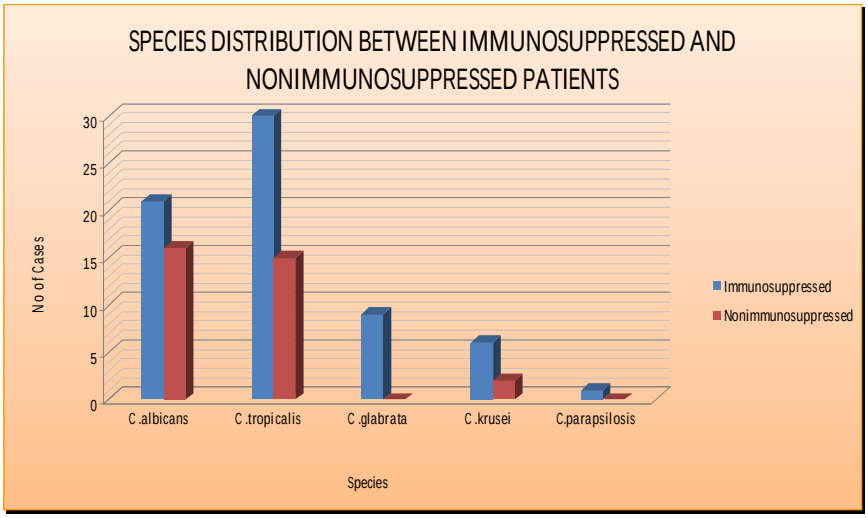

CLINICAL PATTERNS MUCOCUTANEOUS CANDIDIASIS
No of Cases
35
30
25
20
15
10
5
0
OC-Oral Candidiasis VVC-Vulvovaginal Candidiasis
INT G-Intertrigo Groin INT WS-Intertrigo Webspace
INT TC-Intertrigo Toe Cleft BP-Balanoposthitis
INT N-Intertrigo Neck
OC
VVC
INT G
INT WS
INT TC
BP
INT N
Clinical Patterns
M
F

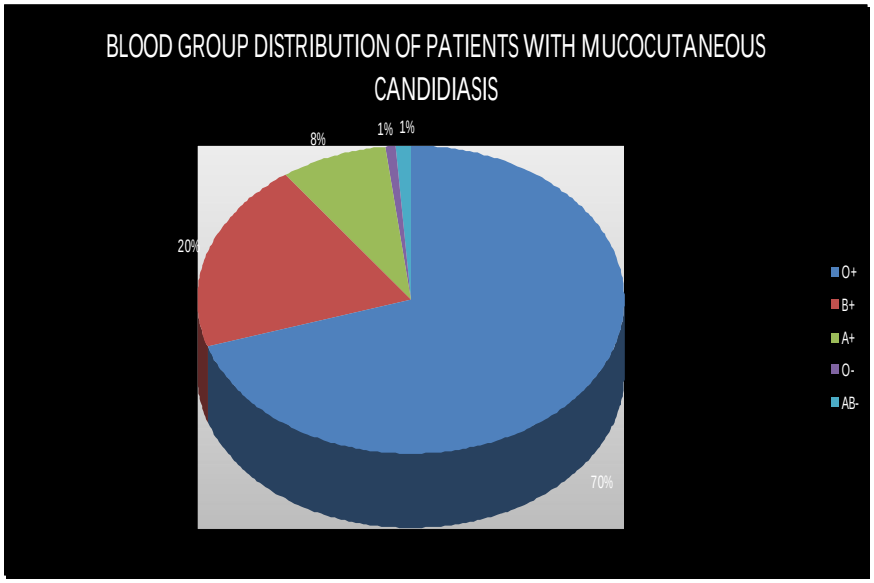

CLINICAL PATTERNS OF ORAL CANDIDIASIS
No of Cases
30
25
20
15
10
5
0
Pseudomembranous candidiasis
Angular chelitis
Acute erythematous type
Patterns
No of cases


SPECIES DISTRIBUTION AMONG DIFFERENT AGE GROUPS
No of Cases
12
10
8
6
4
2
0
0-10
11-20
21-30
31-40
41-50
51-60
61-70
Age Groups
C.albicans
C.tropicalis
C.glabrata
C.krusei
C.parapsilosis


SPECIES DISTRIBUTION OF MUCOCUTANEOUS CANDIDIASIS
Species
C .parapsilosis
C .krusei
C .glabrata
C .albicans
C .tropicalis
0
5
10
15
20
25
30
35
40
45
C .tropicalis
C .albicans
C .glabrata
C .krusei
C .parapsilosis
No of cases
45
37
9
8
1
No of Cases


CLINICAL PATTERN AND SPECIES DISTRIBUTION MUCOCUTANEOUS CANDIDIASIS
25
20
15
10
5
0
OC
VVC
BP
IG
INTWS
INTTC
INTN
Clinical Pattern
C.tropicalis
C.albicans
C.glabrata
C.krusei
C.parapsilosis


SPECIES DISTRIBUTION BETWEEN IMMUNOSUPPRESSED AND NONIMMUNOSUPPRESSED PATIENTS
No of Cases
30
25
20
15
10
5
0
C .albicans
C .tropicalis
C .glabrata
C .krusei
C.parapsilosis
Species
Immunosuppressed
Nonimmunosuppressed


BLOOD GROUP DISTRIBUTION OF PATIENTS WITH MUCOCUTANEOUS CANDIDIASIS
1%
1%
8%
20%
70%
O+
B+
A+
O-
AB-

DISCUSSION

DISCUSSION

In this study of 100 patients with mucocutaneous candidiasis, maximum number of patients were in the 4th and 5th decade of life. The minimum age of presentation was a one month old infant and the maximum age was 70 years. This implies that candidiasis can affect any age group.

In the present study, immunosuppressed patients (67%) developed candidiasis more than the immunocompetent individuals (33%). Drezen et al, Hawking et al proposed candidiasis to be the commonest mycoses in immunosuppressed patients [85,86] Most of the immunosuppressive patients (77.61%) in this study were diabetics. Safia et al, Reeding et al proposed diabetes to be the predisposing factor for various fungal infections especially *Candida spp*[87,88]

Oral candidiasis (48%) has been observed the most common manifestation of mucocandidiasis in this study. Females (62.5%) had higher occurrence than males (37.5%). Shaheen et al and Bart et al showed higher number of males than females in contrast to this study.[89,90] There were more number of patients in the age group of 31-50. Zaremba et al observed maximum no of patients in the age group of 33-44 yrs.[91] Bezali et al have speculated that oral carriage cannot be directly related to age.[92] Immunosuppression was found to the major cause in 70.8% of patients with oral candidiasis. Among the immunosuppressed, diabetes was found in 58.8% patients. This is similar to the study by Shaheen et al who noted the prevalence

of oral candidiasis to be higher in immunosuppressed individuals.[89] Tapper Jones et al, Aly et al and Abu Elteen et al reported the prevalence of yeast carriage in diabetic individual to reach upto 54%.[93,94,95] In this study it was found that all patients had type II diabetes and their blood sugar levels were between 200-290 mg/dl. The relationship between the blood glucose level and carriage rate of *Candida* is controversial. Hill et al proposed that long duration of diabetes rather than diabetes by itself puts the patient at risk of oral candidiasis [96] Gray et al proposed that there is no correlation between glycemic level and the *Candida* carriage rate.[97] Yet another study by Lamey et al showed the lack of association between HbA1c or blood glucose level and the *Candida* carriage rate[98]. Similar reports were also given by Kumar et al who stated that glycemic control and antidiabetic drugs have no correlation with the Candida carriage[99].

Of the diabetic patients, *Candida albicans* was isolated in 40% patients followed by *Candida tropicalis* in 30% patients and *Candida glabrata* and *Candida krusei* in 15% of patients each. *Candida albicans* was the common isolate which is similar to the study done by Khaled et al and Lee et al which showed *C.albicans* to be more prevalent in diabetes followed by *C.tropicalis*.[100,101] Tapper Jones et al showed 60% of them harbor *C.albicans* and Yarahmadi et al reported higher carriage of *Candida albicans* in the mouth of diabetics (40.2%) compared to controls (16.2%)[93,102]

In this study, 37.5% of patients with oral candidiasis were suffering from pemphigus vulgaris. Oral candidiasis occurred as a complication of steroids. Pemphigus was shown to be associated with oral candidiasis in 24% in a study by Shaheen et al.[89]

Among the clinical patterns of oral candidiasis, pseudomembranous candidiasis was found to be the most common manifestation seen in 62.5% patients followed by angular cheilitis in 20.8% patients, erythematous type in 16.7% patients. Similar observations were made by Shaheen et al and Gravina et al who also observed pseudomembranous type as the most common clinical pattern. [89,103]The species isolated in this study are *Candida tropicalis* in 41.7% patients followed by *C.albicans* in 39.6% patients, *C.glabrata* in 12.5% patients and *Candida krusei* in 6.2% patients. They were isolated in comparable rates to *C. albicans* in the present study. *C.albicans* and *C.tropicalis* were reported in equal proportion by Kamat et al, Kumar et al and Ariyawardana et al[104,105,106]. This is in contrast to other studies which showed *C.albicans* as the most common isolate (Shaheen et al, Zaremba et al)[89,91].

