Abstract
Fungi are ubiquitous. Some of them are commensal organisms living on our skin, mucosal surfaces, intestines and urinary tract. Given the availability of nutrients in the human body, it is not surprising that for some fungal species, this represents a prime location for colonization and infection. But fortunately the human immune system is capable of evading fungal infections to such an extent that till 20 years back, fungi were assumed to be innocuous and rarely identified as human fungal pathogens. However during the 1980s there was a sudden increase in fungal infections due to raise in incidence of immunocompromised patients namely AIDS, cancer and transplant recipients.

The first study was made to find the prevalence of *albicans* and non *albicans* in pregnant and non-pregnant women. Pregnancy is identified as a risk factor in the occurrence of vaginal candidiasis. The objectives of our study were: to determine the microscopic findings of vaginal swab, frequency of Candida species in the culture of pregnant women and non-pregnant patients, to determine the *Candida* species in all cultures, and to determine the frequency and differences in the frequency of *C. albicans* and non- *albicans* species. In one year study carried out during year 2007, we tested patients of Gynaecology and Obstetrics OPD, AMU, Aigarh. 431 women included in this study were separated into two groups: 197 pregnant (in the last trimester of pregnancy), and 234 non-pregnant woman in period of fertility. The vaginal swabs were examined microscopically. The yeast, number of colonies, and the species of *Candida* were determined on Sabouraud dextrose agar in presence of antibiotics. To determine the *Candida* species, we performed germ tube test for detection of *C. albicans*, and cultivation on the selective medium and assimilation tests for non- *albicans* species detection. The results showed positive microscopic findings in the test group (44.5%) and greater number of positive cultures (42.5) as well. *C. albicans* was the most commonly detected species for the test group (44.5%) and control group(27.8%). The most commonly non- *albicans* species identified for the test group were *C. glabrata* (4.9%) and *C. krusei* (2.4%), and for the control group were *C. glabrata* and *C. parapsilosis*. The microscopic findings and number of colonies in positive cultures had co-relation. In the test group, we observed an increased number of yeasts, and the pseudohyphae and blastopores by
microscopic examination as an indication of infection. In the control group, we observed a lesser number of yeasts, in the form of blastopores, as an indication of the Candida colonisation. The obtained results indicate that pregnancy, as the risk factor for incidence of infection, has the significant role in the incidence of vaginal candidiasis.

The second study aimed to determine the frequency of Candida species in women of different age groups as well as to suggest the criteria for the diagnosis of vulvovaginal candidiasis (VVC). A prospective study of vulvovaginal candidiasis was carried out using laboratory diagnosis, with the estimation of vaginal pH and the direct microscopic and biochemical examination of vaginal discharge/secretions. Vaginal cultures for Candida species were collected from 1050 women with vulvovaginal symptoms. Out of 1050 women, 215 (20.47%) were positive for Candida species. Of 215 women, 172 (80%) had pH within the normal range and 167 (77.67%) were showing yeast cells and mycelia on direct microscopic examination. Candida albicans accounted for 46.9% of cases, Candida glabrata 36.7%, Candida parapsilosis 10.2%, Candida tropicalis 2.8%, Candida krusei 1.4%, and Candida kiefer 1.9%. The frequency of culture positivity was related to pregnancy (P < 0.001), an increase in parity (P < 0.001), and use of oral contraceptives (P < 0.001) and antibiotics (P < 0.001). The most common signs and symptoms in 215 women with positive cultures were pruritus with or without vaginal discharge and vaginal erythema. Conclusion: Our study suggests that vulvovaginal candidiasis can only be diagnosed by using clinical criteria in correlation with vulvovaginal symptoms and Candida cultures.

