CHAPTER 1

Introduction

_Candida_ is one of the frequently encountered fungal opportunists and is now regarded as the most common cause of serious fungal diseases. _Candida species_ are very important human pathogen, _Candida albicans_ is one of the major pathogens incriminated in the etiopathogenesis of vast spectrum of infection that are encountered in human beings.

_Candida_ is found in low numbers on healthy intact skin but rapidly colonizes the damaged skin and intertriginous sites, which are often moist and become shafted. _Candida_ also colonizes the oral and vaginal mucosa and overgrowth may result in disease in these sites. Colonization of neonatal skin and gastrointestinal tract is the first step in pathogenesis of invasive Candidiasis (Mendiratta et al., 2006). They play a major role in causing infection in people having depressed immunity.

Increasing infection rates have become an alarming subject of study as _Candida_ includes many species involvement. There is an increasing trend of infection by non-albicans _Candida_ (Nguyen et al., 1996). These factors have
encouraged colossal interest in research in all facet of biology of all *Candida* species.

The aim of present study is based on the epidemiological picture of *Candida albicans* and non-*albicans Candida* encountered in different infections including HIV/AIDS. It is to be noted that, in Barak Valley, there is no evidence of carrying out the study made elaborately earlier. Hence, this study made shows that, the infections with *C. albicans* and non-*albicans Candida* prevails in this remote land of our country also. The lower socioeconomic condition, lack of awareness on hygiene, temperature and humidity of this geographical area which also contribute much to the significant association of *Candida species* causing infection. The extremes of life that is infancy and old age are associated with a decreased resistance to infection, so chances of getting infection with *Candida* is more. The organism is also well associated with nosocomial infection, e.g., catheter associated urinary tract infection, surgical site infection and central venous catheter related blood stream infection (CRBSI).

Candidiasis is primary or secondary infection involving a member of the genus *Candida*. With the increasing importance of candidiasis, there is a need for practical method for identification of this fungus. The advent of chemotherapeutic and antibiotic agents as well as appearance of HIV infection has lead to emergence of several opportunistic pathogens in the scene of clinical medicine. *Candida albicans* probably the most important pathogen causing vast majority of infection. The genus *Candida* is a heterogeneous group of approximately 150 yeast species. The other species of *Candida* viz., *C. tropicalis, C. krusei, C. guilliermondii, C.*
parapsolosis, C. stellatoidea, C. lusitaniae, C. glabrata, however any one of these can be involved in candidiasis. Candida and other non pathogenic species of Candida are common inhabitant of oral, respiratory, intestinal tract, genitelia, skin of normal healthy adults. Candidiasis is most frequently encountered in patients with diminish host defense.


Realizing the increasing isolation of Candida sp. in immune-compromised and hospital patients, a precise and accurate typing system is necessary for epidemiological investigations. It has been noted from different studies that the tendency for persons who are living with HIV/AIDS in long term harbor Candida albicans as well as other non-albicans Candida. Oropharyngeal candidiasis is the most common opportunistic disease in HIV infected individuals.

**Biology of Candida**

The biology of Candida is found to be similar with other yeast representatives mainly Saccharomyces cerevisiae, but the natural habitats of two species differs considerably; S. cerevisiae is associated with fruits and Candida albicans with warm blooded animals. Candida sp. multiplies by binary fission and can produce true hyphae as well as pseudohyphae.
The cell wall of *Candida* contains polysaccharide. The main constituents of cell wall are glucans, phosphorylated mannans and chitin. Polypeptide and proteins of cell wall play the role of antigenecity of the organism and help in the adhesion with the host cell surface.

*Candida* shows unique morphological forms like budding and blastoconia which grow pseudohyphal form to true hyphae. The hyphal form of fungus confers advantages from the point of view of virulence. Both the form of *Candida* that is yeast and hyphal form can penetrate human tissue and may exert virulence.

**Epidemiology**

The *Candida* species are the one of the most common colonizer of human being and they inhabit different parts of the body for example skin, under the finger nails, gastrointestinal tract, vagina and urethra. Prevalence of *Candida* carriage in human depends on the nature of the site, type of individual habitat and the method of sampling adopted. Many studies have been done which show variation in the carriage or colonization in healthy as well as immunocompromised individual (Pittet et al., 1994).