In this study 6.25% of patients with HIV infection presented with oral candidiasis. All three patients had their CD4 counts were between 374-400 cells /mm^3. Bodhade et al and Campo et al proposed that oral manifestations were common in HIV patients with CD4 counts less than 200 cells /mm^3 .[68,107]The presence of oral candidiasis in HIV patients in this study could be due to other contributing factors like poor oral hygiene and the prolonged use

of antibiotics for prevention of opportunistic infection. The number of patients in this study is small to establish a correlation with the CD4 count and the severity of oral candidiasis. Among the HIV patients of this study, 66.7% had pseudomembranous candidiasis and 33.3% of patients had angular cheilitis. Pseudomembranous candidiasis is found to be common in HIV patients in other reports by Gravina et al and Ranganathan et al.[103,108] Erythematous candidiasis was reported to be common in studies by Bodhade et al, Sharma et al and Moniaci et al.[107,109,110]

C.albicans was isolated in 66.7% patients and *C.tropicalis* in 33.3% patient. This is similar to a study by Ranganathan et al who reported *C. albicans* as the common agent followed by *C.tropicalis*[108]. In HIV patients, rise of *nonalbicans* species has been reported earlier by Baradkar et al (30%)[111]and Kaviarasan et al. (20.2%)[112]. As the sample size in the present study are small, the results are not comparable with the previous studies.

Vulvovaginal candidiasis (VVC) was found in about 32% of patients. In this study it was observed that vulvovaginal candidiasis is more common in third to fifth decade. Similar observation was made in an Indian study by Jindal et al who described increased incidence of VVC in second to fourth decade and he attributed it to the peak sexual activity during this age.[113]. Among the patients with VVC, 84.4 % of patients were diabetic and 15.6% were normal. All patients had type II diabetes. Leon et al reported 61% diabetic patients with VVC which is lesser than the present study.[114]Overall, *C.tropicalis* was

isolated in 53.1% followed by *C.albicans* in 31.2%, *C.glabrata* in 9.5%, *C.krusei* and *C.parapsilosis* in 3.1% each. Among the diabetic patients, organisms isolated were *C.tropicalis* in 63% patients followed by *C.albicans* in 18.5% patients, *C.glabrata* in 11.1% patients, *C.krusei* and *C.parapsilosis* in 3.7% patient each. In contrast, Jindal et al reported *C.albicans* to be common in 74.4% followed by *nonalbicans* species (25.6%) in the order of *C.glabrata* (11%), *C.tropicalis* (5.6%), *C.krusei*(3.6%), *C.parapsilosis* and *C.guillermondi* in equal proportion (2.3%).[113] Similar observation was made by Vermitzky et al describing *C.albicans* to be common and *C. glabrata* to be the second commonest isolate.[115]*C.glabrata* was commonly isolated in diabetic individuals by Goswami et al.[116] In all the immunocompetent patients (15.6%), *C.albicans* was isolated. A single pregnant female with gestational diabetes presented with vulvovaginal candidiasis from whom *C.tropicalis* was isolated

In this study, recurrent VVC was found in 18.75% of females between the age group of 30-40 yrs. Recurrent VVC is known to occur in 5-8% of women (Vermitzky et al).[115] Sobel et al described recurrent VVC in the age group of 21-44 yrs which is similar to the present study.[117] The common organism isolated was *C.tropicalis* in 50% of patients followed by *C.albicans* in 33.3% patients and *C.glabrata* in 16.7% of patients. Ritcher et al described *C.albicans* to be the most common in recurrent VVC followed by *C.glabrata*.[118]

Balanoposthitis was observed in 2% of patients. One of them was a diabetic and other was normoglycemic. *C.albicans* and *C.tropicalis* was isolated from them. Intertriginous lesions of the groin were more common in females (76.9%) than males (23.1%). The predisposing factors in these patients were found to be hot humid climate, excessive sweating and obesity. Intertrigo of the finger web spaces and the toe cleft were observed in 2% each. Prolonged immersion in water was the predisposing factor noted in these patients.

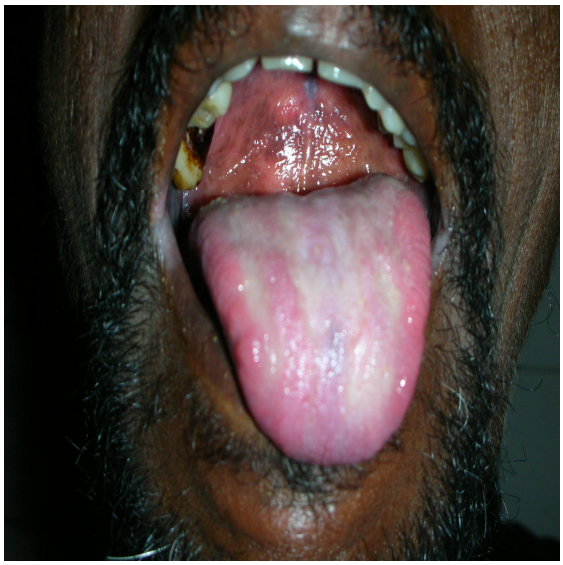
In the present study, patients with O blood group (70%) had higher occurrence of candidiasis than other blood groups (30%). O blood group developed oral candidiasis in 45.7%. Burford et al proposed higher carriage of Candida in patients with O blood group.[119]

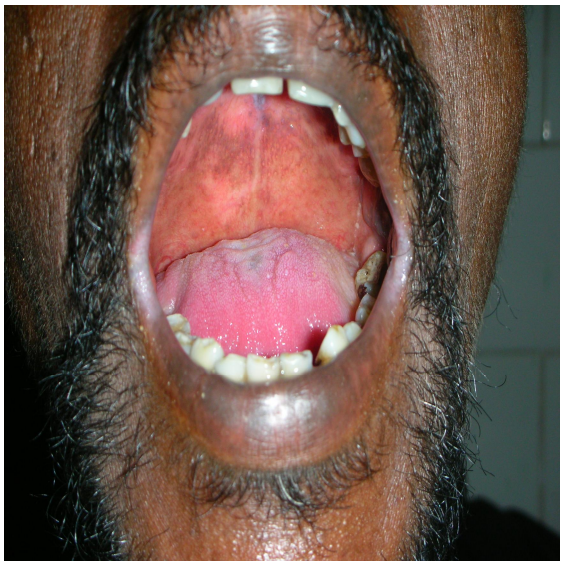
Overall in the present study, 63%of the isolates were non albicans species and 37% was *C.albicans.* The *nonalbicans* species that were isolated in the present study are *C.tropicalis* in 45% followed by *C.glabrata* (9%), *C.krusei*(8%) and *C.parapsilosis* (1%). *C.tropicalis* was isolated in 45% which is higher than *C.albicans* (37%). *C.tropicalis* and *C.albicans* were isolated in equal proportion in oral candidiasis by Kamat et al, Kumar et al and Ariyawardana et al[104,105,106] Further, in the present study *C.glabrata* has been isolated exclusively in immunosuppressed individuals in mucosal candidiasis . *C.krusei* was isolated almost in equal proportion in mucosal and cutaneous samples. In the present study, *C.parapsilosis* was isolated in 3.1% of patients with vulvovaginal candidiasis. Bauters et al described isolation of

C.parapsilosis in 8.9% of vaginal candidiasis patients.[120] The isolation of *C.tropicalis* higher than *C.albicans* has not been reported in mucocutaneous samples. But there have been increasing reports of *C.tropicalis* in other sites such as blood stream and urine samples. Blood stream infections by *C.tropicalis* more than *C.albicans* has been reported by Kothari et al, Shivprakasha et al and Adhikari et al [121,122,123] *C.tropicalis* higher than *C.albicans* has been reported in neonatal septicemia by Rani et al.[124] These reports imply an increase in the incidence of *nonalbicans* species especially *C.tropicalis* in Indian subcontinent. This unexplained increase of this species had led many researchers to undertake DNA studies. Dassanayake et al has demonstrated the evolutionary divergence of distinct genetic subgroups in *C.tropicalis* using DNA finger printing studies.[125]

