Prevalence and Antifungal Susceptibility of *Candida albicans* Causing Vaginal discharge Among Pregnant Women in Lebanon

**CURRENT STATUS:** ACCEPTED

**BMC Infectious Diseases**

Nahed Ghaddar  
Beirut Arab University

Elie Anastasiadis  
Saint George hospital

Rawad Halimeh  
Saint GEorge hospital

Ali Ghaddar  
Lebanese international university

Rita Dhar  
Kuwait university

Wadha AlFouzan  
kkuwait university

Hoda Yusef  
Beirut Arab University

Mira El Chaar  
mira.elchaar@balamand.edu.lb  
University of Balamand  
*Corresponding Author*

**DOI:**  
10.21203/rs.2.12038/v2

**SUBJECT AREAS**  
Infectious Diseases

**KEYWORDS**  
*Candida albicans*, vulvovaginitis, prevalence, pregnant women, antifungal susceptibility.
Abstract

Background: Vaginal candidiasis is frequently prevalent in pregnant women and is associated with sepsis and adverse neonatal outcomes. This study determined the presence of Candida species in symptomatic pregnant women and evaluated the antifungal susceptibility profile of the isolated strains. It also aimed to explore whether Candida species predicts gestational complications and adverse neonatal outcomes.

Methods: A total of 258 pregnant women at 35 to 37 week of gestation participated in this study. Vaginal swabs from these patients were collected at various obstetrics and gynecology clinics in Lebanon for a period of 12 months. Candida isolates were identified at species level and antifungal susceptibility of Candida albicans to fluconazole (FCZ), amphotericin B (AMB), itraconazole (ICZ) and voriconazole (VCZ) was determined by the agar-based E-test method. Results: Among 258 women tested, 100 (39%) were positive for Candida species. C. albicans, C. glabrata and C. krusei were isolated from 42%, 41% and 17% of the women, respectively. C. albicans had significant positive associations with gestational diabetes while C. kreusi or C. glabrata had significant positive associations with gestational complications and vaginal discharge. The antifungal susceptibility tests of C. albicans isolates revealed 97.5%, 90%, 87.5% and 97.5% susceptibility to AMB, FCZ, ICZ and VCZ, respectively. Conclusion: The current study revealed high incidence of both C. albicans and non-C. albicans strains causing vulvovaginitis among pregnant women in Beirut, Lebanon. Whereas the susceptibility rates of C. albicans against AMB and VCZ were high, FCZ and ICZ proved comparatively less efficacious. The resistance profile of circulating C. albicans among pregnant women can predict the best outcome of appropriate prophylaxis or treatment of neonatal candidiasis. Vaginal candida colonization might lead to adverse neonatal outcome or gestational complications thus Candida screening as antenatal follow up is advised.
Background

*Candida* species, which are part of the normal flora in the vulvovagina, may cause opportunistic infections under various circumstances that compromise host immunity. *Candida* spp. subsist in symbiotic relationship with vaginal microbiota, therefore asymptomatic colonization is common and may persist for years. The rate of genital *Candida* colonization ranges from 20% in asymptomatic young women to up to 30% in pregnant women [1-6]. The risk factors associated with increased rate of Vulvovaginal candidiasis (VVC) in pregnant women are immunologic alterations, increased estrogen levels, and increased vaginal glycogen production mechanism [3]. VVC is the result of *Candida albicans* in 85–95 % of cases whereas incidence rate of Non-*C. albicans Candida* (NCAC) in pregnant women is less than 10% [7].

Treatment of VVC is recommended only in the presence of symptoms since over 20% of women may have yeast as part of their natural vaginal microbiome and are asymptomatic [8]. However, pregnant women may have severe and prolonged symptoms of VVC requiring longer courses of therapy [9]. Recent studies have shown an increase in the development of drug-resistance among *C.albicans*, less is known about the burden and effects of drug resistant fungal infections.

Candidiasis in newborns has been associated with increased risk of pregnancy complications, such as premature rupture of membranes, preterm labor, chorioamnionitis, and congenital cutaneous candidiasis. Colonization with *Candida* spp. in neonates may occur by vertical transmission from the mother during the perinatal period or by horizontal transmission in the nursery or the neonatal intensive care unit (NICU) [10-12]. It has been shown that 5% to 30% of all colonized preterm neonates will develop invasive *Candida* infection (ICI) during their stay in the NICU [13-15]. *C.albicans* was shown to play a major role in neonatal colonization in the first days of life and were also documented in a group
of premature infants [16].