*Candida* sp. also play important role in causing infection in hospitalized patients and account for the one of the major pathogen in hospital acquired infection. The condition of host is important in determining the infection rather the organism itself. Adherence of *Candida* sp. contributes the tissue invasion and production of virulence factors or pathogenicity.
Clinical disease

*Candida albicans* perhaps the most common protean infectious agent that affects man. The clinical manifestation Candidiasis can be classified as follows.

**a) Cutaneous candidiasis**

Intertriginous and generalized Candidiasis:

Intertriginous candidal infection is most commonly seen in axilla, groin, inter- and sub mammary folds, intergluteal folds, interdigital spaces and umbilicus. In men infection occur due to increased moisture in crural folds, usually near the scrotum (Rippon, 1988). The upper medial thigh is most commonly affected area and buttocks. However moisture, heat, maceration of skin are predisposing factors in normal individuals and diabetes mellitus, occlusion of skin over weight and use of broad spectrum antibiotics are additional factors for the infection. The initial lesions of superficial cutaneous Candidiasis (intertrigo) are papules or vesicopustules that later enlarge and become confluent. The lesions become erythematous and have an irregular margin. Itching are common symptoms.

**Paronychia and onychomycosis:**

The food handlers, dishwashers, health-care workers, and children who suck their thumbs, farmers who have prolonged exposure of their hands to moisture have an increased risk of developing candidal paronychia. Occasionally, manipulation of the cuticle by a manicurist may precede the infection. Initially, the proximal nail fold becomes red and edematous. Damage or loss of the cuticle and a
purulent discharge from the nail fold soon follows. Chronic infections may result in nail dystrophy (William and Roderick, 2005).

Candidal onychomycosis may follow candidal paronychia. *Candida sp.* first attacks the soft tissue around the nail and then invades the nail plate. Infection of the nail matrix may result in transverse depressions (Beau’s lines), rough, irregular nail plates, and dystrophy (Andre and Achten, 1987). A second, much less common form of candidal onycholysis occurs in chronic mucocutaneous Candidiasis. Here the organism invades the nail plate directly and may affect the entire thickness of the plate (Elewski, 1995). A third variety of candidal onychomycosis resembles dermatophytic distal subungual onychomycosis, occurs more often on the hands, and is characterized by onycholysis and distal subungual hyperkeratosis (William and Roderick, 2005).

**Diper disease (napkin candidiasis):**

It has been shown that the causative organisms of diper rash in infants are commonly *Candida sp.*, this is also known as napkin candidiasis. Maceration and wet diaper for prolong period favour the growth of this organism. Progressive macular erythematous rash may develop during the course of infection.

**Candidal granuloma:**

In this condition there is vascularised papules covered with a thick adherent yellowish brown crust over face, scalp, finger-nails, trunk, leg and pharynx. This condition is found in children.
b) Mucocutaneous Involvement

Oral thrush:

Oropharyngeal candidiasis is most common in infants, patient with diabetes mellitus, leukemia, lymphoma, malignancy, neutropenia, patient receiving antibacterial antibiotics and in HIV patients. The classical symptom of oral thrush is with congestive reddening of mucous membrane which gives dry shiny appearance. The thrush can be diffused or confined to gums, palate, tongue or buccal mucosa.

Oral candidiasis is common early oral manifestation of AIDS and a reliable prognostic indication of this disease (Samaranayake and Hoimstrup; 1989). Oral candidiasis perhaps the most frequent opportunistic infection associated with HIV disease and AIDS. It has been noticed about 11-96 % of HIV infected individuals develop oral candidiasis during their disease span (Samaranayake and Hoimstrup, 1989).

Vaginitis and balanitis:

Vulvovaginal candidiasis is a significant problem for women of child bearing age. Approximately 75% of women experience atleast one episode of vulvovaginal candidiasis during their life time (Sobel et. al., 1998). It is a common condition in women often associated with the use of broad spectrum antibiotics, third trimester of pregnancy, low vaginal pH and diabetes mellitus, contraception and sexual activity also play role in infection. Infection spread to perineum, the vulva, and the entire inguinal area. Vaginal candidiasis along with oral candidiasis
may also be a presentation of HIV infection or AIDS. Symptoms include intense vulval pruritus, burning, erythema, dyspareunia associated with creamy white, curd-like discharge.

In case of balanitis symptoms include erythema, pruritus and vesiculopustules on the glans penis or prepuce.

