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PROFILING VULVOVAGINAL CANDIDIASIS IN PREGNANCY: CLINICAL OUTCOME AND MICROBIAL LANDSCAPE IN PATIENTS ATTENDING A TERTIARY CARE CENTRE

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ABSTRACT

Background: Vulvovaginal candidiasis (VVC) remains one of the most common fungal infections among pregnant women, attributed to hormonal and immunological changes in pregnancy that promote Candida colonization and infection.

Aim and Objectives: To assess the prevalence, species distribution, virulence characteristics, and antifungal susceptibility profiles of Candida species isolated from pregnant women presenting with symptoms of VVC.

Materials and Methods: A cross-sectional study was carried out on 250 pregnant women attending the antenatal clinic with vaginal discharge, itching, or discomfort. High vaginal swabs were collected under aseptic precautions and processed using standard microbiological methods. Species identification was done using CHROMagar and biochemical tests. Virulence factors including biofilm formation and phospholipase activity were assessed, and antifungal susceptibility was tested as per CLSI M44-A guidelines.

Results: Out of 250 samples, 128 (51.2%) were culture positive for Candida species, while 122 (48.8%) were negative. Among isolates, C. albicans constituted 48 (37.5%) and non-albicans Candida (NAC) 80 (62.5%). The predominant NAC species was C. tropicalis (66.2%), followed by C. krusei (18.7%), C. glabrata (10%), and C. parapsilosis (5%). Biofilm formation was detected in 104 isolates (81.2%), and phospholipase activity in 19 (14.8%). Resistance was highest against nystatin (88.5%) and cotrimoxazole (82.3%), while voriconazole (87.5%) and amphotericin-B (93.7%) showed the highest sensitivity.

Conclusion: Non-albicans Candida, particularly C. tropicalis, are emerging as dominant pathogens in VVC during pregnancy, showing high biofilm-forming capacity and azole resistance. Routine culture, species identification, and antifungal susceptibility testing are essential for guiding effective and safe therapy during pregnancy.

Keywords: Vulvovaginal candidiasis, Candida tropicalis, biofilm, antifungal resistance, pregnancy

INTRODUCTION

Vulvovaginal candidiasis (VVC) is one of the most frequent mucocutaneous infections among women of reproductive age, caused predominantly by Candida species. It accounts for nearly 20–25% of all vaginal infections worldwide and is estimated to affect up to 75% of women at least once during their lifetime, with 40–45% experiencing recurrent episodes [1,2]. Pregnancy represents a particularly vulnerable period for the development of VVC due to profound physiological, hormonal, and immunological alterations that promote fungal colonization and infection [3,4].

During pregnancy, elevated levels of estrogen and progesterone increase the glycogen content of vaginal epithelial cells, providing an abundant carbohydrate substrate for fungal proliferation. Estrogen also enhances Candida adhesion to epithelial cells by inducing specific receptor expression and altering epithelial permeability [5]. Meanwhile, progesterone suppresses cell-mediated immunity by reducing the activity of neutrophils and macrophages, thereby limiting the host's ability to clear fungal pathogens . These changes, combined with a shift in vaginal pH and a reduction in protective Lactobacillus species, create an environment conducive to fungal overgrowth and symptomatic infection .

Physiological elevations in estrogen and progesterone during pregnancy increase vaginal epithelial glycogen content, leading to a carbohydrate-rich environment conducive to Candida proliferation [4]. Additionally, suppression of cell-mediated immunity and reduced activity of neutrophils and macrophages allow fungal persistence [5]. The resulting alteration in the vaginal microbiota — particularly a reduction in protective Lactobacillus species — enhances the risk of symptomatic infection [6].

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While C. albicans has traditionally been the principal etiological agent, recent studies indicate a global epidemiological shift toward non-albicans Candida (NAC) species such as C. tropicalis, C. glabrata, and C. krusei. NAC species often exhibit intrinsic or acquired resistance to azole antifungals, complicating management and increasing recurrence risk. Biofilm formation, one of the most important virulence traits of Candida, enhances antifungal tolerance, contributes to chronicity, and facilitates mucosal invasion.

