



Influence of recurrent vulvovaginal candidiasis on quality of life issues

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Abstract

Purpose More than 370 million women will experience recurrent vulvovaginal candidiasis (RVVC) during their lifetime. However, RVVC is often trivialized as clinically insignificant and not worthy of research funding. We evaluated the influence of RVVC on the quality of life in affected women.

Methods The validated World Health Organization Quality of Life Abbreviated Assessment (WHOQOL-Bref) questionnaire was administered to 100 women with RVVC and to 101 epidemiologically matched women with no history of vulvovaginal candidiasis. RVVC was defined as at least four episodes of clinical and culture-positive vaginal candidiasis within a 1 year period. Data were analyzed by Chi square, Student *t* test and analysis of variance. Internal consistency of responses to questions was evaluated by Cronbach alpha.

Results The Cronbach alpha coefficient was > 0.80 for responses to generalized questions and > 0.65 for answers to more specific questions, indicating substantial internal consistency. Perception of quality of life and satisfaction with their health was greatly reduced in the RVVC group ($p < 0.001$). Diminished responses to physical and psychological well-being were also reported by women with RVVC ($p < 0.001$). Various aspects of social relations including sexual activity were similarly reduced ($p < 0.001$) as were satisfaction with issues such as home environment, financial resources and employment ($p < 0.001$).

Conclusion RVVC affects multiple aspects of a woman's well-being. Women with this condition deserve serious attention from clinicians and research into susceptibility, prevention and treatment of this infection deserves much greater emphasis.

Keywords Health questionnaire · Quality of life · Recurrent vulvovaginal candidiasis

Introduction

Candida albicans exists as a harmless commensal microorganism in the vagina in a variable number of healthy reproductive age women [1]. Under a variety of circumstances [2], but in many cases involving a transient decrease in local immunity [3, 4], vaginal *C. albicans* proliferates and undergoes a morphogenetic change from a yeast-like organism to a

more invasive hyphal form. This induces clinical symptoms such as pruritis, inflammation, dysuria, dyspareunia and a curd-like vaginal discharge [5]. It has been estimated that about 75% of women will experience at least one episode of a symptomatic *Candida* infection during their lifetime [5, 6]. In the majority of these affected women, short-duration treatment with any one of a number of anti-fungal agents is sufficient to reduce the level of this organism to a concentration under which host immunity can again prevent its proliferation and symptoms which are ameliorated. However, in about 5% of women, a symptomatic episode of *Candida* vaginitis leads to its frequent recurrence. The presence of at least four culture-positive symptomatic occurrences of *Candida* vaginitis within a 12 month period is called recurrent vulvovaginal candidiasis (RVVC) [5, 7]. While symptoms may be alleviated by anti-fungal agents this is only temporary and once treatment is completed another clinical episode shortly commences. Multiple reasons for this susceptibility to develop RVVC following an initial episode have

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been advanced [3, 4, 8]. To date, there is no successful long-term treatment that is effective in preventing recurrences in the majority of affected women [9]. A recent review estimated that about 138 million women will develop RVVC annually and that > 370 million women will suffer from this disorder during their lifetime [10].

While not life-threatening RVVC may have a major negative impact on quality of life. However, only a few studies have investigated this systematically. A study of South Asian women living in England reported that even a single occurrence of vaginal candidiasis induced feelings of embarrassment, stigmatization and depression [11]. A cross-sectional study of women in five European countries plus the United States concluded that RVVC was associated with anxiety, depression and a loss of productivity [12]. Subsequent studies of women in China [13] and Australia [14] observed similar negative influences of RVVC on mental health issues.

Using a World Health Organization-validated questionnaire, we investigated the influence of RVVC on a range of quality of life issues in women residing in Sao Paulo, Brazil.

