

Vulvovaginal candidosis caused by *Candida Non-Albicans*, proportion and clinical characteristics in the Dr. Cipto Mangunkusumo National General Hospital, Jakarta

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Abstrak

Angka kejadian Kandidosis vulvovaginalis (KVV) yang disebabkan *C.non-albicans* belakangan ini cenderung meningkat. Namun di RSCM, sampai saat ini belum ada data tentang proporsi dan karakteristik KVV yang disebabkan *C.non- albicans*. Untuk itu dilakukan penelitian deskriptif dengan rancangan studi potong lintang. Subyek penelitian adalah wanita yang datang ke Poliklinik Kulit dan Kelamin serta Poliklinik Kebidanan dan Kandungan RSCM yang mengeluh keputihan dan gatal, serta pada pemeriksaan sediaan apus dengan pewarnaan Gram ditemukan blastospora dengan atau tanpa pseudohifa, tanpa infeksi genital spesifik lain. Kultur dibuat dengan menggunakan media CHROMagar *Candida* untuk membedakan spesies *Candida* penyebab. Didapatkan subyek terbanyak pada kelompok usia 26 – 44 tahun, dengan nilai tengah 29 tahun. Dari 69 subyek yang menderita KVV, sebanyak 30,4% disebabkan oleh *C.non- albicans*, terdiri atas : *C. glabrata* (61,9%), *C. tropicalis* (28,6%) dan *C. parapsilosis* (9,5%). KVV yang disebabkan oleh *C.non-albicans* cenderung terjadi pada pasien dengan usia lebih dari 45 tahun, menggunakan KB non-hormonal, memiliki pasangan dengan keluhan gatal dan kemerahan pada ujung penis dan keluhan terjadi lebih dari satu tahun. Tidak ditemukan perbedaan gejala klinis KVV yang disebabkan oleh *C. albicans* dan *C. non-albicans*. (*Med J Indones* 2003; 12: 142-7)

Abstract

The prevalence of Vulvovaginal candidosis (VVC) caused by *C.non-albicans* tends to increase, recently. The aim of this study was to obtain data about proportion and clinical characteristic of *C.non-albicans* VVC at dr. Cipto Mangunkusumo General Hospital, Jakarta. This is a cross-sectional study on all female patients with symptoms of VVC visiting Obstetri-gynaecology and Dermatovenereology outpatient clinics at Dr. Cipto Mangunkusumo General Hospital, Jakarta. All subjects had positive Gram stain, showed *Candida* spp. on culture with CHROMagar *Candida*, and had no other specific genital infections. Sixty nine subjects aged 26 – 44 years old (averaged 29 years old) were included in this study. *Candida non-albicans* was found in 30.4% subject, and consisted of: *C. glabrata* (61.9%), *C. tropicalis* (28.6%) and *C. parapsilosis* (9.5%). We found that *C.non-albicans* VVC infections are more common in women above 45 years old, using non-hormonal contraceptives, whose sexual partner has erythema and pruritus in glands penis, and having the disease for more than 1 year. No differences in clinical symptoms were noted between *C. albicans* and *C.non-albicans* infection. We concluded from this study that the proportion of *C. non-albicans* infections at dr. Cipto Mangunkusumo General Hospital, Jakarta, with *C. glabrata* represents the most prevalent species. No characteristic clinical symptoms were found from the subjects with *C.non-albicans* VVC when compared with those infected by *C. albicans*. (*Med J Indones* 2003; 12: 142-7)

Keywords : vulvovaginal candidosis, *Candida non-albicans*, CHROMagar *Candida*

Vulvovaginal candidosis (VVC) is a mucosal infection caused by *Candida* spp. The estimated incidence of

VVC is 5 to 20%, and 1 to 5% of cases become recurrent.¹⁻⁴ *Candida albicans* is responsible for 80 – 90 % of VVC episodes and the rest are caused by *non-albicans* species.⁵⁻⁷ A tendency of increasing frequency of *C. non-albicans* VVC in many places and countries has been reported as high as 2 – 57 %, recently. The most common *non-albicans* species are: *Candida glabrata*, followed by *Candida tropicalis* and *Candida parapsilosis*.⁶⁻¹⁰

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C. non-albicans infection now becomes a medical problem, due to the increasing prevalence especially in immunocompromised patients, the emergence of newly recognized pathogens, the discovery of resistance species to anti-fungal azoles as well as recurrent infections.^{8,9,11} It is also suggested to be associated with inadequate treatment with broad spectrum anti-fungal.