The epidemiology of antifungal resistance among *C. albicans* in pregnant women in Lebanon remains poorly reported. Therefore, the objective of this study was to determine the prevalence of *Candida* species in symptomatic pregnant women with vaginal discharge at 35 to 37 weeks of gestation and to evaluate the antifungal susceptibility profile of the isolated strains of *C. albicans*. In addition, the study evaluated the association between the presence of *Candida* species and gestational complications and outcomes.

**Methods**

**Study sample and procedure of collection**

In this study, a cross-sectional design was adopted for determining the prevalence of *Candida* species in Lebanese pregnant women. Clinical samples were collected from 258 pregnant women with vaginal discharge in three obstetrics and gynecology clinics in Lebanon during a period of 14 months (June 2015-July 2016). Women were approached by a registered gynecologist who explained the objectives of the study and asked them to participate. Participation was voluntary and anonymous. This study was approved by the institutional review board of Beirut Arab University. A written informed consent was obtained from all eligible women before entering the study. Two vaginal swabs were collected from each patient. The samples were stored in Stuart media (Oxoid, UK) at room temperature and transported to the clinical diagnostic laboratory.

**Data collection**

Socio-demographic data, clinical status and gestational history of 165 (64%) patients were collected through a questionnaire that included information about mothers’ risk factors for adverse neonatal outcomes such as gestational diabetes, previous miscarriage, anemia and recurrent urinary tract infections (UTI). The 165 participants were followed up after delivery to gather information about delivery time, delivery type, induced labor,
gestational complications and neonatal outcomes (newborn height, weight and Apgar score).

**Culture and identification:**

Vaginal swabs were cultured on both Sabouraud dextrose agar (SDA) and Chromatic Candida medium (Liofilchem, Italy). The latter allows the selective isolation and differentiation of Candida spp. based on colony color and morphology; it has been well documented in previous studies as for its high sensitivity and specificity for the identification of the most commonly encountered Candida spp. [17-19]. Both plates were incubated at 37°C for 48 to 72 hrs. The chromatic characteristics of the colonies were the following: green colonies were identified as *C. albicans*, creamy colored colonies as *C. glabrata*, and pink with a whitish border colonies as *C. krusei*. All isolates were confirmed by API 20 C AUX strip (BioMerieux, Marcy l’Etoile, France). Further phenotypic testing was done to differentiate between *C. dubliniensis* and *C. albicans* by growing the germ tube positive yeast isolates at 45°C on SDA for up to 10 days. *C. albicans* isolates were identified by their ability to grow at 45°C.

**Antifungal susceptibility testing**

The in vitro activity of the antifungal agents against each isolate was determined by the E-test (HiMedia, Mumbai, India) in accordance with the manufacturer’s instructions. The E-test strips of fluconazole (FCZ; 0.016∼256 μg/mL), itraconazole (ICZ; 0.002∼32 μg/mL), voriconazole (VCZ; 0.002∼32 μg/mL), and amphotericin B (AMB; 0.002∼32 μg/mL) were used [20]. Interpretive susceptibility criteria for antifungal breakpoints were adapted from the Clinical and Laboratory Standards Institute (CLSI), 2017 [21]. The breakpoints used for *C. albicans* are: FCZ (S ≤ 2; SDD= 4; R ≥ 8); VCZ (S ≤ 0.12; R ≥ 1), ICZ (S ≤ 0.12; R ≥ 1) and AMB (S ≤ 2; R > 2). For quality control, *C. albicans* (ATCC 10231) was used as reference strain and tested simultaneously with the clinical isolates.
**Statistical Analysis**

The presence of *Candida* species was correlated with the newborn height, weight and Apgar score (overall assessment of new born well-being used immediately following the delivery of the baby) as dependent variables using linear multiple regression analysis. The models took into consideration to control other possible confounding effect of various independent variables including mother’s age, mother’s education, delivery type, delivery week, induced labor, recurrent urinary tract infection (UTI), gestational diabetes, anemia and other gestational complications. Statistical significance was calculated using p-value and confidence intervals. The presence of *Candida* species effect on categorical outcome variables (Gestational diabetes, vaginal discharge, induced labor and recurrent UTI) was explored by comparing frequencies using the test of independence Chi-square. P values were computed considering $p \leq 0.05$ as significant results.