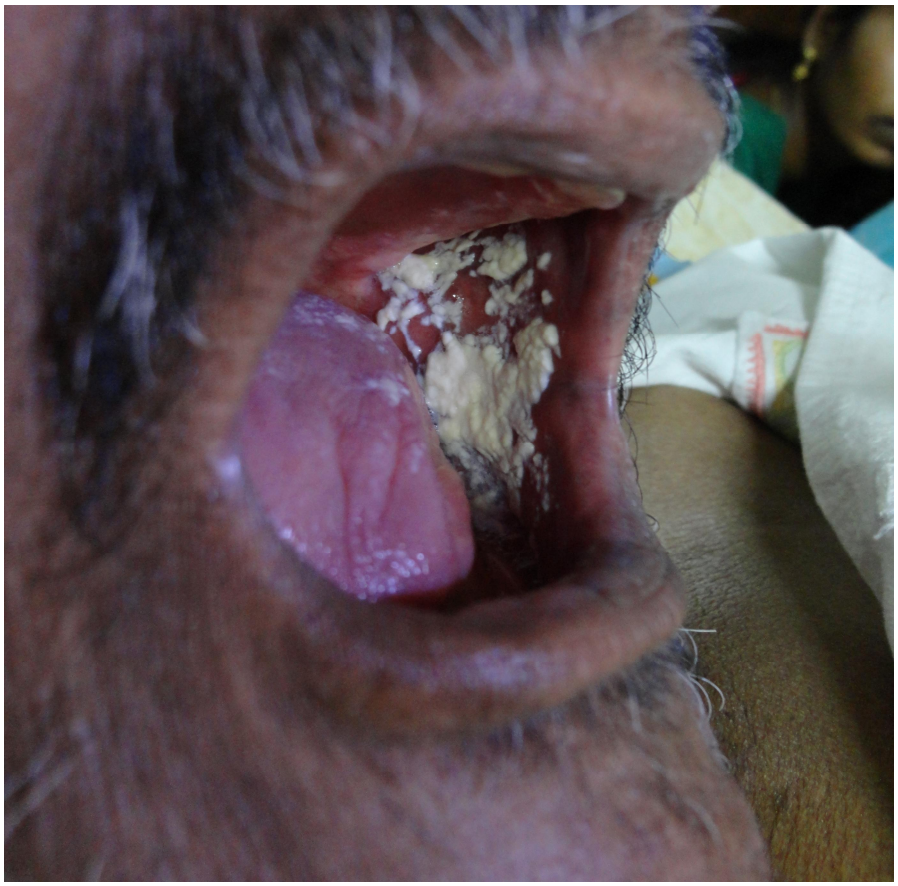
ORAL CANDIDIASIS

Pseudomembranous type with angular cheilitis



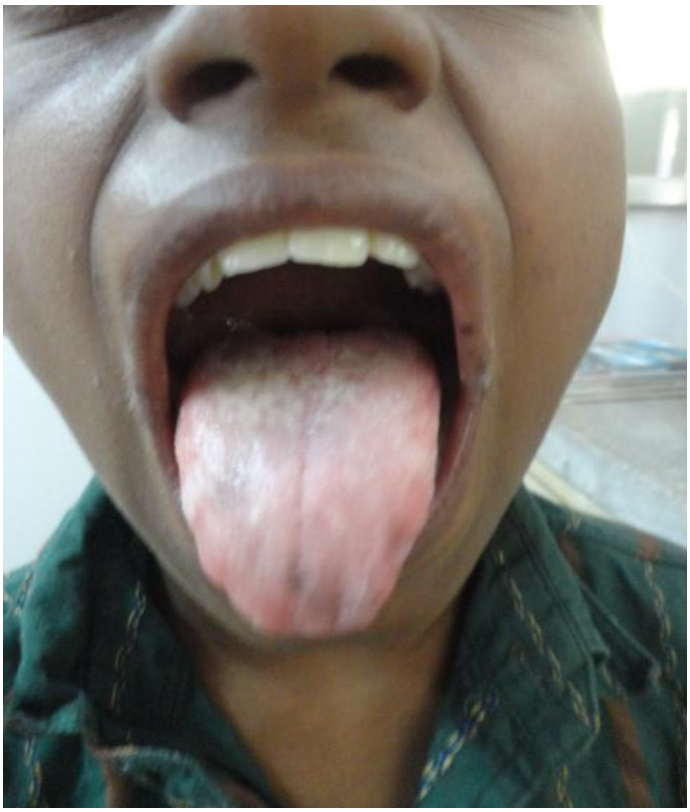


Plaque type of oral candidiasis

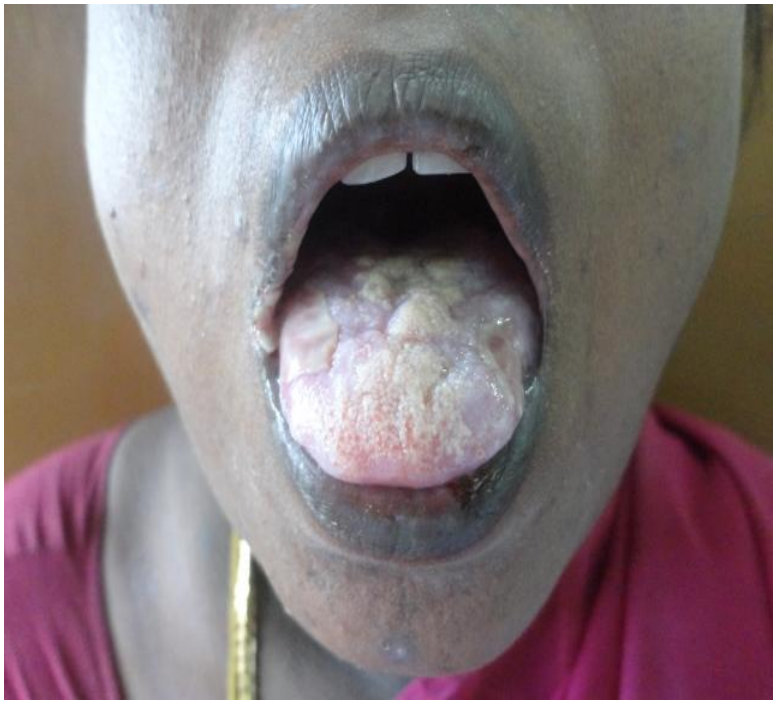


ORAL CANDIDIASIS IN HIV PATIENT –

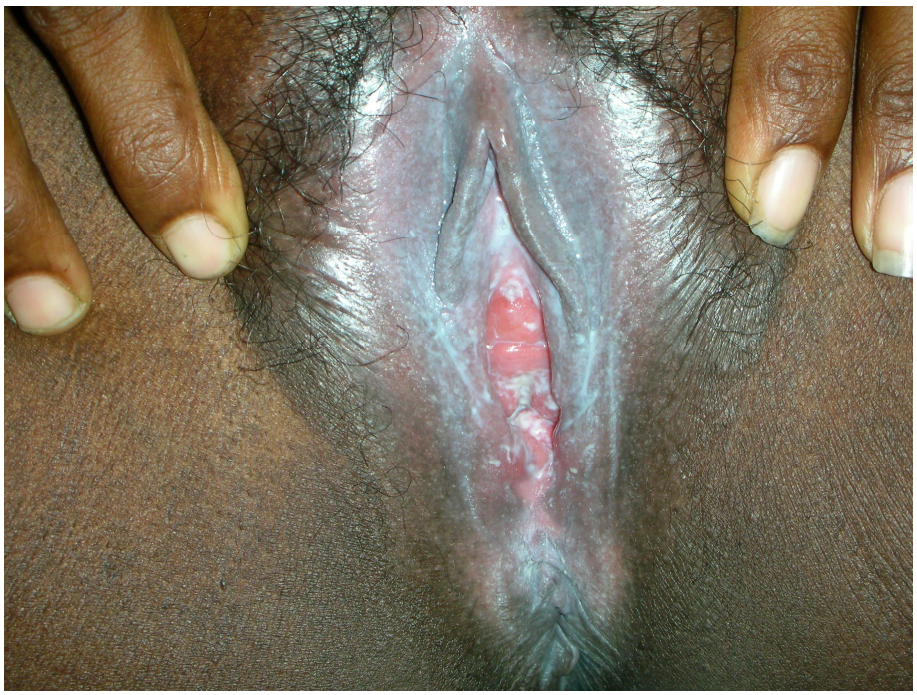
Pseudomembranous type with angular cheilitis