The third study was conducted to assess the molecular epidemiology and drug susceptibility of Candida causing invasive candidiasis in a NICU and to compare C. albicans and non-albicans Candida spp. infections. Species identification was performed by conventional methods. Susceptibility testing was carried out for amphotericin B, flucytosine, fluconazole, posaconazole and itraconazole using the broth microdilution method. Molecular biotyping of Candida albicans was performed by DNA fingerprinting with CARE-2 probe. RAPD analysis was also performed for non albicans. Statistical analysis was performed by Student’s t test,
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Fisher's exact test wherever applicable. During the study period, invasive candidiasis developed in 80 neonates, resulting in an overall incidence of 1.3% that demonstrated a declining tendency over the study epoch. During the study period 2005-2006, *C. albicans* was predominantly isolated, while during the period 2009-2010, non- *albicans* *Candida* species, particularly *C. parapsilosis*, was found to be the most common species (*P*<0.001). Although the overall mortality due to candidemia was observed as 30%, mortality related to *C. albicans* and *C. parapsilosis* was found to be 39.5% and 11.1%, respectively (*P*=0.032). Virtually all isolates were found susceptible to amphotericin B, flucytosine, and posaconazole. Moreover, three genotypically non-identical clusters of *C. albicans* were found during the study period. This study concludes that the infection caused by *C. parapsilosis* and *C. tropicalis* have been found increasing in the subsequent years during the study period, which may lead to the reduced mortality in NICU. Although no change in susceptibility was observed over the study periods.

The fourth study aimed to understand the mode of transformation of Candida infection from mother's vaginal mucosa to their full-term neonates. Samples were collected from vaginal mucosa of 100 mothers at the time of birth, and on the oral mucosa of their respective newborns, on the 1st, 3rd, and 9th days after birth by vaginal (75 cases) and caesarean (25 cases) routes. In each case where concordance at the level of species was found between the isolate from the mother and that from the neonate, tests were made to check for concordance between the genotypic and phenotypic profiles (susceptibility to killer toxins, susceptibility to antifungal agents, serotyping, proteinase and phospholipase production, RAPD profile, and by DNA fingerprinting with CARE-2 probe). For the vaginal-route group, Candida species were recovered from the vaginal mucosa of the mothers (44.4%) and from neonates (20%). For the caesarean-route group, these rates were 40% and 4%, respectively. Most frequently found species in the samples from the mothers and the neonates were *C. tropicalis* and *C. albicans* respectively. For the vaginal-route group, the rate of mother/neonate concordance at the level of species was 28.1% and no case of concordance for the caesarean births were found. RFLP analysis with CARE-2 probe revealed only 9.4 % concordance out of 28.1 %
shown by conventional analysis. This study concludes that vaginal mucosa is not the main route of transmission of the *Candida* species to the neonate.

The fifth study deals with the effect of maternal flora on *Candida* colonization of VLBW infants. Body site samples were collected within 24 hours of delivery from mothers who gave birth to VLBW infants, from their infants at birth, and then weekly for 12 weeks or until death or discharge. Yeast isolates were identified as *Candida albicans* by standard methods and typed by DNA fingerprinting using a *C. albicans* strain-specific DNA probe (*CARE-2*). Sixty-five percent (52/80) of mothers were colonized with Candida and 37.5% (30/80) of their infants had a *Candida* species isolated at least once. Of 52 infants born to *C. albicans*-colonized mothers, 17 (32.7%) became colonized with *C. albicans*. Twenty percent (16/80) of the infants in the study were colonized with *C. albicans* by 1 week of age; 69% of these infants (11/16) were born to *C. albicans*-colonized mothers suggesting vertical transmission. DNA fingerprinting was performed on 17 mother–infant pairs and 9 pairs demonstrated identical band patterns, confirming vertical transmission. However, of all infants colonized with *C. albicans* by the first week of age, just 50% (8/16) had a maternal source, and among all infants colonized at any time point, only 27.7% (8/30) became colonized by vertical transmission. Both vertical and horizontal transmission contributes to *Candida* colonization of ELBW infants in the neonatal intensive care unit.

The study concludes the understanding the mode of transmission of various *Candida* infections in neonates from their mothers and their molecular epidemiology under different conditions of infection. Moreover, the data presented in the thesis might be helpful in updating the empirical antibiotic regimen and minimizing risk factors for infection among patients, particularly in this region (Uttar Pradesh, India).