We performed this study to obtain further data on the proportion and clinical characteristic of *C. non-albicans* VVC in dr. Cipto mangunkusumo General Hospital, Jakarta. We hope the results of this study will help the health providers to perform optimal management of patients with VVC, especially those who do not respond to standard therapy.

METHODS

We conducted a cross-sectional study at Dr. Cipto Mangunkusumo General Hospital, Jakarta, from February to April 2002. The subjects were female patients who attended Obstetric Gynaecology and Dermatovenereology outpatient clinics. The subjects must have a distinct clinical symptoms associated with VVC, a positive vaginal smear with Gram stain (blastospore and or pseudohyphae), a positive *Candida* spp. with CHROMagar Candida culture and had no other specific genital infections. Subjects were not allowed to take any oral or topical antifungal for 2 and 4 weeks, respectively, before entering this study.

Informed consents were taken from all subjects. Epidemiological characteristics, history of illness, predisposing factors, physical examination of the external genitalia and the surrounding skin, the result of vaginal specimen with Gram stain and *Candida* spp. identified in CHROMagar Candida media are reported.

Data were analyzed using SPSS 10.0 for Windows and Epi Info 2000. Chi-square test or Fisher exact test were applied for data value less than 5, to compare the *C. albicans* versus *C.non-albicans* infection but not for mixed infection.

RESULTS

Sixty-nine women aged 26-44 years old (mean: 29 years) were included in this study. Fifty-seven subjects were married (82.6%). Most of them were in

the middle education group (59.4%), and only 23 subjects had a permanent job, as a government or private employee (8.7% and 24.6%, respectively).

Table 1. Proportion of the *Candida* spp as the cause of VVC

<i>Candida</i> spp	n	%	% among <i>C. non albicans</i>
<i>C. albicans</i>	43	62.3	0
<i>C non-albicans</i> :	21	30.4	0
<i>C. glabrata</i>	13	61.9	61.9
<i>C. tropicalis</i>	6	28.6	28.6
<i>C. krusei</i>	0	0.0	0.0
<i>C. parapsilosis</i>	2	9.5	9.5
Mixed infection	5	7.3	0

n, numbers

C. non-albicans is found in 30.4 % subjects, with *C. glabrata* as the most common species. Mixed infection of *C. albicans* + *C. tropicalis*, and *C. albicans* + *C. parapsilosis*, were found in 3 and 2 subject, respectively. (Tabel 1)

Table 2 lists the history of illness and subjective findings.

Pruritus is the most frequent chief complaint (49.3%) followed by fluor albus (46.4%). Severe pruritus seems to be more associated with *C. albicans* VVC but there was no significant different compared to *C. non albicans*. (p>0.05, OR 2.29, 95% CI 0.41-32.62).

Among fifty-six subjects (81.2%) who had a husband or sexual partner, four (5.8%) reported that their partner also had pruritus and erythema at the gland penis. One married subject did not have a husband/sexual partner anymore. Subjects who had a husband or sexual partner with erythema and pruritus at the gland penis seemed to have a greater tendency to get *C. non-albicans* infection. (p > 0.05, OR 6.40, 95% CI 0.51 –174.56).

Most of the subjects had pruritus and fluor albus for less than 1 year (91.3%). Those with duration of illness more than 1 year tend to have *C. non-albicans* VVC. (OR 3.42, 95% CI 0.41-32.62).

We found no relationship between subjects with *C non-albicans* VVC with history of recurrent illness of more than 4 times during the last 1 year and those who had already been treated by antifungal.

Table 2. History of illness and subjective findings

	<i>C. albicans</i> n (%)	<i>C. non- albicans</i> n (%)	Mixed n (%)	n (%)	p	OR; CI 95%
Chief complaint						
Pruritus	25 (73.5)	7 (20.6)	2 (5.9)	34(49.3)		
Fluor albus	16 (50.0)	13 (40.6)	3 (9.4)	32(46.4)		
Pruritus	39	17	5		0.2359	2.29 (0.41-12.79)
Partner’s symptom	1 (25.0)	3 (75.0)	0	4(5.8)	0.1200	6.40 (0.51-174.56)
Duration > 1 year	2 (33.3)	3 (50.0)	1 (16.7)	6(8.7)	0.1939	3.42 (0.41-32.62)
Previous illness						
1 – 3 x / last 1 year	13 (72.2)	4 (22.2)	1 (5.6)	18(26.1)		
≥ 4 x / last 1 year	7 (63.6)	3 (27.3)	1 (9.1)	11(15.9)	0.5252	0.72 (0.09-5.72)
Previous anti-mycotic treatment						
Doctor/Health sevicees	16(69.6)	5(21.7)	2(8.7)	23(33.3)	0.5024	1.60 (0.15-16.43)
None	4(66.7)	2(66.7)	0	6(8.3)		

