LABupdate

Candida Species Identification by NAA

Background

Vulvovaginal candidiasis (VVC) occurs as a result of displacement of the normal vaginal flora by species of the fungal genus *Candida*, predominantly *Candida albicans*. The usual presentation is irritation, itching, burning with urination, and thick, whitish discharge.[1] VVC accounts for about 17% to 39% of vaginitis[1], and most women will be diagnosed with VVC at least once during their childbearing years.[2]

In simplistic terms, VVC can be classified into uncomplicated or complicated presentations. Uncomplicated VVC is characterized by infrequent symptomatic episodes, mild to moderate symptoms, or *C albicans* infection occurring in nonpregnant and immunocompetent women.[1] Complicated VVC, in contrast, is typified by severe symptoms, frequent recurrence, infection with *Candida* species other than *C albicans,* and/or occurrence during pregnancy or in women with immunosuppression or other medical conditions.[1]

Diagnosis and Treatment of VVC

Traditional diagnosis of VVC is accomplished by either: (i) direct microscopic visualization of yeast-like cells with or without pseudohyphae; or (ii) isolation of *Candida* species by culture from a vaginal sample.[1] Direct microscopy sensitivity is about 50%[1] and does not provide a species identification, while cultures can have long turnaround times. Today, nucleic acid amplification-based (NAA) tests (eg, PCR) for *Candida* species can provide high-quality diagnostic information with quicker turnaround times and can also enable investigation of common potential etiologies of vaginitis symptoms from a single sample.

In uncomplicated VVC, usually caused by *C albicans*, short-course treatment with –azole therapies resolve the infection in about 80% to 90% of cases.[3] Recurrent VVC caused by *C albicans* also typically responds well to short duration –azole therapy, although some specialists recommend longer duration of initial therapy and/or maintenance regimens to maintain success rates.[3] Since a significantly higher proportion of non-*albicans Candida* species have been isolated in women with recurrent and complicated VVC[2], species identification is important in such cases because of differential susceptibility to –azole antifungal agents.[3]

C glabrata is the predominant non-*albicans Candida* species associated with VVC in the United States, Europe, and Australia.[2] According to two large US studies, *C albicans* and *C glabrata* comprise approximately 93% to 97% of all *Candida* species.[4,5] Other species are comparatively rare.

Table 1. *Candida* Species Prevalence in VVC

Species	Prevalence (n=93,775)[4]	Prevalence (n=429)[5]
C albicans	89.0%	77.3%
C glabrata	7.9%	15.9%
Subtotal	**96.9%**	**93.2%**
C parapsilosis	1.7%	3.9%
C krusei	--	1.6%
C tropicalis	1.4%	1.1%
C lusitaniae	--	0.2%

The primary rationale for differentiating *Candida* species in cases of VVC is due to the increased incidence of resistance to the principal oral –azole agent fluconazole among certain *Candida* species isolates. In an extensive survey of –azole susceptibility among *Candida* species isolated from women with VVC, 67.0% of *C glabrata* isolates (n=112) demonstrated decreased *in vitro* susceptibility to fluconazole.[5] *C krusei* is considered intrinsically resistant to fluconazole.

Table 2.[5] *Candida* Species with Decreased Susceptibility to Fluconazole

Candida Species	% Resistant	% Susceptible-Dose Dependent	Total % Decreased Susceptibility	Antifungals without Decreased Susceptibility
C glabrata	15.2%	51.8%	67.0%	Flucytosine, Imidazoles, Nystatin
C krusei	Intrinsically resistant	Intrinsically resistant	Intrinsically resistant	Imidazoles, Nystatin

In the same study, *C albicans, C parapsilosis, C tropicalis, C lusitaniae* did not exhibit any significant decreased fluconazole susceptibility.

The optimal treatment of non-*albicans* VVC remains unclear because of this phenomenon and its presumed correlation with lack of response to oral –azole antifungal therapy.[1] Treatment options for non-*albicans* VVC include longer duration of therapy with nonfluconazole –azole drugs or non-azole therapy, such as flucytosine, nystatin, or vaginal boric acid.[3,6]

C albicans and *C glabrata* by NAA Test Performance

LabCorp offers identification tests for up to six *Candida* species, but the *C albicans* and *C glabrata* by NAA test detects and differentiates the two *Candida* species responsible for the vast majority of VVC in the US.