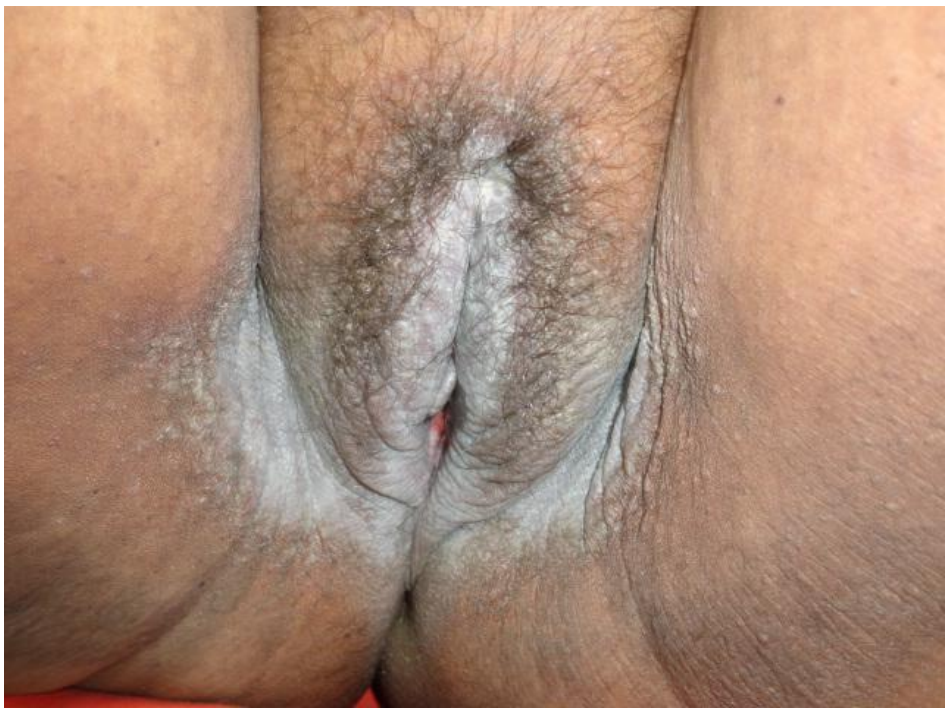
Pseudomembranous type in a patient on prolonged steroids



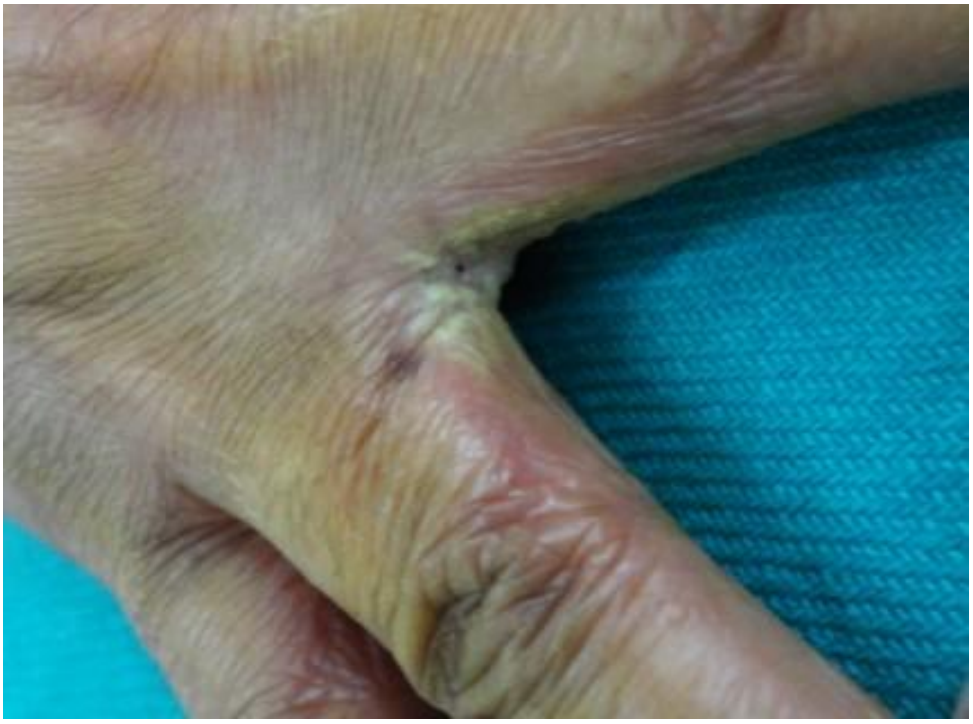
VULVOVAGINAL CANDIDIASIS



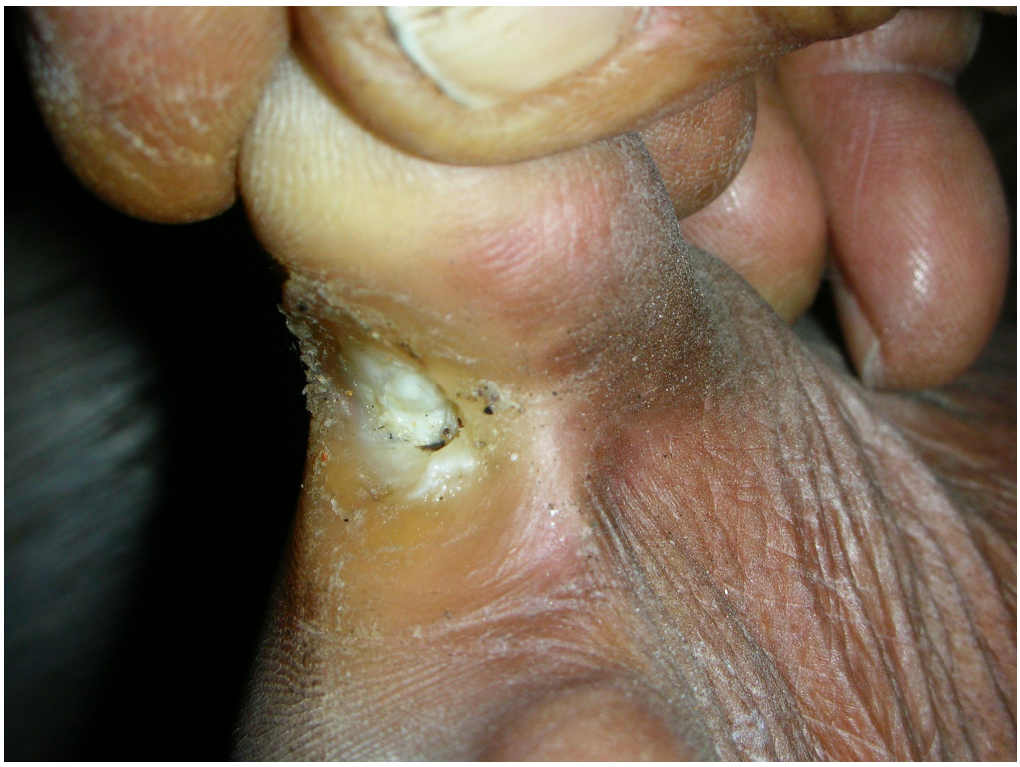
VULVOVAGINAL CANDIDIASIS WITH INTERTRIGO GROIN