n, numbers; OR, Odds Ratio; CI, Confidence interval

Table 3 shows that the patients aged more than 45 years old (premenopausal) also seems to be related with *C. non-albicans* VVC. (OR 4.32, 95% CI 0.60 – 37.75). Subject with pregnancy and overweight tend to suffer *C. albicans* VVC more frequently. (p > 0.05, RO 1.46, 95% CI 0.35-6.47 and p > 0.05, RO 1.61, 95% CI 0.13 – 43.89, respectively).

Subjects with contraceptives devices tend to be infected by *C. albicans* VVC. (p=0.0069, OR 5.7, 95% CI 1.37-24.86). Meanwhile, non-hormonal contraceptive users

have association with *C. non-albicans* VVC. (p>0.05, OR 5.0, 95% CI 0.41 – 12.79).

No significant statistical association between systemic antibiotics’ and corticosteroids’ user with *C. non-albicans* VVC.

C. albicans is the most prevalent species found in the subjects with clinical symptoms of vulvar erythema, edema, erosion, ample and cheese-like appearance of the discharge, satellite lesions surrounding genitalial skin and sour odour. But no specific symptoms were noted on *C. non-albicans* VVC.

Table 3. Predisposing factors

Predisposing factors	<i>C. albicans</i> n (%)	<i>C. nonalbicans</i> n (%)	Mix n (%)	Total n (%)	p	RO; CI (95%)
Age > 45 year	2 (33.3)	4 (66.7)	0	6(8.7)	0.1050	4.32 (0.60-37.75)
Associated diseases						
DM	2 (100)	0	0	2(2.9)		
TB	3 (100)	0	0	3(4.3)		
Pregnancy	11 (61.1)	4 (22.2)	3 (16.7)	18(26.1)	0.4031	0.68 (0.15-2.85)
Contraceptive						
Hormonal	4 (40.0)	4 (40.0)	2 (20.0)	10(14.5)		
Non-hormonal	1 (16.7)	5 (83.3)	0	6(8.7)	0.2378	5.0 (0.26-179.03)
Weight						
Underweight	1 (50.0)	1 (50.0)	0	2(2.9)	0.5899	0.54 (0.01-21.40)
Normoweight	28 (62.2)	15 (33.3)	2 (4.4)	45(65.2)		
Overweight	3 (75.0)	1 (25.0)	0	4(5.8)	0.5677	1.66 (0.13-44.99)
Antibiotics	12 (57.1)	9 (42.9)	0	21(30.4)	0.2317	0.52 (0.15-1.76)
Corticosteroids	2 (50.0)	2 (50.0)	0	4(5.8)	0.3979	0.46 (0.04-5.09)

n, numbers; OR, Odds Ratio; CI, Confidence interval

Cheese-appearance discharge is more frequently found in *C. albicans* VVC. ($p > 0.05$, OR 2.13, 95% CI 0.53–9.18). Negative Gram staining examination was found in 8.7 %.

DISCUSSION

We used CHROMagar Candida to isolate *Candida* spp. CHROMagar Candida is a new differential isolation medium, which allows identification of *C. albicans* and *C. non-albicans*, especially *C. tropicalis*, *C. glabrata* dan *C. krusei*, on the basis of their colour and appearance.¹² Compared with the standard or conventional isolation methods, this method provide a quicker result within 24 – 48 hours, simpler and easier.¹³⁻¹⁵ Multiple yeast species can be detected in one specimen more easily.¹⁴ The sensitivity and specificity of this method were also reported high.²

The majority of the subject is on childbearing age, and this is consistent with other studies.⁶⁻⁹ The relationship between *C. non-albicans* VVC with age, sexual activity, job and education is still unclear. Eventhough one previous study found a relation between *C. glabrata* VVC with low education level.¹⁶

Incidence of *C. non-albicans* VVC at dr. Cipto Mangunkusumo General Hospital (30.4 %) tends to increase, with *C. glabrata* being the most frequent. The same result has been reported on other studies.^{3,8,9}

Several studies in other centers suggested that these infections were caused by an inappropriate use of antifungal.⁸⁻¹⁰ However, we failed to show this association in this study.

Severe pruritus seems to be associated with *C. albicans* infections. While husband/sexual partner's symptom tends to correlate with *C. non-albicans* VVC. Physical examination and culture from the partner should be performed to get a more reliable data.

