

Recurrent vulvovaginal candidiasis in Colombian women: Main clinical and microbiological characteristics

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Background

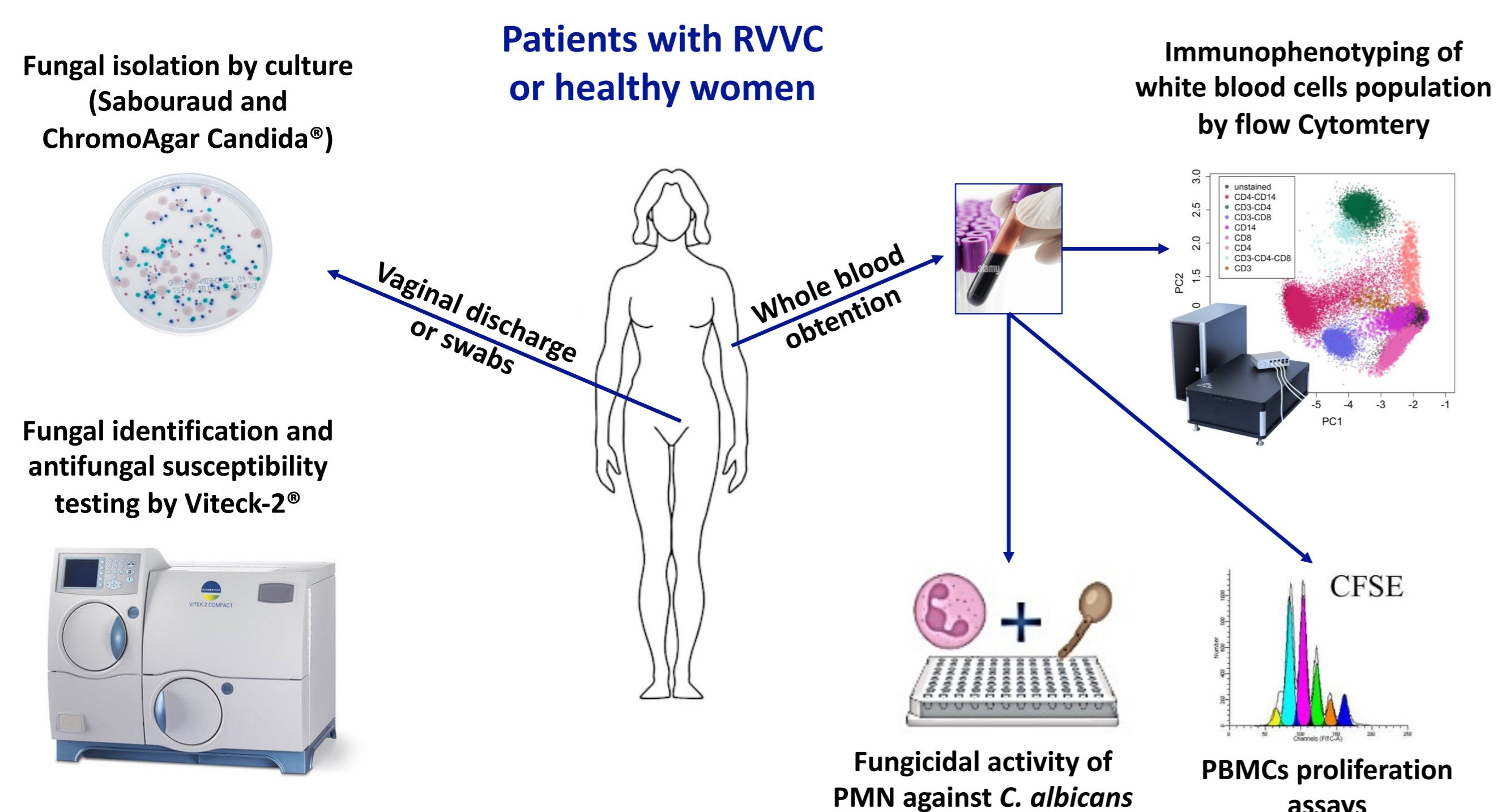
Vulvovaginal candidiasis (VVC) is the second cause associated with genital tract infections; Approximately 75% of the female population will suffer from VVC at least once in their life (1,2). It is estimated that 138 million people worldwide have recurrent vulvovaginal candidiasis (RVVC), which is defined as four or more episodes of VVC in one year (3,4). This condition is mainly caused by *C. albicans*, although an increase in other species has been reported. Among the different risk factors associated with the development of RVVC, the following are described: pregnancy, use of therapy with broad-spectrum antibiotics and steroids, hormone replacement therapy, genetic mechanisms, immune (HIV, uncontrolled diabetes and other underlying diseases) and some hygiene, behavioral and idiopathic habits. A failure in the natural or primary immune response is also considered a predisposing factor for suffering RVVC, when the patient does not present any of the aforementioned factors (5).