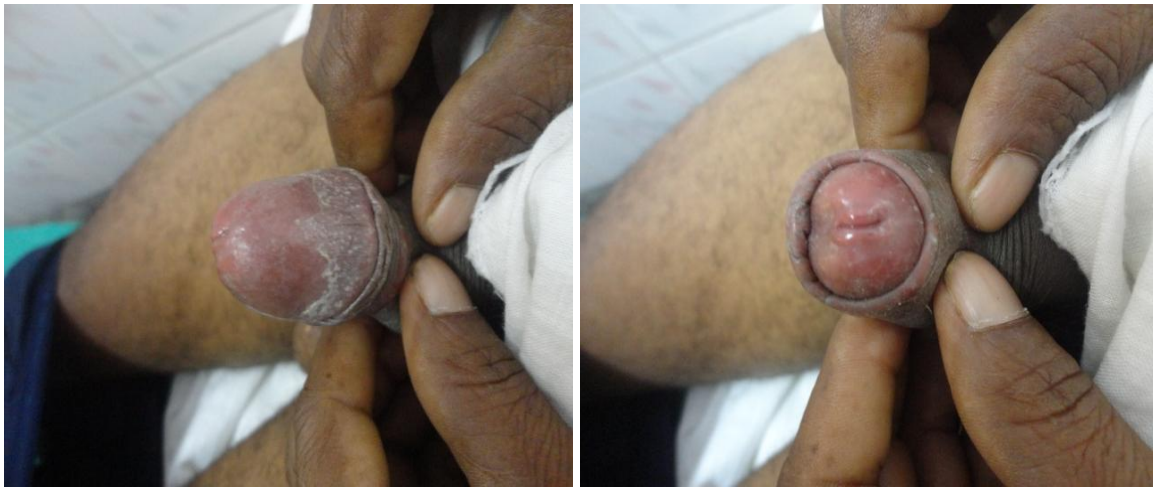
INTERTRIGO FINGER WEB SPACE



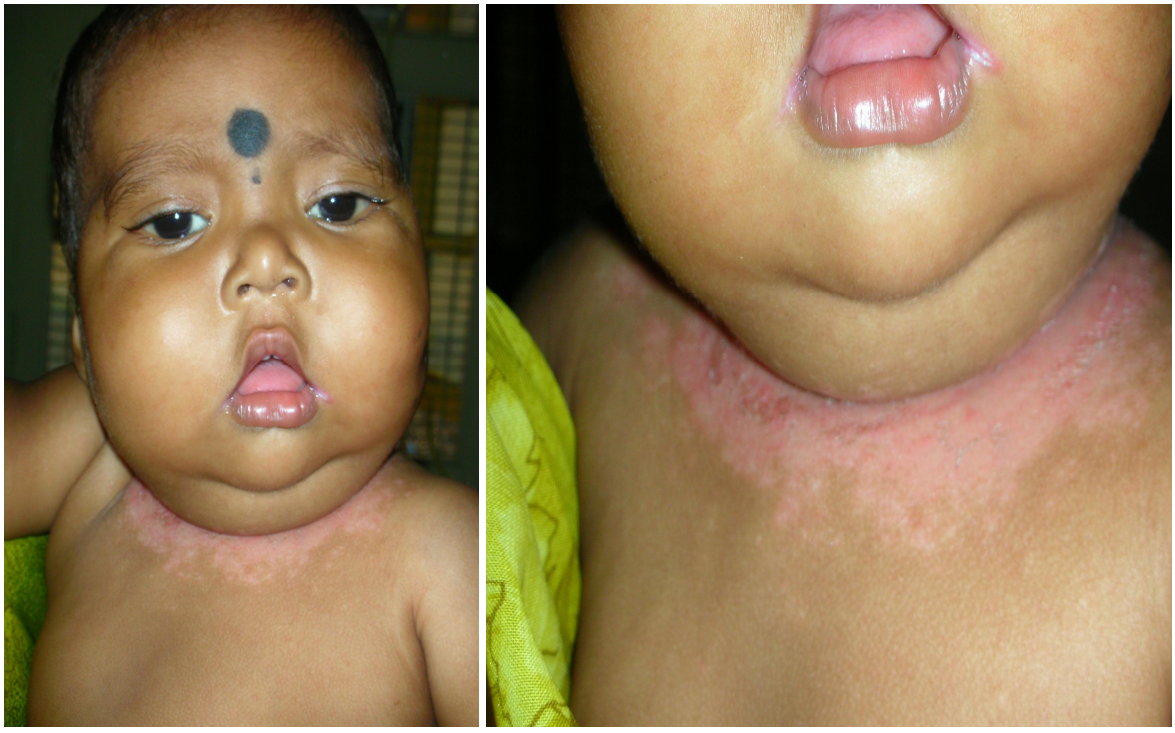
INTERTRIGO TOE CLEFT – EROSIO INTERDIGITALIS BLASTOMYCETICA



Balanoposthitis in a diabetic patient



Intertrigo Neck- with perleche in an infant with Nephrotic syndrome



CONCLUSION

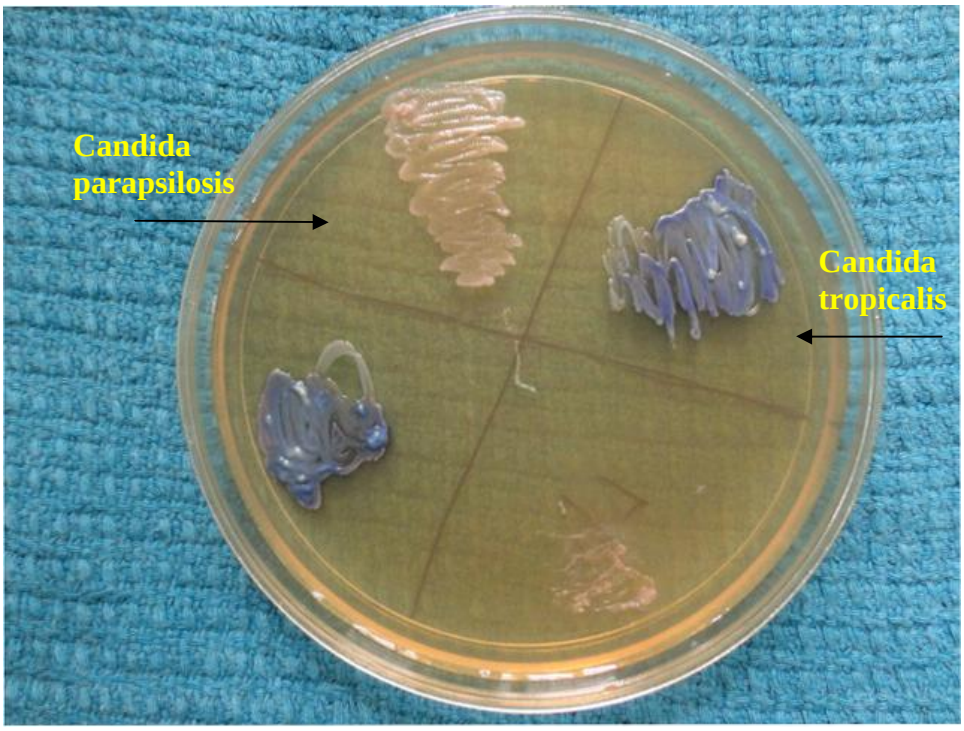
CONCLUSION

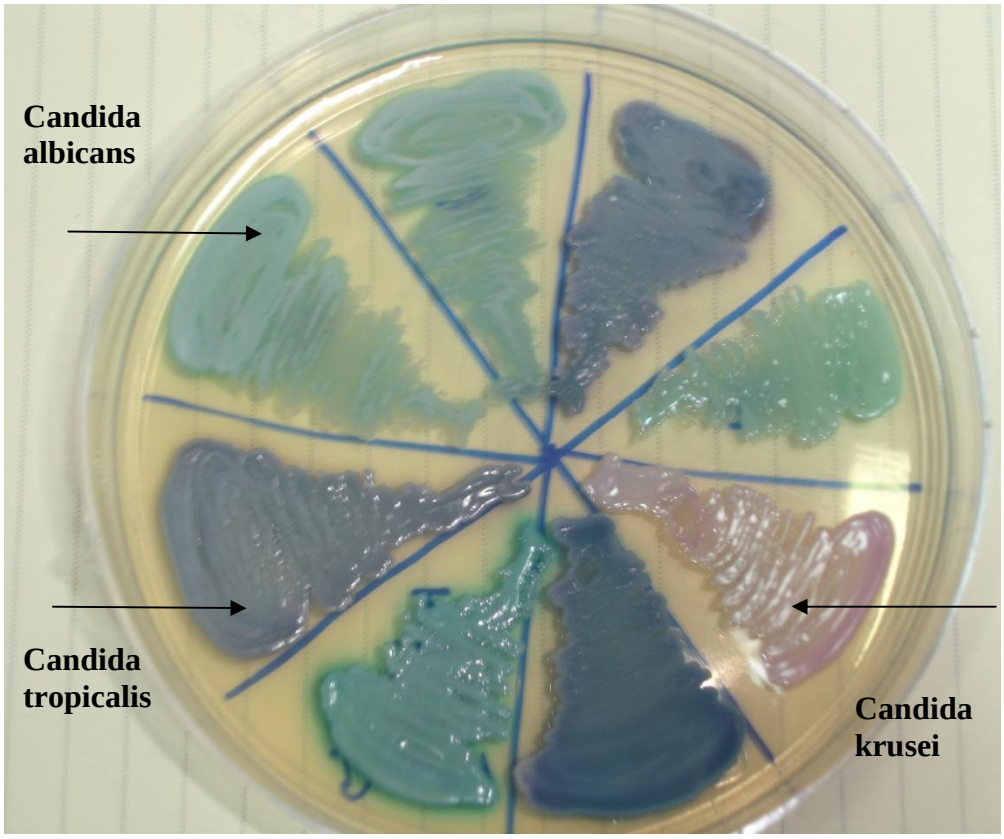
- Mucocandidiasis can occur in all age groups with majority of the affected individuals in the age group of 31-50 years.
- Females outnumbered the males and the male to female ratio was 1:2.7
- Mucocandidiasis was more common in immunosuppressed individuals than immunocompetent individuals.
- Mucosal candidiasis was more common than cutaneous candidiasis.
- Oral candidiasis was the most common clinical presentation followed by vulvovaginal candidiasis.
- Among the patients with oral candidiasis, pseudo membranous type was the most common presentation. The common predisposing factor was found to be immunosuppression. *Candida albicans* and *Candida tropicalis* were isolated in almost equal proportion in oral candidiasis.
- Vulvovaginal candidiasis was more common among the immunosuppressed individuals. *Candida tropicalis* was isolated in higher number than *Candida albicans.*
- *Nonalbicans* species were isolated in higher number than *albicans* species.
- The *nonalbicans* species isolated were *C.tropicalis, C.glabrata, C.krusei* and *C.parapsilosis*.