**Bronchial and pulmonary:**

Pulmonary candidiasis may be caused due to extension of oropharyngeal candidiasis; it can also be acquired by haematogenous dissemination causing pneumonia. Invasive pulmonary candidiasis has been found in many adult cases (Oblath et al., 1951), in children (Joshi and Wang, 1923), and in neonates (Linhartova and Chung, 1963).

Clinical bronchopulmonary candidiasis was first described by Castellani (1914) among tea plantation workers in Cylon. First well documented case of bronchopulmonary was described by Lewis in 1933 (Gupta et al., 1996). Latter many reports came from India. Various *Candida sp.* found to be reported from respiratory tract infection. Healthy person do harbor many species of *Candida.* It has also reported by Wessler et al., (1945) that there is remarkable increase in bronchopulmonary candidiasis due to use of broad spectrum antibiotics therapy (Woods et al., 1957, Kobza et al., 1976, Masur et al., 1977).
Gastrointestinal: Esophagitis, Gastritis, Peritonitis, Enteric and Perianal disease:

Esophageal candidiasis is often the extension of lesions from oral cavity or from the thrush in new born. Mostly it is asymptomatic or may have burning pain in the substernal area, epigastrium or throat (Zillessen et al., 1986) worse pain while patients with hematological malignancy or patients with acute leukemia may have ulceration of the stomach which can be secondarily invaded or colonized by *Candida*. This often can be detected by presence of *Candida* in stool.

Chronic mucocutaneous candidiasis (CMC):

Chronic mucocutaneous Candidiasis gives a heterogeneous picture in which oral candidiasis is the primary source. It is generally confined to infants or late childhood with the poor cell-mediated immunity. The heterogeneous picture of clinical symptoms includes skin, nail, and mucous membrane involvement. Four types of CMC exist including familial CMC, CMC with endocrinopathy, CMC with familial susceptibility and endocrinopathy and CMC with onset after 10 years of age (Ruhnke, 2002). Several disorders are associated with CMC including hypo-endocrine function, autoimmune diseases, immunosupression, hepatitis, diabetes, thymoma, dental enamel dysplasia, vitiligo, alopecia, and infectious diseases (Filler and Edwards, 1993; Kirkpatrick,1994).
c) Systemic Involvement

Urinary tract:

Urinary tract candidiasis often seen associated with prolonged catheterization and may originate from colonizer of genital tract which is common in women. Other predisposing factors of candida involvement could be diabetes mellitus, diseases associated with incomplete bladder emptying, chronic outlet obstruction from prostatic hypertrophy. Candida sp. other than C. albicans are mostly common in urinary tract (John, 2011). Pyuria in presence of candiduria can suggest bladder candidiasis, but often associated with bladder disease. Asymptomatic candiduria may occur due to prolonged antibiotic or steroid treatment. Renal candidiasis can occur due to ascending infection or may be haematogenous dissemination from other organ. The development of fungus ball in renal pelvis can complicate the infection.

Endocarditis:

Subacute candidiasis can cause due to haematogenous spread of candida in patients with abnormal native valve or prosthetic heart valve. The predisposing factor for endocarditis is intravenous drug users and use of intravenous catheter.

Meningitis:

Haematogenous spread of candida in low weight neonates is found to cause meningitis (Chander, 2009).
Disseminated Candidiasis:

Disseminated candidiasis occurs in immunocompromised patients or in patients who are admitted in the hospital for longer period and use of broad spectrum antibiotics. Patients with intravenous catheter, urinary catheter, surgical procedure, neutropenia, severe burn are also prone to acquire disseminated candidiasis. Intravenous catheter patients are prone to infection of cardiac valves, retina and the vein where the catheter is located (Kown Chung and Bennett, 1992).

New born who receive long term antibiotics therapy or parental nutrition by umbilical or intravenous catheters are prone to candidemia. Candidemia in neonates can cause meningitis, endocarditis and arthritis of knee (Kown Chung, and Bennet, 1992).

Objectives of the study:

1. To study the frequency and profile of Candida sp. from different clinical specimens in immunocompromised and immunocompetent in health care hospital.

2. To characterize the Candida sp. isolated from clinical specimens.

3. Characterization of Candida sp. according to morphological and biochemical tests.

4. Susceptibility to antimycotic agents in invitro condition.

5. Comparison of susceptibility testing pattern of Candida sp. isolated from different clinical specimens.

6. Analysis of prevalence of Candidiasis.