Objective

To determine the main clinical and microbiological characteristics in a cohort of patients with diagnosis of recurrent vulvovaginal candidiasis (RVVC).

Methods

A cross-sectional study was carried out for 57 women, 34 with diagnosis of RVVC, and 23 healthy women as a control. Basic data of personal history as well as lower genital tract symptoms and signs were analyzed.



Results

The median age of the patients and healthy women was 29 (IQR 34-23) and 24 (IQR 30-23) years, respectively. All RVVC patients presented at least two of the following symptoms: discharge, irritation, or burning sensation. Eight (33.5%) patients presented four episodes per year while 26 (76.5%) presented more than five episodes per year. Of note, 29 (85.3%) patients used azoles as treatment for VVC during the last year. In all patients with RVVC, *Candida* spp. was isolated, of which 31 (91%) corresponded to *C. albicans* and three (9%) to *C. lusitanae*. Three isolates of *C. albicans* were resistant to fluconazole, while one isolate were resistant to voriconazole, amphotericin B, and flucytosine each, respectively; one isolate of *C. lusitanae* resistant to flucytosine was found.

Table 1. Main socio-demographic characteristics of patients with RVVC

	Control (n=23)	RVVC (n=34)
Age groups (in years)		
<20	-	1 (2.9)
20-29	16 (69.5)	16 (47)
30-39	5 (21.8)	12 (35.4)
40-49	2 (8.7)	5 (14.7)
Menarche (in years)		
8-11	7 (30.4)	10 (29.4)
12-15	16 (69.6)	21 (61.8)
>15	-	3 (8.8)
Ethnicity		
Afrocolombian	3 (13)	4 (11.8)
Caucasian	3 (13)	-
Mixed-race	13 (56.6)	27 (79.4)
Other	4 (17.4)	3 (8.8)
Contraceptive use		
Implant	1 (4.3)	1 (2.9)
Caps or diaphragms	6 (26.1)	12 (35.3)
Contraceptive injection	1 (4.3)	2 (5.9)
IUD (Intrauterine device)	3 (13)	5 (14.7)
No use	12 (52.3)	14 (41.2)
Number of sexual partners		
1	4 (17.4)	3 (8.8)
2	4 (17.4)	7 (20.7)
3	2 (8.7)	2 (5.9)
4	-	6 (17.6)
5	3 (13)	6 (17.6)
>5	10 (43.5)	10 (29.4)

Table 2. Main clinical characteristics of patients with RVVC

	Control (n=23)	RVVC (n=34)
RVVC symptoms		
Burning sensation, Discharge, & irritation	-	27 (79.4)
Burning Sensation & Discharge	-	5 (14.7)
Discharge	-	2 (5.9)
Number of VVC episodes in the last year		
4	-	8 (23.5)
5-8	-	15 (44.1)
>8	-	11 (32.4)
Antifungal use		
Azoles	-	29 (85.3)
Polyenes	-	3 (8.8)
None	-	2 (5.9)
Allergies		
Yes	12 (52.2)	16 (47)
Not	11 (47.8)	18 (53)
Family history of VVC		
Yes	1 (4.3)	5 (14.7)
Not	22 (95.7)	29 (85.3)

Table 3. In vitro susceptibility of *Candida* spp. to the main antifungal in clinical use (n = 34)

Antifungal drugs	<i>Candida</i> spp.	S n (%)	SDD n (%)	I n (%)	R n (%)	Total n (%)
Fluconazole	<i>C. albicans</i>	27 (87.1)	1 (3.2)	-	3 (9.7)	31 (100)
	<i>C. lusitanae</i>	2 (66.6)	-	1 (33.3)	-	3 (100)
Voriconazole	<i>C. albicans</i>	27 (87.1)	-	3 (9.7)	1 (3.2)	31 (100)
	<i>C. lusitanae</i>	3 (100)	-	-	-	3 (100)
Caspofungin	<i>C. albicans</i>	31 (100)	-	-	-	31 (100)
	<i>C. lusitanae</i>	3 (100)	-	-	-	3 (100)
Micafungin	<i>C. albicans</i>	31 (100)	-	-	-	31 (100)
	<i>C. lusitanae</i>	3 (100)	-	-	-	3 (100)
Amphotericin B	<i>C. albicans</i>	30 (96.8)	-	-	1 (3.2)	31 (100)
	<i>C. lusitanae</i>	3 (100)	-	-	-	3 (100)
Flucytosine	<i>C. albicans</i>	30 (96.8)	-	-	1 (3.2)	31 (100)
	<i>C. lusitanae</i>	2 (66.6)	-	-	1 (33.3)	3 (100)

S, Susceptible; SDD, Susceptible Dose Dependent; I, Intermediate susceptibility; R, Resistant

Noteworthy, in patients with CVVR, a significant increase in neutrophils were observed, but with an altered fungicidal capacity; furthermore, PBMCs had a lower proliferative capacity compared to healthy controls.