- Patients with O blood group had higher occurrence of mucocutaneous candidiasis.

- In this study, *C.tropicalis* was isolated in higher number than *C.albicans.* Further studies in a larger population would provide more conclusive information on the changing trends in the epidemiology of candidal infections and would aid in the optimal treatment of patients.

SUBCULTURE IN HI - CHROME MEDIA



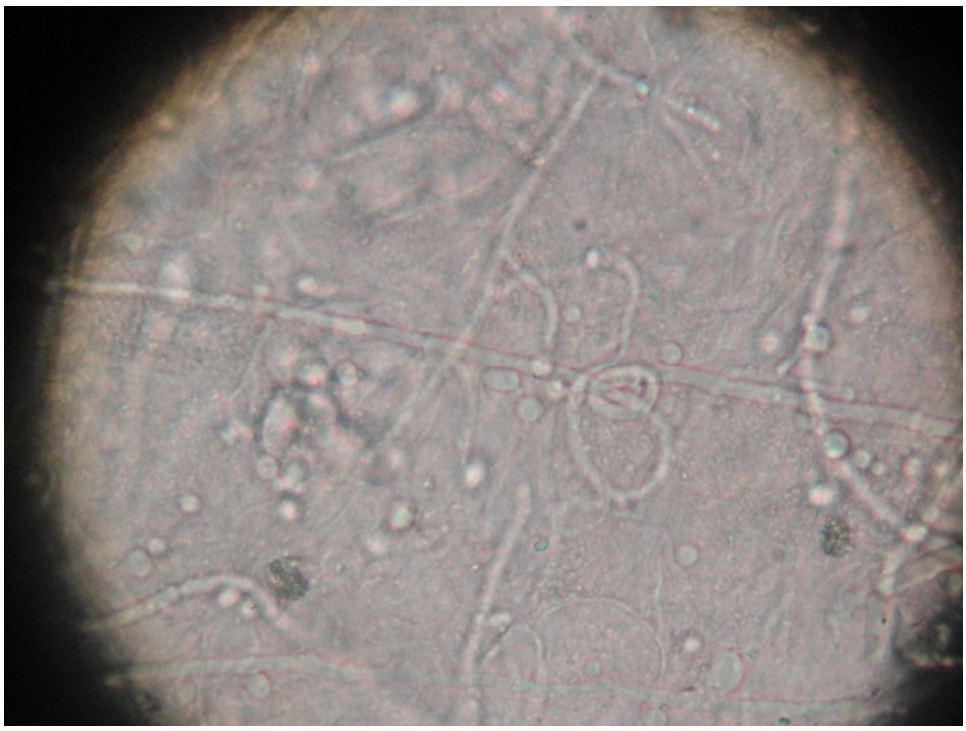


MACROSCOPIC COLONIES IN SDA AGAR

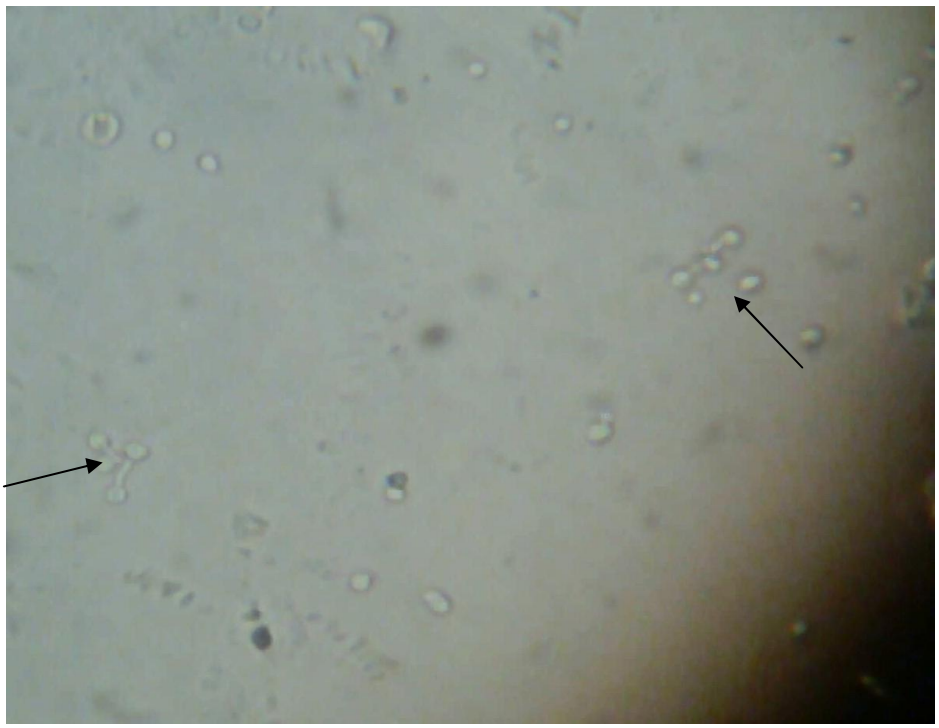
COLONIES IN CORN MEAL AGAR

SUBCULTURE IN HI - CHROME MEDIA SHOWING COLONIES OF CANDIDA ALBICANS

KOH mount showing pseudohyphae

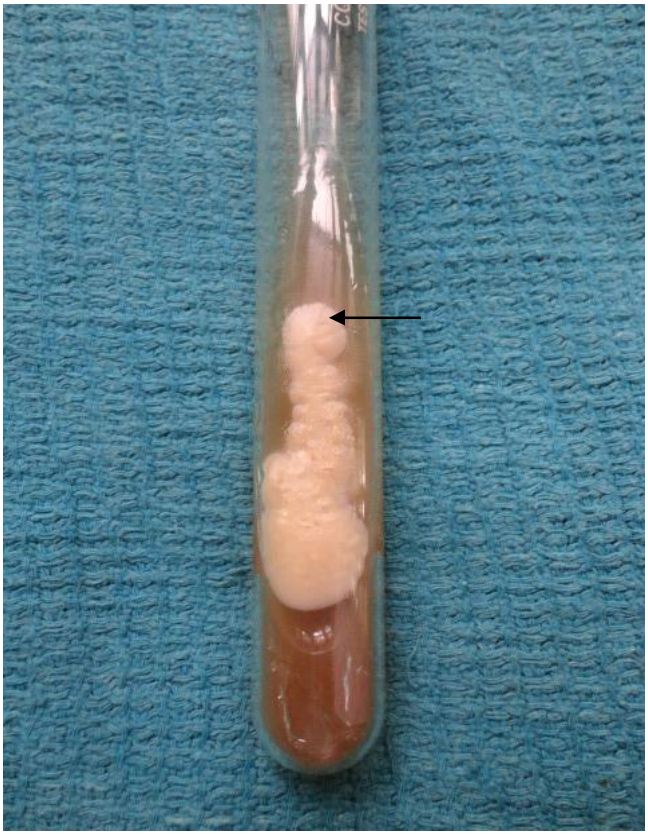


GERM TUBE TEST



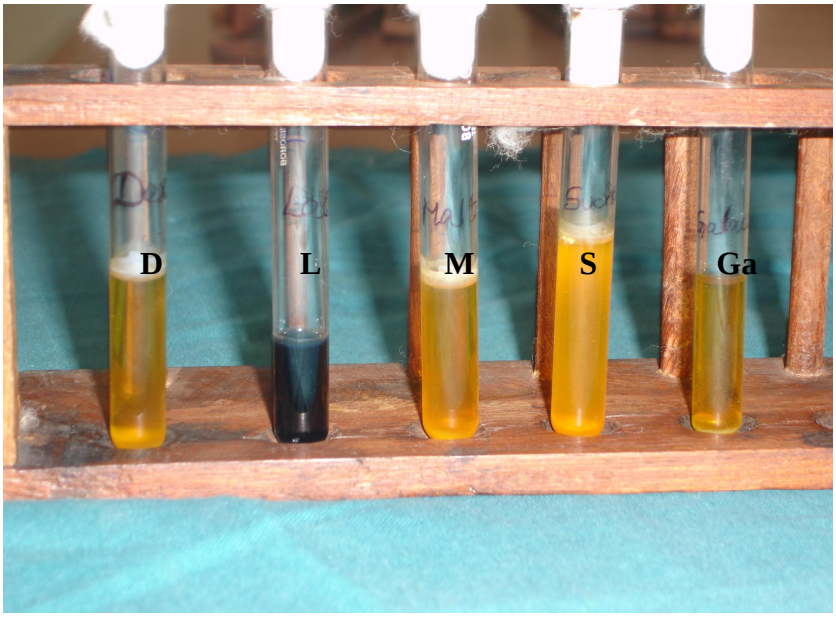
COLONIES IN SABOURAUD'S DEXTROSE AGAR

CANDIDAL COLONIES IN SABOURAUD'S DEXTROSE AGAR SHOWING MYCELIAL FRINGE



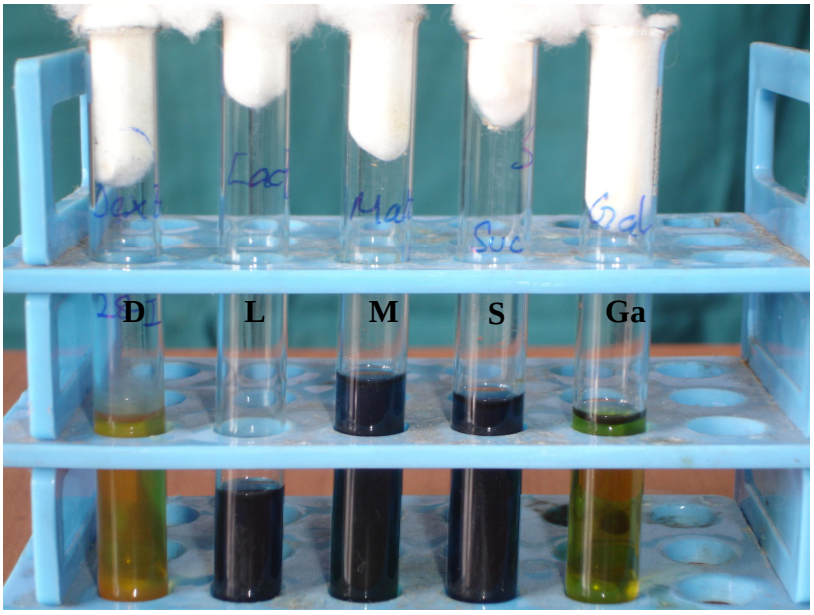
SUGAR FERMENTATION TESTS

Candida albicans



Dextrose, Sucrose , Maltose-fermented ; Lactose – not fermented

Candida parapsilosis



Dextrose - not fermented ; Lactose, Sucrose, Maltose - fermented

D- Dextrose, S- Sucrose, M- Maltose, Ga-Galactose ; Blue – not fermented ; Yellow – fermented

BIBLIOGRAPHY

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PROFORMA

PROFORMA

NAME :

AGE :

SEX :

OCCUPATION :

ADDRESS :

PRESENTING COMPLAINTS:

DURATION :

FAMILY HISTORY :

MARITAL HISTORY :

PREDISPOSING FACTORS:

- Diabetes
- Immunosuppressive drugs-details
- Pregnancy
- Malnutrition
- Systemic illness
- HIV

ASSOCIATED DERMATOLOGICAL DISORDER:

GENERAL EXAMINATION

- Anemia
- obesity

- nutritional status
- weight

SYSTEMIC EXAMINATION

- CVS:
- RS:
- ABDOMEN:
- CNS:

DERMATOLOGICAL EXAMINATION