**Results**

The socio-demographic characteristics of 165 respondents are summarized in Table 1; 49% of women who participated were between the ages of 36 to 40 years old. The majority completed their university degree (62.4%). The rate of normal vaginal delivery was 43.6% and 69.7% of women had labor induction. Gestational complications occurred in 59.1% of women and 25.5% of women had gestational diabetes mellitus. Anemia was reported in 14.5% of women.

Among the cultures from the 258 women tested, 100 (39%) were positive for *Candida* species. *C.albicans* was isolated from 42% of the women (N=42) and *Non-C.albicans Candida* (NCAC) from the remaining 58%. The main identified NCAC were *C.glabrata* (71%, N=41) followed by *C.krusei* (29%, N=17). Four women were co-infected with both *C.albicans* and *C.glabrata*. All of the three identified *Candida* species were isolated from women in the
The observed susceptibility rates of *C. albicans* isolates to AMB, FCZ, ICZ and VCZ were 97.5%, 90%, 87.5% and 97.5%, respectively. MIC$_{50}$ and MIC$_{90}$ of the antifungal agents tested against 40 strains of *C. albicans* are presented in Table 2. Two of the isolates were lost during processing, although ICZ presented the lowest MIC$_{90}$ value of 0.125 µg/mL, it showed highest resistance rate (12.5%) among all the agents tested.

The association between the presence of *Candida species*, isolated from 48 women who filled the questionnaire, was assessed with preterm delivery, delivery type, gestational complications, gestational diabetes, recurrent UTI infection and induced labor (Table 3). The Chi-square test revealed that *C. albicans* had significant effects only on patients with gestational diabetes; 33% of *C. albicans* positive and 24% of *C. albicans* negative participants had gestational diabetes (p=0.04). *C. albicans* had non-significant associations with gestational complications, induced labor and recurrent UTI. On the other hand, the presence of *C. kreusi* and *C. glabrata* had strong significant association with premature delivery and gestational complications (p<0.05): 94% of women with *C. glabrata* and 71.4% of women with *C. krusei* had gestational complications compared to 28.4% and 29.7% of women who did not have *C. glabrata* and *C. krusei* respectively (p-value ≤0.001). No significant associations were observed between the isolated *Candida* species and induced labor or recurrent UTI (Table 3).

Results of the three multiple regression models with neonatal outcomes (weight, height and Apgar score) as dependent variables are displayed in Table 4. Results revealed significant positive association between delivery time and neonatal height and significant negative association between C-section and height. Height increased 0.41 centimeter with one week increase in delivery time (p=0.001) and decreased 0.46 centimeter with C-section (p=0.002). Height also decreased with the presence of all identified *Candida*
species. This reduction was statistically significant in both \textit{C.krusei} or \textit{C.glabrata} infections (Beta=-0.46, p=0.05 for \textit{C.albicans} and Beta=-0.77; p=0.006). The other covariates did not yield significant associations with height. Neonatal weight had significant positive association with delivery time and significant negative association with \textit{C-section}. There was 0.32g increase in weight with an additional delivery week (p=0.01) and 0.34g decrease in weight with \textit{C-section} (p=0.02). Although weight decreased with the presence of \textit{Candida} species (\textit{C.albicans}: Beta=0.16, \textit{C. krusei} or \textit{C.glabrata}: Beta=0.43), this reduction was not statistically significant. The other covariates did not yield significant associations with weight. Apgar score did not show significant correlation with the presence of any \textit{Candida} species or with any of the other independent variables.