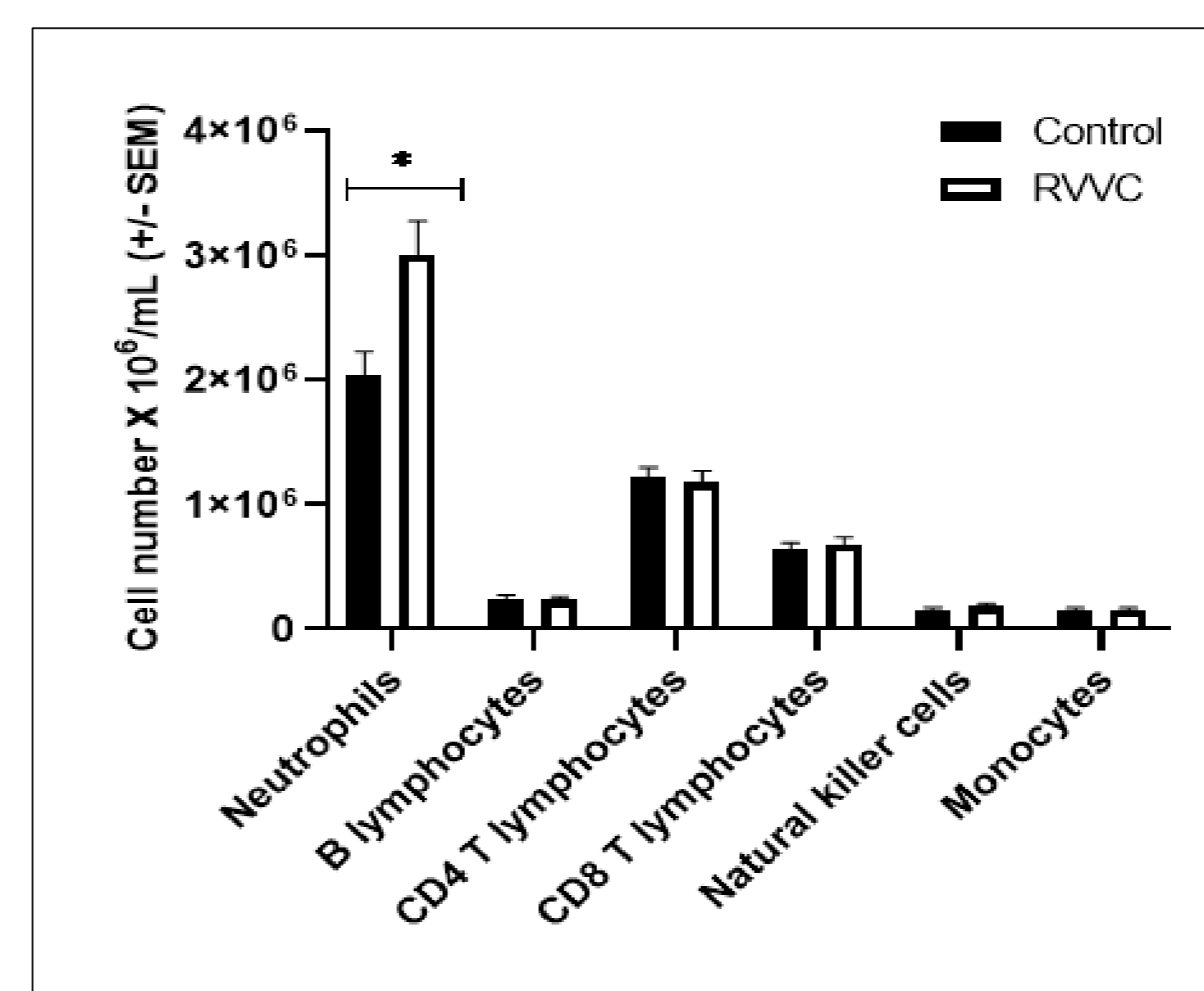


Figure 1. Absolute number of circulating white blood cell populations in patients suffering RVVC and healthy women. Immunophenotyping was determined using monoclonal antibodies against specific surface markers and by flow cytometry. Differences between groups were calculated using Mann-Whitney test. Significant differences are expressed as * P < 0.05, ** P < 0.01, *** P < 0.001.