- SITE
- MORPHOLOGY

INVESTIGATIONS:

BLOOD: TC,DC,ESR ,VDRL

ELISA FOR HIV

BLOOD GROUPING

PLASMA BLOOD GLUCOSE

MYCOLOGICAL:10 %KOH MOUNT

CULTURE IN SDA AGAR

SUBCULTURE IN CHROME AGAR

SUGAR FERMENTATION TEST

MASTER CHART

MASTER CHART

Sl.no	Age	Sex	Blood Group	Clinical Type	DM	HIV	other assotiations	Colour in hichrome media	candida species
1	55	M	o+	oc	N	P	N	LG	C.a
2	49	M	O+	OC	N	N	CS	B	C.t
3	28	F	B+	VVC	N	N	prg	B	C.t
4	50	M	O+	BP	N	N	N	B	C.t
5	1	M	O+	INT N	N	N	NS	LG	C.a
6	52	M	A+	OC	N	N	N	B	C.t
7	34	F	O+	OC	II	N	PV	LG	C.a
8	40	F	O-	OC	II	N	PV	LG	C.a
9	60	F	O+	OC	N	N	N	B	C.t
10	44	M	O+	INT G	N	N	N	B	C.t
11	65	F	B+	OC	N	N	N	LG	C.a
12	36	F	O+	OC	N	N	N	LG	C.a
13	36	F	O+	INT G	N	N	N	B	C.t
14	65	F	B+	INTG	N	N	N	B	C.T
15	45	M	O+	OC	II	N	PV	B	C.t
16	29	M	O+	OC	II	N	PV	LG	C.a
17	34	F	O+	INT G	N	N	N	LG	C.a
18	55	F	O+	INT G	N	N	N	LG	C.a
19	28	M	O+	OC	II	N	PV	B	C.t
20	47	M	O+	INT G	N	N	N	B	C.t
21	35	F	O+	INT G	II	N	N	P	C.k

Sl.no	Age	Sex	Blood Group	Clinical Type	DM	HIV	other assotiations	Colour in hichrome media	candida species
22	28	F	O+	BP	II	N	N	LG	C.a
23	2	F	B+	OC	N	N	N	LG	C.a
24	43	M	O+	OC	N	N	CA/SC	LG	C.a
25	26	F	O+	INT G	II	N	PV	P	C.k
26	25	F	O+	OC	N	N	N	LG	C.a
27	46	M	A+	OC	N	N	N	LG	C.a
28	32	F	B+	OC	N	N	N	LG	C.a
29	32	F	O+	VVC	II	N	N	Pu	C.g
30	44	F	O+	OC	II	N	N	LG	C.a
31	50	F	O+	OC	II	N	N	LG	C.a
32	38	F	B+	INT G	II	N	N	LG	C.a
33	53	F	O+	INT G	II	N	N	LG	C.a
34	37	F	AB-	VVC	N	N	Ps	LG	C.a
35	28	F	O+	VVC/R	II	N	N	Pu	C.g
36	30	F	O+	OC	II	N	PV	LG	C.a
37	43	F	O+	INT G	II	N	PV	LG	C.a
38	57	M	O+	OC	II	N	PV	Pu	C.g
39	14	M	B+	OC	N	N	RF	B	C.t
40	52	M	O+	OC	N	N	MRH	Pu	C.g
41	45	F	A+	OC	II	N	PV	B	C.t
42	36	F	B+	OC	II	N	PV	B	C.t
43	55	F	O+	VVC/R	II	N	BP	B	C.t
44	63	F	B+	VVC	II	N	N	B	C.t