VVC during pregnancy can negatively affect maternal wellbeing, causing pruritus, burning, and discomfort, and may contribute to adverse obstetric outcomes such as preterm labor, chorioamnionitis, and premature rupture of membranes, although evidence remains inconclusive.

While C. albicans has traditionally been the principal etiological agent, recent studies indicate a global epidemiological shift toward non-albicans Candida (NAC) species such as C. tropicalis, C. glabrata, and C. krusei [7,8]. NAC species often exhibit intrinsic or acquired resistance to azole antifungals, complicating management and increasing recurrence risk [9]. Biofilm formation, one of the most important virulence traits of Candida, enhances antifungal tolerance, contributes to chronicity, and facilitates mucosal invasion [10,11].

VVC during pregnancy can negatively affect maternal wellbeing, causing pruritus, burning, and discomfort, and may contribute to adverse obstetric outcomes such as preterm labor, chorioamnionitis, and premature rupture of membranes, although evidence remains inconclusive [12,13].

Diagnosis relies on direct microscopy and culture, while advanced tools such as CHROMagar and PCR allow rapid species identification and differentiation [14]. Accurate diagnosis and

susceptibility profiling are essential in pregnancy, where systemic antifungal therapy (e.g., fluconazole) is generally contraindicated due to potential teratogenicity [15]. Current guidelines favor topical azoles for seven days as first-line therapy [16].

Despite its clinical significance, there is limited Indian data on the microbiological profile, virulence attributes, and antifungal susceptibility of Candida isolates in pregnancy.

This study aims to evaluate the prevalence, species distribution, virulence factors, and antifungal resistance among Candida isolates causing VVC in pregnant women attending a tertiary care center

MATERIAL AND METHODS

This cross-sectional study was conducted in the Department of Physiology in collaboration with the Department of Microbiology at a tertiary care teaching hospital. A total of 250 pregnant women attending the antenatal clinic with symptoms of vulvovaginal discharge, itching, burning, or discomfort were included after obtaining informed consent.

Sample Collection

High vaginal swabs were collected using sterile cotton swabs under aseptic precautions. Swabs were transported immediately to the microbiology laboratory for processing.

Microbiological Identification

Samples were cultured on Sabouraud's Dextrose Agar (SDA) with chloramphenicol and incubated at 37°C for 48 hours. Colonies were further identified using Gram staining, germ tube test, chlamydospore formation on cornmeal agar, and CHROMagar Candida for species differentiation. Confirmation was done using biochemical tests (sugar assimilation).

Virulence Factor Testing

1. Biofilm formation was assessed by the tube adherence method.
2. Phospholipase activity was detected on egg yolk agar, with zone measurement indicating enzyme production.

Antifungal Susceptibility Testing

Performed by CLSI M44-A disc diffusion method against fluconazole, itraconazole, voriconazole, amphotericin-B, micafungin, cotrimoxazole, and nystatin. Results were interpreted as sensitive or resistant according to CLSI guidelines.

Data Analysis

Results were expressed as frequency and percentage. Statistical analysis was performed using SPSS software, version 22.0.

RESULTS

Out of the total 250 pregnant women included in the study, 128 (51.2%) samples were culture positive for Candida species, while 122 (48.8%) yielded no fungal growth. This indicates that approximately half of the antenatal women presenting with vaginal discharge, itching, or discomfort were affected by vulvovaginal candidiasis, highlighting its high burden among pregnant women in this population.

Among the 128 Candida-positive isolates, Candida albicans accounted for 37.5% (48 isolates), while non-albicans Candida (NAC) species collectively made up 62.5% (80 isolates). The most frequently isolated NAC species was C. tropicalis, which constituted 41.4% (53 isolates), followed by C. krusei (11.7%), C. glabrata (6.2%), and C. parapsilosis (3.1%). This clear predominance of C. tropicalis over C. albicans reflects the growing epidemiological shift toward NAC species in vaginal infections during pregnancy.