Materials and methods

Subjects

The study population consisted of 100 women with RVVC and 101 control women seen for a routine yearly examination in the outpatient vaginitis clinic at Hospital das Clinicas, University of Sao Paulo Medical School. RVVC was defined as at least four instances of a culture-positive symptomatic episode of vaginitis due to *C. albicans* within a 1 year period. Controls were matched to patients by epidemiological characteristics and had no reported history of vaginal candidiasis. All subjects were of reproductive age, over 18 years old and were sexually active. Exclusion criteria were pregnancy, HIV-positive or a present or prior history of diabetes mellitus, autoimmune disease or malignancy. The study was approved by the ethical committee of the University of Sao Paulo Medical School and all subjects gave informed written consent.

Questionnaire

In an analytic transversal case–control study, the World Health Organization Quality of Life Abbreviated Assessment (WHOQOL-Bref) questionnaire [15] was administered to patients and controls. The WHOQOL-Bref consists of 26 questions. The first two questions evaluate the subjects' perception of her quality of life and satisfaction with her health. The remaining 24 questions delve more deeply into patients' self-perceptions and facets of life in four different areas (physical health, psychological well-being, social

relations, and environmental issues such as home environment, physical resources and availability of recreational outlets). Each question is composed of a scale of five possible responses and subjects selected the response most appropriate for them. The subjects completed all questions under the supervision of a physician who was available to clarify any uncertainties about the meaning of a specific question.

Statistics

Scores from each individual question were transformed to scores of 1–100 according to norms established for utilization of this instrument by WHOQOL-Bref. Mean and standard deviation values for each question were compared by absolute and relative frequencies. Analyses utilized the χ^2 test, Student *t* test and analysis of variance as appropriate. Linear multiple regression analysis was utilized to control for the influence of competing variables. A two sided *p* value < 0.05 was considered significant. All analyses utilized Statistical Package for Social Sciences.

To analyze internal consistency and confidence in validity of the questionnaire (the expected correlation between subjects' answers that measure the same construct) the Cronbach's alpha (tau-equivalent reliability) statistic was utilized [16]. The higher the value obtained the more reliable is the subjects' consistency in their responses.

Results

Table 1 describes the sociodemographic characteristics of subjects and controls. Most women in both groups were White, had a high school education, were of comparable age and married or in civil unions. The only significant difference was that more women in the control group were actively employed (75.3%) than were women with RVVC (57.0%) ($p = 0.006$).

The alpha coefficient for Cronbach's alpha test for the total questionnaire and for each domain is shown in Table 2. For both RVVC patients and controls the internal consistency of responses to similar questions was highly reliable and indicated substantial internal consistency.

Table 3 compares the responses of women with RVVC and controls to questions about overall quality of life and satisfaction with their health as well as their more detailed responses to questions about satisfaction in the physical, psychological, social and environmental domains. Women in the control group reported significantly higher levels of satisfaction overall and in each of the domains ($p < 0.001$ in both univariate and multivariate analyses). Physically, perception of pain, lack of energy, sleep problems, reduced daily activity, reliance on medications or treatments were increased in women with RVVC ($p < 0.001$). Psychologically, patients

Table 1 Sociodemographic characteristics of the study population

Variables	RVVC N = 100	Controls N = 101	<i>p</i> value
Age in years (SD)	34.0 (6.9)	32.2 (7.6)	0.072
Employed	57 (57.0%)	76 (75.3%)	0.006
Marital status			0.198
Married/civil unions	64 (64.0%)	55 (54.5%)	
Single	30 (30.0%)	39 (38.6%)	
Divorced/separated	4 (4.0%)	7 (6.9%)	
Widowed	2 (2.0%)	0	
Education			0.139
Less than primary school	6 (6.0%)	4 (4.0%)	
Primary school	28 (28.0%)	38 (37.6%)	
Secondary school	53 (53.0%)	54 (53.5%)	
University	13 (13.0%)	5 (4.9%)	
Ethnicity			0.468
White	82 (82.0%)	89 (88.1%)	
Black	4 (4.0%)	1 (1.0%)	
Mixed race	13 (13.0%)	10 (9.9%)	
Asian	1 (1.0%)	1 (1.0%)	