Sl.no	Age	Sex	Blood Group	Clinical Type	DM	HIV	other assotiations	Colour in hichrome media	candida species
45	51	F	O+	VVC	II	N	N	B	C.t
46	35	F	O+	VVC/R	II	N	N	B	C.t
47	45	F	O+	OC	II	N	PV	LG	C.a
48	26	F	O+	VVC	II	N	N	B	C.t
49	35	F	O+	OC	N	N	PV	B	C.t
50	13	M	O+	OC	N	N	RF	Pu	C.g
51	42	M	O+	OC	N	N	RT	B	C.t
52	39	F	O+	OC	N	N	BP	B	C.t
53	29	F	O+	OC	II	N	SLE	Pu	C.g
54	47	M	O+	OC	II	N	PV	P	C.k
55	32	F	B+	VVC	II	N	PV	LG	C.a
56	40	F	O+	INT W	N	N	N	B	C.t
57	45	F	A+	OC	N	N	N	B	C.t
58	32	F	A+	VVC	N	N	N	LG	C.a
59	34	F	B+	VVC	II	N	N	B	C.t
60	48	F	B+	VVC	II	N	N	LG	C.t.
61	54	F	O+	INT G	N	N	N	P	C.k
62	57	F	O+	OC	II	N	PV	LG	C.a
63	23	F	O+	OC	N	N	PV	LG	C.a
64	65	F	O+	VVC	N	N	N	lg	C.a
65	50	F	O+	VVC	N	N	N	LG	C.a
66	64	F	A+	VVC	II	N	N	Pu	C.g
67	65	F	O+	VVC	II	N	N	B	C.t

Sl.no	Age	Sex	Blood Group	Clinical Type	DM	HIV	other assotiations	Colour in hichrome media	candida species
68	64	M	O+	INT G	N	N	N	B	C.t
69	36	M	O+	INT T	N	N	N	P	C.k
70	35	F	O+	OC	N	N	SLE	B	C.t
71	46	F	O+	VVC	N	N	N	LG	C.a
72	67	F	B+	VVC	N	N	N	LG	C.a
73	26	F	O+	VVC	II	N	N	LG	C.a
74	45	F	O+	VVC	N	N	N	LG	C.a
75	55	F	O+	VVC	II	N	N	B	C.t
76	65	F	B+	VVC	II	N	N	W	C.p
77	23	F	O+	VVC	II	N	N	B	C.t
78	25	F	O+	VVC	II	N	N	B	C.t
79	45	F	O+	VVC	II	N	N	B	C.t
80	56	M	B+	OC	N	N	N	B	C.t
81	22	F	O+	VVC	II	N	N	B	C.t
82	37	F	A+	OC	II	N	PV	B	C.t
83	24	F	O+	OC	N	N	N	LG	C.a
84	24	F	O+	OC	N	N	P.Ps	PP	C.g
85	70	F	B+	OC	II	N	PV	PP	C.g
86	48	F	O+	VVC	II	N	N	Pi	C.k
87	35	F	O+	OC	N	N	PV	B	C.t
88	31	F	O+	VVC/IG	II	N	N	B	C.t
89	60	F	B+	OC	N	N	N	B	C.t
90	63	F	O+	VVC	N	N	N	B	C.t

Sl.no	Age	Sex	Blood Group	Clinical Type	DM	HIV	other assotiations	Colour in hichrome media	candida species
91	13	M	B+	OC	N	P	N	B	C.t
92	48	F	A+	VVC	II	N	N	LG	C.a
93	45	M	O+	OC	N	P	N	LG	C.a
94	29	M	O+	IWS	N	N	N	B	C.t
95	62	M	O+	ITC	N	N	N	LG	C.a
96	42	F	O+	OC	II	N	N	Pi	C.k
97	25	F	O+	OC	II	N	SLE	B	C.t
98	40	M	O+	OC	II	N	N	PI	C.k
99	44	M	B+	OC	N	N	ERY	B	C.t
100	64	F	B+	VVC	II	N	N	B	C.t

ABBREVIATIONS

ABBREVIATIONS

M	**-**	**Male**
F	**-**	**Female**
OC	**-**	**Oral candidiasis**
VVC	**-**	**Vulvovaginal Candidiasis**
IG	**-**	**Intertrigo groin**
IWS	**-**	**Intertrigo web spac**
INT TC	**-**	**Intertrigo Toe cleft**
INT N	**-**	**Intertrigo neck**
Ps	**-**	**Psoriasis**
PPs	**-**	**Pustular psoriasis**
BP	**-**	**Balanoposthitis**
PV	**-**	**Pemphigus vulgaris**
ERY	**-**	**Erythroderma**
SLE	**-**	**Systemic lupus erythematosus**
MRH	**-**	**Multicentric reticulohistiocytosis**
N	**-**	**Nil**
P	**-**	**Positive**
C.t	**-**	**Candida tropicalis**
C.a	**-**	**Candida albicans**
C.p	**-**	**Candida parapsilosis**
C.k	**-**	**Candida krusei**
C.g	**-**	**Candida glabrata**
B	**-**	**Blue**
LG	**-**	**Light Green**
Pi	**-**	**Pink**

INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI -3

Telephone No: 04425305301
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CERTIFICATE OF APPROVAL

To
Dr. M. Subhashini
PG In MDDVL
Madras Medical College, Chennai -3

Dear Dr. M. Subhashini

The Institutional Ethics Committee of Madras Medical College reviewed and discussed your application for approval of the project / proposal / clinical trail entitled " A clinicomycological study of Mucocutaneous candidiasis" No. 13102010.

The following members of Ethics Committee were present in the meeting held on 22.10.2010 conducted at Madras Medical College, Chennai -3.

1. Prof. S.K. Rajan, MD	-- Chairperson
2. Prof. J. Mohanasundaram, MD,Ph.D,DNB Dean, Madras Medical College, Chennai -3	-- Deputy Chairman
3. Prof. A. Sundaram, MD Vice Principal , MMC, Chennai -3	-- Member Secretary
4. Prof R. Nandhini, MD Director, Institute of Pharmacology, MMC, Ch-3	-- Member
5. Prof. Pregna B. Dolia , MD Director, Institute of Biochemistry, MMC, Ch-3	-- Member
6. Prof. C. Rajendran , MD Director, Institute of Internal Medicine, MMC, Ch-3	-- Member
7. Prof. Md. Ali, MD, DM Professor & Head ,,Dept. of MGE, MMC, Ch-3	-- Member
8. Thiru. S. Govindasamy BA.BL	-- Lawyer
9. Tmt. Arnold Soulina	-- Social Scientist

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, any SAE occurring in the course of the study, any changes in the protocol and patient information / informed consent and asks to be provided a copy of the final report

Member Secretary, Ethics Committee

A CLINICOMYCOLOGICAL STUDY OF MUCOCUTANEOUS CANDIDIASIS

ABSTRACT

Background : *Candida* is an ubiquitious organism causing superficial fungal infection that is commonly encountered in clinical practice. The knowledge of the change in the epidemiology, clinical spectrum and antifungal susceptibility may aid for the appropriate treatment decisions.

Aim and Objective : This study has been designed to study the age wise & sex wise distribution, the predisposing factors, the common clinical features, different species of candida and common blood group susceptible to mucocutaneous candidiasis.

Materials and Methods : One hundred patients with symptoms and signs of mucocutaneous candidiasis attending the OPD, Mycology section of the Department of Dermatology were included in the study. Culture in SDA, subculture in Hichrome agar and sugar fermentation tests were done for all patients with positivity for candida in 10% KOH examination.

Results : The minimum age group affected was a one month old infant and maximum age group affected was 70 years female. The maximum number of patients were in the age group of 31 – 50 years with mean age 41.5 years. There was female predominance with 73% and males were 27%. The male to female ratio was 1:2.7. Mucosal candidiasis was found in 82 patients and 18 patients had cutaneous candidiasis. Oral candidiasis was detected in 48 patients, followed by Vulvovaginal candidiasis in 32 patients, Balanoposthitis, intertrigo toe cleft and intertrigo finger webspace in 2 patients each.Pseudomembranous candidiasis was present in 30 patients (62.5%), followed by angular cheilitis 10 patients (20.8%) and acute erythematous type in 8 patients (16.7%). Immunosuppression was the major predisposing factor found in 67% of patients. Among the immunosuppressed, 52 patients (77.61%) had diabetes mellitus. *Nonalbicans* species was isolated in 63% and *albicans* in 37%. Of the *nonalbicans* species, *C.tropicalis* was isolated in 45 patients followed by *C.glabrata* in 9 patients, *C.krusei* in 8 patients and *C.parapsilosis* in 1 patient. `O' blood group patients had higher occurrence of mucocutaneous candidiasis.

Conclusion : In summary, maximum number of patients were in the 4^{th} and 5^{th} decade with females outnumbering the male patients. Mucosal candidiasis were more common than cutaneous candidiasis. *Nonalbicans* species were the most common isolate of which *C.tropicalis* were isolated in higher number than *C.albicans.* However, further studies in larger population would provide conclusive information on the changing epidemiology of mucocutaneous candidiasis.

Key words : Mucocutaneous candidiasis, oral candidiasis, vulvovaginal candidiasis, *nonalbicans spp, C.tropicalis, C.albicans.*