We should consider about the recall bias since some data were obtained through history taking.

Recurrent VVC could be caused by relapse (due to the same organism which is temporally suppressed by anti fungal therapy)^{7,17} or reinfection (from natural gastrointestinal source or sexual transmission).^{7,10,17,18} VVC patients can transmit the infection to her partner^{17,18} but, relationship between *C. non-albicans* infection and the partner's symptoms is not known.

Table 4. Objective finding of genitalia external, the surrounding skin and laboratory examination.

Objective findings	C. albicans C. non-albicans Mix			Total n(%)	p	RO; CI (95%)	
	n (%)	n (%)	n (%)				
Erythema	Mild	14 (60.9)	6 (26.1)	3 (13.0)	23(33.3)	0.6985	0.80 (0.21-2.90)
	Distinct	26 (61.9)	14 (33.3)	2 (4.8)	42(60.9)		
Edema		20 (66.7)	8 (26.7)	2 (6.7)	30(43.5)	0.5239	1.41 (0.43-4.70)
Erosion		13 (65.0)	6 (30.0)	1 (5.0)	20(29.0)	0.8914	1.08 (0.30-3.99)
Discharge							
No		1 (100)	0	0	1(1.4)		
Limited in vagina		28 (59.6)	17 (36.2)	2 (4.3)	47(68.1)		
Come out from vagina		14 (66.7)	4 (19.0)	3 (14.3)	21(30.4)	0.2367	2.13 (0.53-9.18)
Consistency of discharge							
Cheese-appearance		19 (67.9)	5 (17.9)	4 (14.3)	28(40.6)	0.1139	2.53 (0.69-9.69)
No coagulated		24 (58.5)	16 (39.0)	1 (2.4)	41(59.4)		
Involvement of surrounding genitalia skin							
Sour Odour		9 (69.2)	4 (30.8)	0	13(18.8)	0.8605	1.13 (0.26-5.13)
Gram Stain		20 (60.6)	8 (24.2)	5 (17.2)	33(47.8)	0.7011	1.40 (0.18-10.64)
Positive		39 (61.9)	19 (30.2)	5 (7.9)	63(91.3)	0.6491	1.03 (0.12-7.47)
Negative		4 (66.7)	2 (33.3)	0	6(8.7)		

n, numbers; OR, Odds Ratio; CI, Confidence interval

Subjects with VVC symptom lasting more than 1 year tend to have *C. non-albicans* infections. The same result was reported by Nyirjesy et al.¹⁰ But recurrent infections during the last one year did not seem to correlate with *C. non-albicans* VVC. Opposite finding was reported by Sobel et al.⁸ The cause of this difference is not well understood, but the infection pattern in different region might have influence the results.

It seems that *C. non-albicans* infection is related with age. Spinillo et al., likewise, found a tendency of *C. glabrata* infection in the patients of more than 38 years old, but not with other *C. non-albicans*.¹⁶ Pregnancy and overweight might be a predisposing factors for VVC, but there is no clear association with *C. non-albicans* VVC.^{4,8}

Non-hormonal contraceptive tends to associate with *C. non-albicans* VVC. Other studies, however, reported a higher incidence of *C. albicans* VVC among condom⁶ and intrauterine device user.¹⁶ We could not find any reasons for this microbiological difference.

We did not find any specific symptoms associated with *C. non-albicans* VVC. Other study also found no characteristic differences between clinical symptoms of *C. albicans* and *C. non-albicans* infections.¹⁰ But Ryan et al.¹ found that vulvar erythema and edema were associated with *C. albicans* VVC.¹ Schaaf et. al. reported that *C. albicans* VVC is less frequently had unpleasant odor.¹⁹

Negative Gram staining in this study might be caused by technical problems, especially with *C. glabrata* infections, the only *Candida* spp that not produce pseudohypha.⁸

We hope that the results of this study will drive the health providers to consider the possibility of *C. non-albicans* infection, in the case of non responsiveness to conventional therapy. In such patients, species identification and resistancy test should be performed.²⁰

From this study, we found that the proportion of *C. non-albicans* infection at dr. Cipto Mangunkusumo General Hospital, Jakarta, is 30.4%, with *C. glabrata* as the most prevalent species.

No specific clinical symptoms were found in the subjects with *C. non-albicans* VVC. We also found

that *C. non-albicans* VVC infections are more common in women with age more than 45 years, using non-hormonal contraceptive, have a sexual partner with symptoms of erythema and pruritus on the glands penis, and a history of complaint for more than 1 year.

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