Table 2 The Cronbach's alpha coefficient for subjects' responses to the WHOQOL-bref questionnaire

Section	Coefficient	Number of questions
All sections	0.88	26
Overall quality of life and health	0.81	2
Physical domain	0.65	7
Psychological domain	0.68	6
Social relationships domain	0.72	3
Environmental domain	0.74	8

reported lowered affection, cognition, self-esteem and body image ($p < 0.001$). All aspects of social relations including satisfaction in sexual activity and support from friends and family were also reduced ($p < 0.001$). Patients reported a less

Table 3 Responses of women with RVVC and controls to questions about overall quality of life and satisfaction with their health and more detailed responses to satisfaction in the physical, psychological, social and environmental domains

Area	Mean value (standard deviation)			
	RVVC	Controls	<i>p</i> value	
			Univariate	Multivariate
Perception of life quality	59.7 (19.4)	71.3 (14.7)	<0.001	<0.001
Satisfaction with health	46.7 (20.0)	67.1 (17.3)	<0.001	<0.001
Physical domain	54.5 (11.2)	68.5 (10.7)	<0.001	<0.001
Psychological domain	56.8 (12.1)	65.8 (10.8)	<0.001	<0.001
Social domain	51.5 (18.8)	69.1 (16.7)	<0.001	<0.001
Environmental domain	43.5 (12.0)	57.4 (10.5)	<0.001	<0.001

satisfactory home environment, lower financial resources, lower frequency of recreational activities and higher unemployment ($p < 0.001$).

Analyzing by multivariable analysis, perceived overall quality of life ($p = 0.02$) and satisfaction in the physical domain ($p = 0.037$) were lowest in Black women compared to the other ethnicities. In the psychological domain, the most uneducated group of women scored lowest in satisfaction in the psychological ($p = 0.041$) and social ($p = 0.042$) domains. Married women and those in civil unions scored lowest on questions in the environmental domain than did women who were single or separated/divorced ($p = 0.004$).

Discussion

The quality of life in all areas evaluated is significantly diminished in women with RVVC as compared to a comparable group of women who have not experienced this disorder. Based on results from a validated questionnaire, women with RVVC are less satisfied with their overall health and well-being as well as self-perceptions of physical and psychological health. They also had lower scores on satisfaction with social interactions and their ability to successfully engage with their environment.

These findings, using a novel instrument for measurement, confirm and expand on prior investigations on the debilitating and widespread adverse consequences of having RVVC. Furthermore, it should now be apparent that these negative feelings universally apply to women living in different countries and with various cultures.

There are several limitations to this investigation. We did not collect information on the number of episodes of RVVC experienced by each subject, her age at the first episode as well as the frequency and duration of each episode. It was also not determined if the episodes coincided with menstruation and associated symptoms. Strengths of the study include the high number of subjects evaluated, collection of comparison data from control women being seen at the same clinic and utilization of a validated questionnaire.

Given the large numbers of women with RVVC and its devastating effects on overall life quality there can be no rational excuse for the lack of a sufficient research effort and the availability of adequate funding for this disorder. Concerted efforts are urgently needed to identify sub-populations of women with increased susceptibility to develop RVVC, development of protocols to prevent a single episode of vulvovaginal candidiasis from transforming into RVVC and for novel interventions to successfully end repeated cycles of *Candida* proliferation and symptom initiation. At the present time, a greater emphasis on providing psychological counseling for affected women is also needed. Effective counseling will help to keep self-perceptions related to RVVC in a more realistic framework and prevent its progression to diminished feelings of self-worth and enjoyment in all areas of life.

We conclude that RVVC has a major negative influence on multiple areas of life quality. Women with RVVC deserve more extensive support and counseling and there needs to be a much greater focus on research into this prevalent problem.