Table 1. Culture Positivity among 250 Pregnant Women

Result Type	Frequency (n)	Percentage (%)
Culture Positive	128	51.2
Culture Negative	122	48.8
Total	250	100

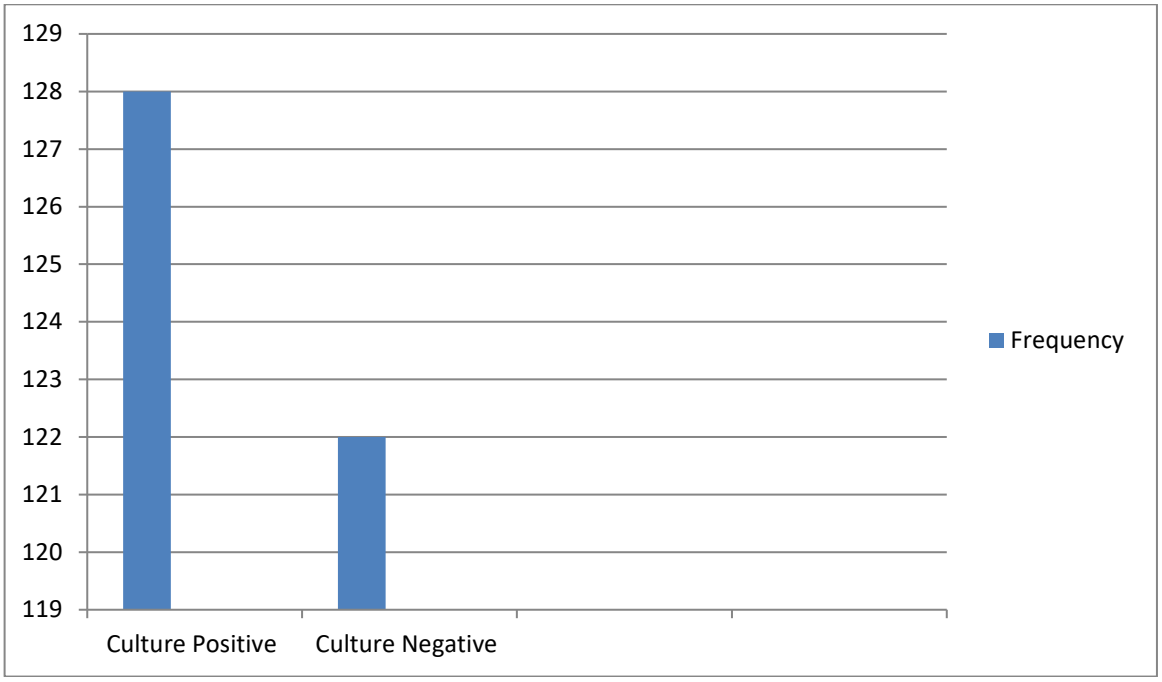

Table 2. Distribution of Candida Species (n = 128 isolates)

Species	No. of Isolates	Percentage (%)
Candida albicans	48	37.5
Candida tropicalis	53	41.4
Candida krusei	15	11.7
Candida glabrata	8	6.2
Candida parapsilosis	4	3.1

Table 3. Virulence Factor Distribution among Candida Isolates (n = 128)

Virulence Factor	Positive Isolates (n)	Percentage (%)	Predominant Species
Biofilm Formation	104	81.2	C. tropicalis, C. albicans
Phospholipase Activity	19	14.8	C. albicans

Assessment of virulence traits showed that biofilm formation was present in 104 (81.2%) of the isolates, with the highest biofilm-forming potential observed in C. tropicalis and C. albicans. Biofilm-positive isolates exhibited dense adherence along the walls of the test tubes, indicative of robust biofilm matrix production. Phospholipase activity was detected in 19 (14.8%) isolates, predominantly among C. albicans, suggesting that enzymatic tissue invasion remains a key pathogenic mechanism for this species.