\section*{Discussion}

The prevalence of \textit{Candida} species causing vaginitis is pregnant women vary from one population to another. In our study, 39\% of participating women were infected by \textit{Candida} species. NCAC were more frequently isolated (58\%) than \textit{C.albicans} (42\%). NCAC were also shown to increase in non vaginal clinical samples isolated from Lebanon; that was observed in a previous retrospective clinical study published where the authors have shown that among all \textit{Candida} strains isolated, \textit{C.albicans} rates had decreased from 86\% in 2005 to around 60\% in 2014. However, the NCAC rates increased from 14\% in 2005 to around 40\% in 2014, comprising mainly of \textit{C.tropicalis}, \textit{C.glabrata}, and \textit{C.parapsilosis} [21]. Recent emergence of NCAC, such as \textit{C.glabrata} and \textit{C. krusei} has been seen in the post FCZ era and in settings with azole selection pressure [22]. Worldwide, there is a variation in the distribution of \textit{Candida} spp. identified from vaginal swabs and depends largely on the location as well as the population studied. Figure 1 summarizes the distribution of \textit{Candida} species isolated from vaginal swabs from population-based studies conducted in different countries. China, Brazil, Tunis, Kuwait, India and Turkey have reported that
*C. albicans* remains the most commonly isolated yeast (60%-80%) in women diagnosed with VVC [23-28]. On the other hand, an increasing trend in the occurrence of NCAC (58%-60%) over time has also been observed in Pakistan and Burkina Faso [29, 30] (Figure 1). Treatment of vaginal candidiasis is successfully achieved by use of azoles [31]. NCAC related disease is less likely to respond to azole therapy, alternative treatment with AMB suppositories with or without topical azole is recommended. In the current study, isolates showed high susceptibility to AMB (97.5%) and this observation has been corroborated by studies done in various other countries including Lebanon [21, 32-34]. Resistance rates of *C. albicans* to VCZ, FCZ, and ICZ and in this study were 2.5%, 10%, and 12.5%, respectively, which are in contrast to earlier data from Lebanon reporting susceptibility to FCZ (94-100%), VCZ (94-97%) and ICZ (62%) [21]. However, despite high susceptibility rates against FCZ and VCZ in the previous study, their MIC$_{90}$ showed an elevated trend over 10 year of study period [21]. The increase in azole resistance in our study can be attributed to the frequent empiric prescription of FCZ for sporadic VVC, which may result in FCZ-resistant *C. albicans* causing recurrent VVC infection to emerge [35]. Identification of the most common molecular mechanism of resistance among our clinical isolates would help in understanding if there is any spread of resistance gene between *C. albicans* and NCAC. Since through vertical or horizontal transmission, 5-30% of all colonized preterm neonates may develop invasive *Candida* infection [13-15], prophylaxis with antifungal agents in this group of patients has proven effective in preventing such an infection. However, an increase in MIC against antifungal agents may have major consequences resulting in poor outcomes and higher mortality rate among neonates with ICI. Although treatment of asymptomatic pregnant women with *Candida* colonization in the genital tract is not yet recommended, some countries such as Germany have started to implement the process of screening and treatment of women found to be colonized
vaginally by *Candida* spp. or those who present with VVC in the third trimester [36]. In Lebanon, unlike group B streptococcus (GBS), routine screening for the presence of *Candida* spp. in pregnant women in the third week of gestation is not considered as part of a routine surveillance by the obstetricians. Since Invasive candidiasis in neonates is becoming a serious and common cause of late onset sepsis, with mortality rates reaching as high as 25-35% [10], screening simultaneously for both GBS and *Candida* spp. in pregnant women would reduce the rate of sepsis, meningitis, oral thrush and diaper dermatitis in newborns with these organisms acquired during vaginal delivery.

It is reported that vaginitis in pregnancy is related to adverse perinatal outcome [37]. In the current study, we aimed to correlate between the presence of candidiasis and pregnancy outcome. Our results showed that height decreased with the presence of *Candida* species. This reduction was statistically significant in the presence of *C. kreusi* or *C. glabrata*. However no effect was observed on the weight of the baby. This finding was consistent with a study done previously in Iran where they found no association between vaginal *Candida* colonization and low birth weight [38]. The current study has also shown that *Candida species* cause gestational complications which is also in agreement with a previous study done in China [39].

Among the different studied variables which may be affected by *Candida*, such as gestational complications, gestational diabetes, vaginal discharge, induced labor and recurrent UTI, the present study confirmed that the presence of *C. albicans* had the most significant effects on women with gestational diabetes and both *C. kreusi* and *C. glabrata* on women with gestational complications. Future case control studies should be performed to compare the clinical outcome of pregnant women infected with any microorganism versus non infected women.