Author contributions EI Fukazawa and IM Linhares: trial conception and design and wrote original draft. EI Fukazawa, R Robial, and JG Vinagre: patient interviews and initial data analysis. IM Linhares and SS Witkin: final data analysis and interpretation, and wrote final version of manuscript. IM Linhares and EC Baracat: study supervision.

Compliance with ethical standards

Conflict of interest None of the authors have any conflict of interest.

References

- Giraldo P, von Nowaskonski A, Gomes FA, Linhares I, Neves NA, Witkin SS (2000) Vaginal colonization with *Candida* in asymptomatic women with and without a history of recurrent vulvovaginal candidiasis. *Obstet Gynecol* 95:413–416
- Goncalves B, Ferreira C, Alves CT, Henriques M, Azeredo J, Silva S (2016) Vulvovaginal candidiasis: epidemiology, microbiology and risk factors. *Crit Rev Microbiol* 42:905–927
- Linhares LM, Witkin SS, Miranda SD, Fonseca AM, Pinotti JA, Ledger WJ (2001) Differentiation between women with vulvovaginal symptoms who are positive or negative for *Candida* species by culture. *Infect Dis Obstet Gynecol* 9:221–225
- Ilkit M, Guzel AB (2011) The epidemiology, pathogenesis, and diagnosis of vulvovaginal candidiasis: a mycological perspective. *Crit Rev Microbiol* 37:250–261
- Sobel JD (2016) Recurrent vulvovaginal candidiasis. *Am J Obstet Gynecol* 214:15–21
- Babula O, Lazdane G, Kroica J, Ledger WJ, Witkin SS (2003) Relation between recurrent vulvovaginal candidiasis, vaginal concentrations of mannose-binding lectin, and a mannose-binding lectin gene polymorphism in Latvian women. *Clin Infect Dis* 37:733–737
- Witkin SS, Jeremias J, Ledger WJ (1988) A localized vaginal allergic response in women with recurrent vaginitis. *J Allergy Clin Immunol* 81:412–416
- Cassone A (2015) Vulvovaginal *Candida albicans* infections: pathogenesis, immunity and vaccine prospects. *BJOG* 122:785–794
- Sobel JD, Weisenfeld HC, Martens M, Danna P, Hooton TM, Rompalo A et al (2004) Maintenance fluconazole therapy for recurrent vulvovaginal candidiasis. *N Eng J Med* 351:876–883
- Denning DW, Kneale M, Sobel JD, Rautemaa-Richardson R (2018) Global burden of recurrent vulvovaginal candidiasis: a systematic review. *Lancet Infect Dis* 18(11):e339–e347
- Chapple A (2001) Vaginal thrush: perceptions and experiences of women of south Asian descent. *Health Educ Res* 16:9–19
- Aballea S, Guelfucci F, Wagner J, Khemiri A, Dietz JP, Sobel J et al (2013) Subjective health status and health-related quality of life among women with recurrent vulvovaginal candidiasis (RVVC) in Europe and the USA. *Health Qual Life Outcomes* 11:169
- Zhu YX, Li T, Fan SR, Liu XP, Liang YH, Liu P (2016) Health-related quality of life as measured with the Short-Form 36 (SF-36) questionnaire in patients with recurrent vulvovaginal candidiasis. *Health Qual Life Outcomes* 14:65
- Nguyen Y, Lee A, Fischer G (2017) Quality of life in patients with chronic vulvovaginal candidiasis: a before and after study on the impact of oral fluconazole therapy. *Aust J Dermatol* 58:e176–e181
- World Health Organization. Division of Mental Health (1996) WHOQOL-bref: introduction, administration, scoring and generic version of assessment: field trial version. Dec Geneva. <https://www.who.int/iris/handle/10665/63529>. Accessed Nov 2018
- Tavakol M, Dennick R (2011) Making sense of Cronbach's alpha. *Int J Med Educ* 2:53–55

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