

## SHORT REPORT

Vulvovaginal carriage of yeasts other than *Candida albicans*

J Holland, M L Young, O Lee, S C-A Chen

Sex Transm Infect 2003;79:249–250

**Aims:** We investigated the spectrum of yeasts isolated, and compared the epidemiological and laboratory characteristics of women carrying vulvovaginal *Candida albicans* with those carrying yeasts other than *C albicans*.

**Method:** Between April and June 2001, 5802 consecutively received genital swabs from women were plated onto Candida ID chromogenic media (BioMerieux). Blue colonies were reported as *C albicans*; all other colonies (white and pink) were identified to species level using the Vitek YBC card (BioMerieux). In vitro susceptibility to amphotericin (AMB), fluconazole (FLU), itraconazole (ITZ), and voriconazole (VOR) was determined for approximately 40% of non-*C albicans* yeasts using a standardised microdilution method.

**Results:** Yeast was isolated from 1221 women (21%). Of these, *C albicans* only was isolated from 1087 (89%) and yeasts other than *C albicans* from 129 (11%) women. *C glabrata* comprised 89 (69%) of the latter. Women in whom other yeasts were recovered were older than those with *C albicans* (mean 43, versus 33 years,  $p < 0.001$ ). All isolates tested ( $n=53$ ) were susceptible to AMB and VOR. Seven (24%) *C glabrata* strains were susceptible to FLU with 21 (72%) testing susceptible-dose dependent.

**Conclusion:** Yeasts other than *C albicans* are common vaginal isolates even in a primary care population. The species isolated are less susceptible to FLU than most *C albicans*.

Vulvovaginal candidiasis is a common problem. The majority of infections are caused by *Candida albicans*, but there is increased awareness of the role of yeasts other than *C albicans*. It is important to identify these other yeasts because they tend to be less susceptible to the commonly used topical and oral azole antifungals<sup>1,2</sup> and are associated more frequently with recurrent infection than *C albicans*.<sup>3</sup> Previous studies have been performed in tertiary care settings and included women with recurrent symptoms. Our study investigated the epidemiological and microbiological features of women carrying yeasts other than *C albicans* by examining genital specimens collected in the primary care setting, including those taken for antenatal or sexual health screening purposes. In addition, in vitro susceptibility testing was performed on 40% of yeasts other than *C albicans*.

#### METHOD AND MATERIALS

The study was performed between April and June 2000. Samples were submitted to a large private pathology laboratory in Sydney, Australia, that services the general community. All genital swabs collected in Amies transport medium received from women during the study period were included. If swabs from more than one site were received these were plated out separately but considered as one item for statistical analysis and included as a positive culture if either sample grew yeasts. Swabs were cultured onto quarter plates of Candida ID media (BioMerieux), a chromogenic media that aids identification of

**Table 1** Distribution of yeast species other than *C albicans* recovered from genital swabs

Species	No (%)
<i>C glabrata</i>	89 (69)
<i>C parapsilosis</i>	12 (9)
<i>C krusei</i>	12 (9)
<i>C tropicalis</i>	8 (6)
<i>C kefir</i>	1 (1)
<i>S cerevisiae</i>	6 (5)
<i>C humicolus</i>	1 (1)
Total	129 (100)

*candida* species.<sup>4</sup> Quantitation of yeast colonies was not attempted. All blue colonies were reported as *C albicans*. All white or pink colonies were identified to species level using Vitek YBC cards (Vitek Systems, BioMerieux).

In vitro susceptibility testing was performed for 53 out of 129 isolates of yeast other than *C albicans*. Testing was performed by the broth microdilution technique according to the National Committee for Clinical Laboratory Standards (NCCLS) M27 A protocol against amphotericin B (AMB), fluconazole (FLU), itraconazole (ITZ), and voriconazole (VOR).<sup>5</sup>

Data on age, pregnancy status, presence of diabetes, other pathogens isolated, and reason for submitting the sample were obtained from the request form. Statistical analysis was performed using the *t* test for equality of the means of age, and by the  $\chi^2$  test for other comparisons using SPSS PC+ software (version 7.0; SPSS, Chicago, IL, USA).

#### RESULTS

Swabs were received from 5802 women. No samples were sent from specialists or from hospitalised patients. Yeast was isolated from 1221 women (21%). *C albicans* only was grown from 1087 women (89%) and a single species of other yeast from 129 (11%) (table 1). Five women had infections with both *C albicans* and another yeast (four *C glabrata*, one *C parapsilosis*). These five women were excluded from further statistical analysis.