In conclusion, increasing rates of NCAC strains among pregnant women in Lebanon should
be looked at as both novel and alarming. Extensive surveillance studies should be done on
all clinical specimens yielding significant growth of Candida spp. and the effect of
resistance pattern on invasive Candida infection. As a consequence of selective pressure,
emergence of drug resistance is inevitable. Therefore future studies should focus on the
emergence of drug-resistant Candida strains and their frequencies. The susceptibility
pattern of C.albicans to antifungal agents varies with region and would require constant
monitoring of any unusual increase in resistance.

Declarations

Ethics approval and consent to participate

Study activities were reviewed by Beirut Arab University International Review Board (IRB)
under IRB# 0041-S-P-0336

Consent for publication

A written informed consent was obtained from all eligible women before entering the
study

Availability of data and material

All authors confirm that all data and material are available

Competing interest: All authors declare that they have no competing interests

Funding: No funding

Authors’s contributions

NG was responsible for the study design, performed and analyzed the experiments in
addition to data analysis and writing up the manuscript. MEC was responsible for the study
design, supervised and analyzed the experiments and was responsible for writing up the
manuscript. AE and RH were responsible for sampling and clinical interpretation. AG was
responsible for the epidemiological and statistical analysis of the data. RD, WAF and HY
revised the manuscript. All authors reviewed and approved the manuscript.
Acknowledgements

None

References

1. Aguin TJ, Sobel JD: **Vulvovaginal candidiasis in pregnancy.** Current infectious disease reports 2015, 17(6):462.

2. Beigi RH, Meyn LA, Moore DM, Krohn MA, Hillier SL: **Vaginal yeast colonization in nonpregnant women: a longitudinal study.** Obstetrics and gynecology 2004, 104(5 Pt 1):926-930.

3. Goncalves B, Ferreira C, Alves CT, Henriques M, Azeredo J, Silva S: **Vulvovaginal candidiasis: Epidemiology, microbiology and risk factors.** Critical reviews in microbiology 2016, 42(6):905-927.

4. Holland J, Young ML, Lee O, S CAC: **Vulvovaginal carriage of yeasts other than Candida albicans.** Sexually transmitted infections 2003, 79(3):249-250.

5. Larsen B: **Vaginal flora in health and disease.** Clinical obstetrics and gynecology 1993, 36(1):107-121.

6. van Schalkwyk J, Yudin MH: **Vulvovaginitis: screening for and management of trichomoniasis, vulvovaginal candidiasis, and bacterial vaginosis.** Journal of obstetrics and gynaecology Canada : JOGC = Journal d'obstetrique et gynecologie du Canada : JOGC 2015, 37(3):266-274.

7. Sobel JD: **Vulvovaginal candidosis.** Lancet (London, England) 2007, 369(9577):1961-1971.

8. Farr A, Kiss H, Holzer I, Husslein P, Hagmann M, Petricevic L: **Effect of asymptomatic vaginal colonization with Candida albicans on pregnancy outcome.** Acta obstetricia et gynecologica Scandinavica 2015, 94(9):989-996.
9. Cotch MF, Hillier SL, Gibbs RS, Eschenbach DA: Epidemiology and outcomes associated with moderate to heavy Candida colonization during pregnancy. Vaginal Infections and Prematurity Study Group. *American journal of obstetrics and gynecology* 1998, 178(2):374-380.

10. Wadile RG, Bhate VM: Study of clinical spectrum and risk factors of neonatal candidemia. *Indian journal of pathology & microbiology* 2015, 58(4):472-474.

11. Filippidi A, Galanakis E, Maraki S, Galani I, Drogari-Apiranthitou M, Kalmanti M, Mantadakis E, Samonis G: The effect of maternal flora on Candida colonisation in the neonate. *Mycoses* 2014, 57(1):43-48.

12. Leibovitz E: Strategies for the prevention of neonatal candidiasis. *Pediatrics and neonatology* 2012, 53(2):83-89.

13. Manzoni P, Mostert M, Jacqz-Aigrain E, Stronati M, Farina D: Candida colonization in the nursery. *Jornal de pediatria* 2012, 88(3):187-190.

14. Benjamin DK, Jr., Stoll BJ, Fanaroff AA, McDonald SA, Oh W, Higgins RD, Duara S, Poole K, Laptook A, Goldberg R: Neonatal candidiasis among extremely low birth weight infants: risk factors, mortality rates, and neurodevelopmental outcomes at 18 to 22 months. *Pediatrics* 2006, 117(1):84-92.