The antifungal susceptibility pattern revealed notable resistance trends. High resistance rates were observed against nystatin (88.5%) and cotrimoxazole (82.3%), while moderate resistance was noted for fluconazole (65.6%) and itraconazole (49.2%). In contrast, the majority of isolates remained highly sensitive to amphotericin-B (93.7%) and voriconazole (87.5%). These findings suggest that polyene and newer triazole antifungals continue to be effective treatment options against Candida infections in pregnancy, whereas older azoles exhibit declining efficacy due to emerging resistance.

Taken together, the results indicate that non-albicans Candida species—particularly C. tropicalis—are now dominant in pregnant women with VVC at this centre. The high prevalence of biofilm formation and increasing azole resistance further underscore the necessity of routine fungal culture, species-level identification, and antifungal susceptibility testing for guiding safe and effective management during pregnancy.

DISCUSSION

Vulvovaginal candidiasis (VVC) is one of the most prevalent fungal infections among women of reproductive age, and pregnancy remains a key predisposing factor due to profound hormonal, immunological, and metabolic changes [1,3,5]. In the present study involving 250 pregnant women, the overall prevalence of Candida infection was 51.2%, highlighting the high burden of VVC among antenatal populations. This finding is consistent with the prevalence range of 45–55% reported by Hussen et al. (2024) [12] and Arsić-Arsenijević et al. (2025) [7] in similar antenatal cohorts. These elevated rates are largely attributed to the increased levels of estrogen and progesterone during pregnancy that enhance Candida adherence, hyphal formation, and immune evasion mechanisms [4,6].

Shift Toward Non-albicans Candida Species

A major observation in this study was the predominance of non-albicans Candida (NAC) species (62.5%), particularly C. tropicalis (41.4%). This trend reflects an emerging epidemiological shift that has been documented globally. Studies from Asia and Europe, including those by García-Salazar et al. (2024) [8] and Srb et al. (2025) [19], have reported an increasing proportion of NAC species, often exceeding 55% of all isolates. Similar observations were made by Satora et al. (2023) [9], who found C. tropicalis and C. glabrata to be increasingly associated with recurrent or refractory VVC cases.

The predominance of C. tropicalis in this study aligns with findings from Indian studies (e.g., Donders et al., 2023 [5]) and may be explained by the organism's ability to form dense biofilms and survive environmental stressors. Furthermore, C. tropicalis has a known tendency for azole resistance, likely due to widespread empirical fluconazole use and self-medication practices in low-resource settings [10,23].

Biofilm Formation and Virulence Factors

Biofilm formation was detected in 81.2% of isolates, a rate similar to that reported by Rodríguez-Cerdeira et al. (2020) [10] and Phillips et al. (2022) [11], who described biofilm-mediated antifungal resistance as a major determinant of recurrent VVC. Biofilm structures protect fungal cells from host immune responses and antifungal agents by limiting drug penetration and facilitating horizontal gene transfer. In the current study, biofilm production was most frequent among C. tropicalis and C. albicans isolates, consistent with earlier studies by Kumwenda et al. (2022) [4] and Workowski et al. (2021) [2].

Phospholipase activity, another virulence trait contributing to mucosal invasion and host tissue damage, was observed in 14.8% of isolates, predominantly among C. albicans. This aligns with results by Akinosoglou et al. (2024) [14] and Patel et al. (2024) [6], who found enzymatic activity to be higher in C. albicans due to its greater metabolic adaptability and secretory capabilities.