Comparison of the characteristics of women carrying vulvovaginal *C albicans* and yeasts other than *C albicans* is summarised in table 2.

The mean age of women with vulvovaginal *C albicans* carriage was 33.3 years (SD 13.5) compared to 42.9 (15.9) years for women with other vulvovaginal yeasts ( $p < 0.001$ ). All other yeast species with the exception of *Saccharomyces cerevisiae* and *Cryptococcus humicolus* were isolated from women with a mean age greater than that of women with *C albicans*.

All isolates tested were susceptible to AMB and VOR (proposed breakpoint of 4 mg/l).<sup>6</sup> *C kefir* and *C humicolus* were susceptible to FLU and ITZ. Twenty nine strains of *C glabrata* were tested, of which 21 (71%) tested susceptible-dose dependent (S-DD; MIC 16–32 mg/l), and one isolate was resistant (MIC

**Table 2** Comparison of epidemiological and laboratory features of women carrying *C albicans* with those carrying other yeasts

	<i>C albicans</i> (n=1087)‡	Other yeasts (n= 129)‡	p Value
Mean age (years)	33	43	<0.001
Pregnant	136 (12.5%)	10 (11.2%)	0.6
Diabetes	14 (1.3%)	2 (2.2%)	0.6
Co-pathology*	19 (1.7%)	1 (0.8%)	0.5
Positive microscopy†	706 (64.9%)	93 (72.1%)	0.117
Symptoms noted on request form‡	564 (64.7%)	66 (70.2%)	0.43

\*Presence of another genital tract pathogen.

†Yeast forms plus or minus pseudohyphae seen on directly prepared wet film and/or Gram stain of swab.

‡Reason for submitting sample was not known for 250 women.

64 mg/l) to FLU. Only seven (24%) *C glabrata* isolates were S-DD (MIC 0.25–0.5 mg/l) to ITZ, and 21 (71%) were resistant (MIC  $\geq$  1 mg/l). One isolate of *C krusei* was resistant to ITZ with the remaining strains (n = 8) testing S-DD. *C krusei* is intrinsically resistant to FLU. The MIC<sub>50</sub> obtained when testing four isolates of *S cerevisiae* against FLU was 8 mg/l.

## DISCUSSION

Chromogenic agar such as Candida ID media are commonly used in microbiology laboratories and support the growth of candida to the same extent as Sabouraud's dextrose agar (SDA). Chromogenic agar enables mixed growth to be more easily identified. Neither the germ tube test nor Candida ID media will, however, distinguish *C dublinensis* from *C albicans* as these are both germ tube positive and blue on this medium.<sup>4</sup>

Isolation of yeast from the female genital tract was common. Yeasts other than *C albicans* comprised 11% of our cases, and our study and others worldwide<sup>7</sup> have found *C glabrata* to be the most common yeast other than *C albicans* to be isolated. *S cerevisiae* has been considered to be a rare cause of vaginitis<sup>1</sup>; however, this yeast comprised 5% of our yeasts other than *C albicans* isolates.

We found no difference in the rate of positive microscopy between *C glabrata* vaginal carriage and *C albicans*; others have however reported that the diagnosis of *C glabrata* vaginitis is more difficult because this organism does not form hyphae or pseudohyphae.<sup>2</sup>

Accepted risk factors for candida vaginitis include poorly controlled diabetes and pregnancy. A postulated risk factor for *C glabrata* vaginitis is a more alkaline pH such as occurs with concomitant bacterial vaginosis.<sup>2</sup> We explored these factors in our population but found no difference between *C albicans* and *C glabrata* in the rate of diabetes, pregnancy, or the isolation of co-pathogens. However, reliance on request forms would have limited the information available.