15. Steinbach WJ, Roilides E, Berman D, Hoffman JA, Groll AH, Bin-Hussain I, Palazzi DL, Castagnola E, Halasa N, Velegraki A et al: Results from a prospective, international, epidemiologic study of invasive candidiasis in children and neonates. *The Pediatric infectious disease journal* 2012, 31(12):1252-1257.

16. Waggoner-Fountain LA, Walker MW, Hollis RJ, Pfaller MA, Ferguson JE, 2nd, Wenzel RP, Donowitz LG: Vertical and horizontal transmission of unique Candida species to premature newborns. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America* 1996, 22(5):803-808.
17. Madhavan P, Jamal F, Chong PP, Ng KP: Identification of local clinical Candida isolates using CHROMagar Candida as a primary identification method for various Candida species. Tropical biomedicine 2011, 28(2):269-274.

18. Daef E, Moharram A, Eldin SS, Elsherbiny N, Mohammed M: Evaluation of chromogenic media and seminested PCR in the identification of Candida species. Brazilian journal of microbiology : [publication of the Brazilian Society for Microbiology] 2014, 45(1):255-262.

19. Ouanes A, Kouais A, Marouen S, Sahnoun M, Jemli B, Gargouri S: Contribution of the chromogenic medium CHROMagar((R))Candida in mycological diagnosis of yeasts]. Journal de mycologie medicale 2013, 23(4):237-241.

20. Song YB, Suh MK, Ha GY, Kim H: Antifungal Susceptibility Testing with Etest for Candida Species Isolated from Patients with Oral Candidiasis. Annals of dermatology 2015, 27(6):715-720.

21. Araj GF, Asmar RG, Avedissian AZ: Candida profiles and antifungal resistance evolution over a decade in Lebanon. Journal of infection in developing countries 2015, 9(9):997-1003.

22. Guzel AB, Aydin M, Meral M, Kalkanci A, Ilkit M: Clinical characteristics of Turkish women with Candida krusei vaginitis and antifungal susceptibility of the C. krusei isolates. Infectious diseases in obstetrics and gynecology 2013, 2013:698736.

23. Zhai Y, Liu J, Zhou L, Ji T, Meng L, Gao Y, Liu R, Wang X, Li L, Lu B et al: Detection of Candida species in pregnant Chinese women with a molecular beacon method. Journal of medical microbiology 2018.

24. Mtibaa L, Fakhfakh N, Kallel A, Belhadj S, Belhaj Salah N, Bada N, Kallel K: Vulvovaginal candidiasis: Etiology, symptomatology and risk factors. Journal
25. Alfouzan W, Dhar R, Ashkanani H, Gupta M, Rachel C, Khan ZU: Species spectrum and antifungal susceptibility profile of vaginal isolates of Candida in Kuwait. *Journal de mycologie medicale* 2015, **25**(1):23-28.

26. Dharmik PG, Gomashe AV, Upadhyay VG: Susceptibility pattern of various azoles against Candida species causing vulvovaginal candidiasis. *Journal of obstetrics and gynaecology of India* 2013, **63**(2):135-137.

27. Kalkanci A, Guzel AB, Khalil, II, Aydin M, Ilkit M, Kustimur S: Yeast vaginitis during pregnancy: susceptibility testing of 13 antifungal drugs and boric acid and the detection of four virulence factors. *Medical mycology* 2012, **50**(6):585-593.

28. Brandolt TM, Klafke GB, Goncalves CV, Bitencourt LR, Martinez AM, Mendes JF, Meireles MC, Xavier MO: Prevalence of Candida spp. in cervical-vaginal samples and the in vitro susceptibility of isolates. *Brazilian journal of microbiology : [publication of the Brazilian Society for Microbiology]* 2017, **48**(1):145-150.

29. Khan M, Ahmed J, Gul A, Ikram A, Lalani FK: Antifungal susceptibility testing of vulvovaginal Candida species among women attending antenatal clinic in tertiary care hospitals of Peshawar. *Infection and drug resistance* 2018, **11**:447-456.