Antifungal Susceptibility Trends

The antifungal susceptibility profile in this study revealed high resistance to nystatin (88.5%) and cotrimoxazole (82.3%), with moderate resistance to fluconazole (65.6%) and itraconazole (49.2%). Conversely, amphotericin-B (93.7% sensitivity) and voriconazole (87.5%) were the most effective agents. These patterns are consistent with those reported by Satora et al. (2023) [9] and Nyirjesy (2022) [3], reflecting increasing azole resistance among NAC species.

The high resistance rates observed may be explained by the widespread empirical use of azoles and topical antifungals without culture confirmation. NAC species such as C. tropicalis and C. krusei possess efflux pump mechanisms and alterations in ergosterol biosynthesis pathways that confer reduced susceptibility to azoles [9,11,23]. In contrast, amphotericin-B maintains excellent efficacy as it targets ergosterol directly and bypasses these mechanisms.
Micafungin showed only moderate activity (45.3% sensitivity), likely due to limited exposure and developing resistance mechanisms in NAC species, similar to findings by García-Salazar et al. (2024) [8]. These antifungal trends underscore the need for continuous regional surveillance to guide effective empirical therapy.

Clinical and Obstetric Implications

From a clinical standpoint, symptomatic VVC significantly affects maternal quality of life due to itching, irritation, and vaginal discharge. Although the association between Candida colonization and adverse pregnancy outcomes remains debated, recent studies by Zhang et al. (2025) [13] and Sobel (2024) [1] suggest possible links between high fungal load and increased risk of preterm labor or membrane rupture. However, more controlled studies are required to confirm causality.
Current CDC (2021) [15] and IDSA (2016) [16] guidelines recommend topical azole therapy for seven days as first-line treatment during pregnancy, with oral fluconazole reserved for exceptional circumstances. Given the growing dominance of NAC species and rising azole resistance, empirical therapy without culture confirmation may lead to treatment failure and recurrence. Hence, routine laboratory identification and antifungal susceptibility testing should be considered in symptomatic or recurrent cases.

Comparative Insights with Other Studies

Study	Year	Country	NAC (%)	Dominant Species	Biofilm (%)	Fluconazole Resistance (%)
Hussen et al. [12]	2024	Ethiopia	58.3	C. tropicalis	78	63
García-Salazar et al. [8]	2024	Mexico	61.5	C. glabrata	80	60
Arsić-Arsenijević et al. [7]	2025	Serbia	55	C. albicans	76	50
Present Study	2025	India	62.5	C. tropicalis	81.2	65.6

Our data clearly demonstrate that the proportion of NAC species and azole resistance is increasing worldwide, mirroring the trends seen in our antenatal population. This global convergence indicates the necessity for antifungal stewardship programs, particularly in pregnancy where therapeutic choices are limited.

Public Health and Research Implications

The emergence of azole-resistant NAC species necessitates stricter control of antifungal prescriptions and improved diagnostic capabilities in obstetric clinics. Incorporating CHROMagar and molecular techniques into routine diagnostic workflows can enhance species-level detection and reduce recurrence by enabling targeted therapy [14]. Furthermore, future studies should explore the relationship between virulence factors (biofilm, phospholipase) and clinical outcomes, including pregnancy complications.

CONCLUSION

This study highlights a rising prevalence of non-albicans Candida, particularly C. tropicalis, in vulvovaginal candidiasis during pregnancy. The high rates of biofilm formation and antifungal resistance underscore the need for routine culture and susceptibility testing for appropriate therapy selection. Topical azoles remain the preferred treatment during pregnancy, while systemic antifungals should be reserved for severe or recurrent infections.

LIMITATIONS

1. Single-center, hospital-based study; community prevalence may vary.
2. Molecular typing was not performed.
3. Correlation with pregnancy outcomes was not assessed.
4. Long-term follow-up for recurrence was not conducted.

Declarations:

Conflicts of interest: There is not any conflict of interest associated with this study

Consent to participate: There is consent to participate.

Consent for publication: There is consent for the publication of this paper.

Authors' contributions: Author equally contributed the work.

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