LabCorp validated the *C albicans* and *C glabrata* by NAA assay using 256 specimens collected during a clinical trial, which facilitated comparison of PCR performance on vaginal swabs collected using the GenProbe APTIMA® collection system with conventional yeast culture.

The performance in our validation is summarized in the chart below. Concordant culture and PCR results were obtained for 89.8% (230/256) specimens tested. Seven specimens were positive for *C albicans* and *C glabrata* coinfection when tested by PCR, but not by culture, suggesting that the methodology may be superior to conventional culture for the detection of mixed *Candida* species infections.

Table 3. Concordance of *C albicans* & *C glabrata* PCR vs. Culture

	PCR Result			
Culture Result	*C albicans* Positive	*C glabrata* Positive	*C albicans* and *C glabrata* Positive	Negative
C albicans Positive	91	0	7†	10*
C glabrata Positive	0	3	0	0
C albicans and *C glabrata* Positive	0	0	0	0
Negative	9†	0	0	136

† Confirmed by repeat PCR testing.
*9/10 had <5 colony forming units isolated by culture

Relevant Assays	Test Number	Components	Use
***C albicans* and *C glabrata* by NAA**	**180055**	*C albicans, C glabrata*	Suspected or recurrent cases of vulvovaginal candidiasis
***Candida* Six-species Profile**	**180010**	*C albicans, C glabrata, C tropicalis, C krusei, C parapsilosis, C lusitaniae*	Recurrent or problematic cases of vulvovaginal candidiasis
NuSwab Vaginitis (VG)	**180039**	Bacterial vaginosis by NAA, C *albicans*, C *glabrata*, *Trichomonas vaginalis*	Symptoms of vaginitis/vaginosis such as discharge
NuSwab Vaginitis Plus (VG+)	**180021**	Bacterial vaginosis by NAA, C *albicans*, C *glabrata*, *Trichomonas vaginalis, Chlamydia, Gonorrhea*	Symptoms of vaginitis/vaginosis and/or patients at risk for coinfection with Ct/Ng

Visit the online Test Menu at **www.LabCorp.com** for full test information, including CPT codes and specimen collection requirements.

LabCorp's policy is to provide physicians, in each instance, with the flexibility to choose appropriate tests to assure that the convenience of ordering test combinations/profiles does not prevent physicians who wish to order a test combination/profile from making deliberate informed decisions regarding which tests are medically necessary. All the tests offered in test combinations/profiles may be ordered individually using the LabCorp test request form.

References

1. American College of Obstetricians and Gynecologists. Vaginitis. ACOG Practice Bulletin No. 72. *Obstet Gynecol.* 2006;107:1195-1206.
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3. Centers for Disease Control and Prevention. Recommendations and Reports: Sexually transmitted diseases treatment guidelines, 2010. *MMWR.* 2010;59(RR-12):1-114.
4. Vermitsky JP, Self MJ, Chadwick SG, Trama JP, Adelson ME, Mordechai E, Gygax SE. Survey of vaginal-floral *Candida* species isolates from women of different age groups by use of species-specific PCR detection. *J Clin Microbiol.* 2008; Apr 46(4):1501-1503.
5. Richter SS, Galask R, Messer SA, Hollis RJ, Diekema DJ, Pfaller MA. Antifungal susceptibilities of *Candida* species causing vulvovaginitis and epidemiology of recurrent cases. *J Clin Microbiol.* 2005 May;43(5):2155-2162. (studying additional *Candida* and non-*Candida* species)
6. Gilbert DN, Moellering RC Jr, Eliopoulos GM, Chambers HF, Saag MS, eds. *The Sanford Guide to Antimicrobial Therapy* 2011. 41st ed. Sperryville, Va: Antimicrobial Therapy, Inc; 2011:117.

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