Women with yeasts other than *C albicans*, with the exception of *S cerevisiae* and the one isolate of *Cryptococcus humicolus*, were older than women with *C albicans*. The reason for this is unclear however, it is possible that these patients may have been subjected to longer periods of antifungal therapy or may have recurrent disease.<sup>8</sup> There is also evidence that older people may be more likely to be colonised with *C glabrata*.<sup>9</sup>

Consistent with other reports, yeasts other than *C albicans* generally had higher MICs to FLU, ITZ, and VOR compared to *C albicans*.<sup>10</sup> Our study did not investigate the treatments prescribed to the women; however, the literature indicates that topical or oral azole treatment does not reliably treat *C glabrata* infections. Cure rates are less than 50% even with longer courses of clotrimazole.<sup>11</sup> Alternative therapies for *C glabrata* such as boric acid administered intravaginally once daily for 14 days result in clinical cure or improvement in 81% of patients.<sup>11</sup> The optimal treatment for *C krusei* or *S cerevisiae* vaginitis is not known. Prolonged courses of clotrimazole or the use of boric acid may be effective whereas FLU is likely to

be ineffective.<sup>1,8</sup> There are few clinical data on the use of voriconazole for candida vaginitis; however, all our isolates and most isolates of *C glabrata* and *C krusei* reported from the literature are susceptible in vitro to this new azole which may prove of therapeutic value in the future.<sup>12</sup>

## CONCLUSION

In a primary care population the rate of carriage of yeasts other than *C albicans* is common with *C glabrata* being the most frequently isolated species. Most of the species isolated are less susceptible to the commonly used topical and oral azole agents which has implications for therapy.

## ACKNOWLEDGEMENTS

We thank Karen Byth, Department of Medicine, Westmead Hospital, for expert advice on statistical analysis.

## Authors' affiliations

J Holland, M L Young, Mayne Health-Laverty Pathology, NSW, Australia  
O Lee, S C-A Chen, ICPMR, Westmead Hospital, NSW, Australia

Correspondence to: Dr Juliette Holland, Mayne Health-Laverty Pathology, 60 Waterloo Road, North Ryde, NSW 2113, Australia; juliette.holland@maynegroup.com

Accepted for publication 13 December 2002

## REFERENCES

- Sobel JD, Vazquez M, Lynch M, et al. Vaginitis due to *Saccharomyces cerevisiae*: epidemiology, clinical aspects, and therapy. *Clin Infect Dis* 1993;**16**:93–9.
- Fidel PL Jr, Vazquez JA, Sobel JD. *Candida glabrata*: review of epidemiology, pathogenesis, and clinical disease with comparison to *C albicans*. *Clin Microbiol Rev* 1999;**12**:80–96.
- Spinillo A, Nicola S, Colonna L, et al. Frequency and significance of drug resistance in vulvovaginal candidiasis. *Gynecol Obstet Invest* 1994;**38**:130–3.
- Fricker-Hidalgo H, Orenga S, Lebeau B, et al. Evaluation of Candida ID, a new chromogenic medium for fungal isolation and preliminary identification of some yeast species. *J Clin Microbiol* 2001;**39**:1647–9.
- National Committee for Clinical Laboratory Standards. Reference method for broth dilution antifungal susceptibility testing of yeasts approved standard M27-A. Wayne, PA, USA: National Committee for Clinical Laboratory Standards.
- Kronvall G, Karlsson I. Fluconazole and voriconazole multidisk testing of *Candida* species for disk test calibration and MIC estimation. *J Clin Microbiol* 2001;**39**:1422–8.
- Odds FC, ed. *Ecology of candida and epidemiology of candidiasis*. London: Bailliere Tindall, 1988:85–6.
- Singh S, Sobel J, Bhargava P, et al. Vaginitis due to *Candida krusei*: epidemiology, clinical aspects, and therapy. *Clin Infect Dis* 2002;**35**:1066–70.
- Blot S, Vandewoude K, Hoste E, et al. Outcome in critically ill patients with candida fungaemia: *Candida albicans* vs *Candida glabrata*. *J Hosp Infect* 2001;**47**:308–13.
- Pfaller MA, Diekema DJ, Jones RN, et al. Trends in antifungal susceptibility of *Candida* spp isolated from pediatric and adult patients with bloodstream infections: SENTRY Antimicrobial Surveillance Program 1997 to 2000. *J Clin Microbiol* 2002;**40**:852–6.
- Sobel JD, Chaim W. Treatment of *Torulopsis glabrata* vaginitis: retrospective review of boric acid therapy. *Clin Infect Dis* 1997;**24**:649–52.
- Espinell-Ingroff A, Boyle K, Sheehan DJ. In vitro antifungal activities of voriconazole and reference agents as determined by NCCLS methods: review of the literature. *Mycopathologia* 2001;**150**:101–15.