30. Sangare I, Sirima C, Bamba S, Zida A, Cisse M, Bazie WW, Sanou S, Dao B, Menan H, Guiguemde RT: Prevalence of vulvovaginal candidiasis in pregnancy at three health centers in Burkina Faso. *Journal de mycologie medicale* 2018, **28**(1):186-192.

31. Pappas PG, Kauffman CA, Andes DR, Clancy CJ, Marr KA, Ostrosky-Zeichner L, Reboli AC, Schuster MG, Vazquez JA, Walsh TJ et al: Clinical Practice Guideline for the Management of Candidiasis: 2016 Update by the Infectious Diseases Society
of America. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America* 2016, 62(4):e1-50.

32. Eksi F, Gayyurhan ED, Balci I: In vitro susceptibility of Candida species to four antifungal agents assessed by the reference broth microdilution method. *TheScientificWorldJournal* 2013, 2013:236903.

33. Badiee P, Badali H, Diba K, Ghadimi Moghadam A, Hosseininasab A, Jafarian H, Mohammadi R, Mirhendi H, Najafzadeh MJ, Shamsizadeh A *et al*: Susceptibility pattern of Candida albicans isolated from Iranian patients to antifungal agents. *Current medical mycology* 2016, 2(1):24-29.

34. Mokaddas EM, Al-Sweih NA, Khan ZU: Species distribution and antifungal susceptibility of Candida bloodstream isolates in Kuwait: a 10-year study. *Journal of medical microbiology* 2007, 56(Pt 2):255-259.

35. Whaley SG, Berkow EL, Rybak JM, Nishimoto AT, Barker KS, Rogers PD: Azole Antifungal Resistance in Candida albicans and Emerging Non-albicans Candida Species. *Frontiers in microbiology* 2016, 7:2173.

36. Mendling W, Brasch J, Cornely OA, Effendy I, Friese K, Ginter-Hanselmayer G, Hof H, Mayser P, Mylonas I, Ruhnke M *et al*: Guideline: vulvovaginal candidosis (AWMF 015/072), S2k (excluding chronic mucocutaneous candidosis). *Mycoses* 2015, 58 Suppl 1:1-15.

37. Savita Rathod, Vijayalakshmi S.: Prevalence of vaginitis during pregnancy and its fetomaternal outcome in the rural setup *International Journal of Reproduction, Contraception, Obstetrics and Gynecology* 2016, 5(6):1823-1826.

38. Rasti S, Asadi MA, Taghriri A, Behrashi M, Mousavie G: Vaginal candidiasis complications on pregnant women. *Jundishapur journal of microbiology* 2014, 7(2):e10078.
39. Zhang X, Liao Q, Wang F, Li D: *Association of gestational diabetes mellitus and abnormal vaginal flora with adverse pregnancy outcomes*. *Medicine* 2018, 97(34):e11891.

Tables

**Table 1: Socio-demographic characteristics of 165 respondents**

| Age group       | 20-25 years | n= 19 (11.5%) |
|-----------------|-------------|---------------|
|                 | 26-30 years | n= 14 (8.5%)  |
|                 | 30-36 years | n= 49 (29.7%) |
|                 | 36-40 years | n=81 (49.1%)  |
| ≥41 years       | n= 2 (1.2%) |
| Education status|             |               |
| Primary         |             | n= 32 (19.4%) |
| Secondary       |             | n= 30 (18.2%) |
| University      |             | n= 103 (62.4%)|
| Delivery type   |             |               |
| Normal          |             | n= 72 (43.6%) |
| Cesarean section|             | n= 24 (14.5%) |
| Missing         |             | n=69 (41.8%)  |
| Induced labor   | Yes         | n= 50 (30.3%) |


| Condition                        | Yes          | n=  | (%)   | No          | n=  | (%)   |
|---------------------------------|--------------|-----|-------|-------------|-----|-------|
| Recurrent UTI                   | Yes          | 4   | 2.4%  | No          | 161 | 97.6% |
| Gestational complications       | Yes          | 97  | 59.1% | No          | 67  | 40.9% |
| Gestational diabetes mellitus   | Yes          | 42  | 25.5% | No          | 123 | 74.5% |
| Anemia                          | Yes          | 24  | 14.5% | No          | 141 | 85.5% |

| Antifungal drugs | MIC<sub>50</sub> | MIC<sub>90</sub> | MIC Range | Percentage resistance |
|------------------|------------------|------------------|------------|-----------------------|
| Amphotericin B   | 0.5              | 1                | 0.38-3.00  | 2.5%                  |
| Fluconazole      | 2                | 6                | 0.047-32   | 10.0%                 |
| Itraconazole     | 0.125            | 0.125            | 0.032-32   | 12.5%                 |
| Voriconazole     | 0.094            | 1                | 0.032-256  | 2.5%                  |