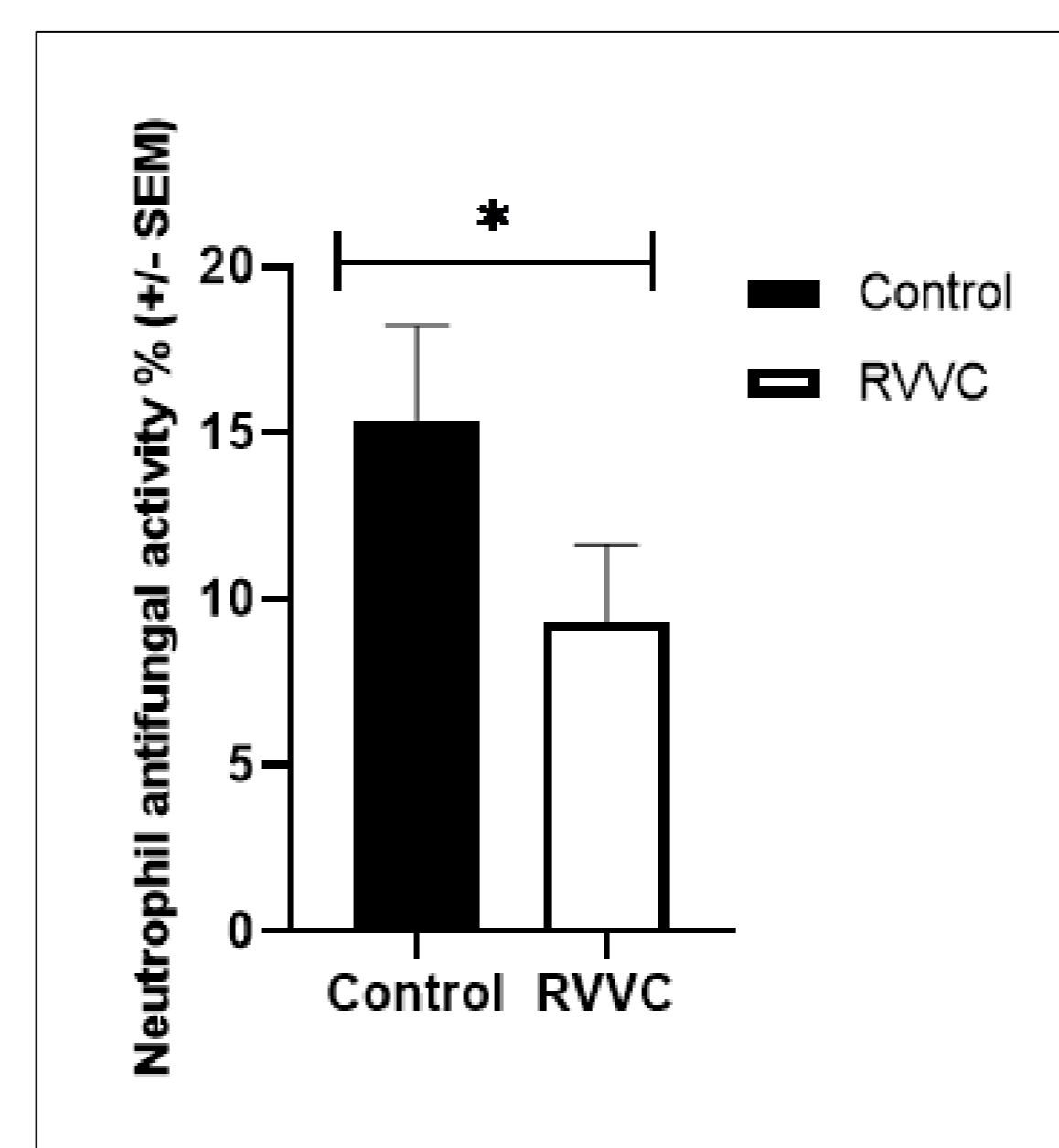


Figure 2. Fungicidal activity of neutrophils against *C. albicans*. Neutrophils were isolated and purified from blood of patients with RVVC and healthy women and then infected with a *C. albicans* ATCC 10231 strain in a MOI of 2. Differences between groups were calculated using Mann-Whitney test. Significant differences are expressed as * P < 0.05, ** P < 0.01, *** P < 0.001.