Table 2: Ranges of MICs, MIC<sub>50</sub> and MIC<sub>90</sub> and percentage resistance in 40 *C. albicans* isolates. MIC<sub>50</sub> = Minimum Inhibitory Concentration required to inhibit the growth of 50% of organisms. MIC<sub>90</sub> = Minimum Inhibitory Concentration required to inhibit the growth of 90% of organisms. MIC range is the range of the lowest and highest MIC values obtained from 40 *C. albicans* isolates tested. Percentage resistance is the percentage of isolates resistant to a specific antifungal drug.
### Table 3: Association between candida species isolated from vaginal swabs of pregnant women and various clinical outcomes (n=165).

*p* value <0.05 is considered significant

| Candida Species | Yes n (n%) | Delivery week (preterm delivery) | p or * | Delivery Type (C-section) | p or * | Gestational Diabetes n (%) | p or * |
|-----------------|-----------|----------------------------------|--------|---------------------------|--------|-----------------------------|--------|
| C.albicans      | Yes n=24  | 15 (62.5%)                       | 0.57   | 5 (20.1%)                 | 0.76   | 8 (33.3%)                   | 0.04   |
|                 | No n=141  | 72 (51.1%)                       |        | 19 (13.5%)                |        | 34 (24.1%)                  | 0.92   |
| C.glabrata      | Yes n=17  | 13 (66.5%)                       | 0.02   | 6 (35.3%)                 | 0.32   | 6 (35.3%)                   | 0.13   |
|                 | No n=148  | 63 (42.6%)                       |        | 38 (25.7%)                |        | 33 (22.3%)                  | 0.51   |
| C.kreusi        | Yes n=7   | 5 (71.4%)                        | 0.01   | 4 (57.1%)                 | 0.24   | 2 (28.5%)                   | 0.19   |
|                 | No n=158  | 55 (34.8%)                       |        | 61 (38.6%)                |        | 33 (20.8%)                  | 0.64   |

### Table 4. Effect of different variables on the height, weight and Apgar score of the neonates

Standardized beta coefficients (Beta) for each individual independent variable was calculated to compare the strength of the effect of each to the dependent variable. The higher the absolute value of the beta coefficient, the stronger the effect.

Coefficient of determination (R2) was calculated to evaluate the proportion of the variance in
the dependent variable that is predictable from the independent variables. The coefficient of
determination assesses how well the model explains and predicts future outcomes.

Confidence interval (CI) is the margin of error of the Beta. P value determines the
significance of the results. P value <0.05 is considered significant.

|                                      | B     | SE   | Lower CI | Upper CI | P     |
|--------------------------------------|-------|------|----------|----------|-------|
| Delivery Week                        | 0.41  | 0.001| 0.34; 1.34 | 0.32     | 0.01  |
| Delivery Type                        | -0.46 | 0.002| -3.30; -0.73 | -0.34 | 0.02  |
| Induced Labor                        | -0.09 | 0.48 | -1.38; 0.65 | -0.07     | 0.61  |
| Gestation Diabetes mellitus          | 0.11  | 0.27 | -0.39; 1.39 | 0.003     | 0.98  |
| Other gestational complications      | 0.18  | 0.10 | -0.14; 1.68 | 0.25     | 0.04  |
| Anemia                               | -0.01 | 0.94 | -1.20; 1.13 | 0.029     | 0.80  |
| Recurrent UTI                        | 0.19  | 0.07 | -0.23; 4.38 | 0.23     | 0.03  |
| Candida albicans infection           | -0.46 | 0.05 | -4.84; 0.08 | -0.16 | 0.53  |
| Candida glabrata/krusei infection    | -0.77 | 0.006 | -6.14; -1.04 | -0.43 | 0.14  |

R² = 0.32

Figures
Figure 1

Distribution of Candida species isolated from vaginal swabs of women from 14 countries.