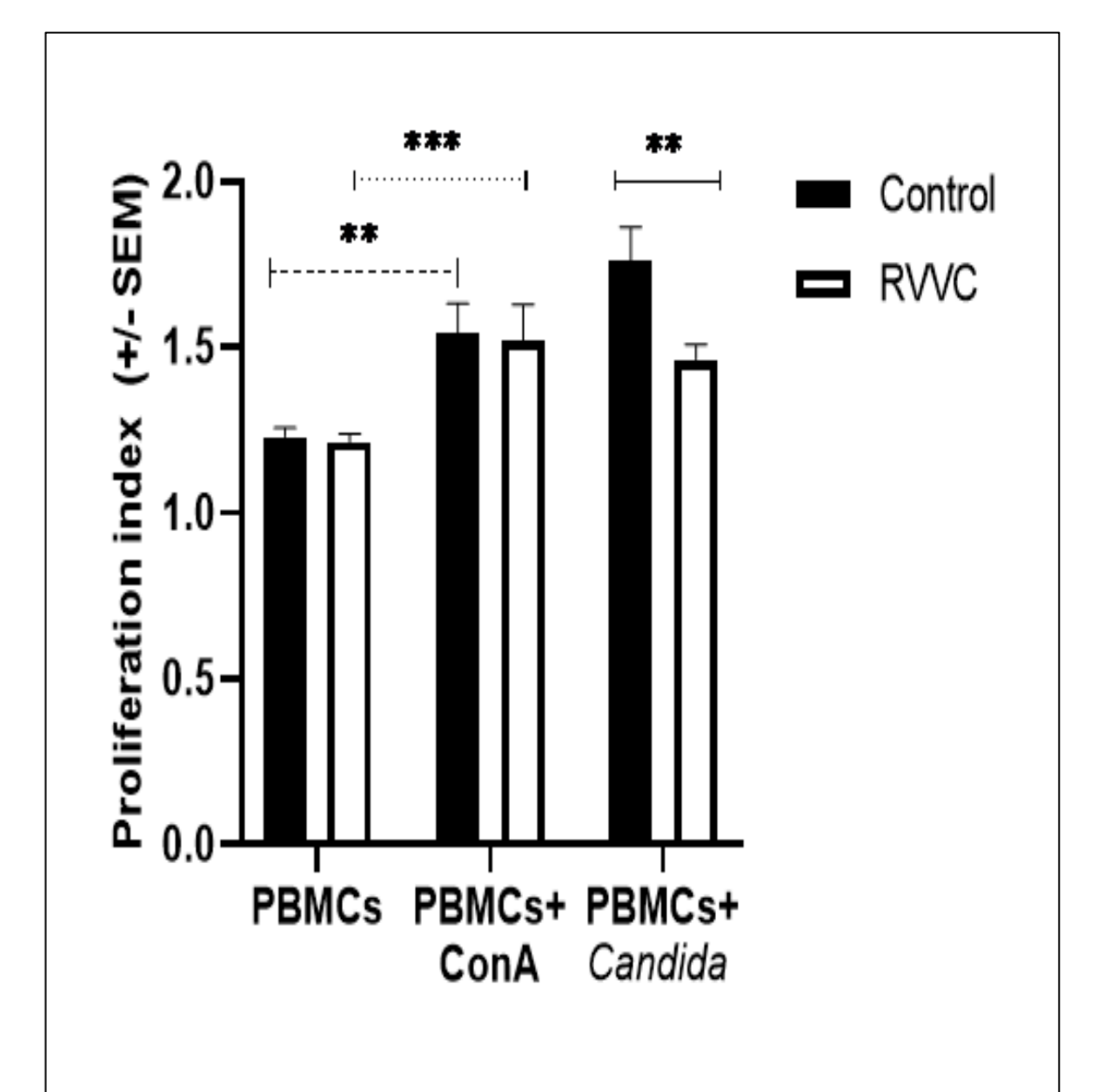


Figure 3. PBMCs proliferation assay. Cell proliferation index was determined by CFSE. PBMCs from patients with RVVC or healthy women were challenged with inactivated *C. albicans* (ATCC 10231) or stimulated with Concanavalin A (ConA). Differences between groups were calculated using Mann-Whitney test. Significant differences are expressed as * P < 0.05, ** P < 0.01, *** P < 0.001.

Conclusions

Contrary to what has been reported in the literature, the predominant species causing RVVC in this study was *C. albicans*. Of interest, no increase in the resistance of *Candida* spp. was observed. Moreover, a decrease in the fungicidal and proliferative capacity of neutrophils and PBMCs, respectively, was observed, which could suggest an alteration of the immune response.

Acknowledgements

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