A SIX-YEAR EPIDEMIOLOGICAL SURVEY

OF VULVOVAGINAL CANDIDIASIS

IN CYTOPATHOLOGY REPORTS

IN THE STATE OF RIO GRANDE DO SUL, BRAZIL

Dariane Castro Pereira, ^{1 e 2} Luana Taís Hartmann Backes, ³ Luciane Noal Calil and Alexandre Meneghello Fuentefria ¹

ABSTRACT

Vulvovaginal candidiasis (VVC) is a common vaginal infectious disease. The constant increase in the incidence of the disease may be associated with factors such as age, HIV infection, diabetes, use of hormonal contraceptive methods and cytopathological alterations. The aim of the study was to survey the prevalence of *Candida* sp. in cytopathology reports in the state of Rio Grande do Sul, Brazil, in the period of 2005-2010. In this observational and retrospective study a total of 121,328 cytopathology reports (CR) of cytopathology were assessed in a period of 6 years. The mean age of patients was 35 years old. Of this total, 8,582 CR (7.1%) were positive for *Candida* sp. More than half of patients (53%) were using oral contraceptive. Alterations in the cervix were present in 49% of the cases. The continuity of epidemiological research is needed to monitor trends over the years to better understand the factors that predispose to VVC in Brazil.

KEY WORDS: Candida. Vulvovaginal candidiasis. Epidemiology.

RESUMO

Levantamento epidemiológico da candidíase vulvovaginal em laudos citopatológicos realizados durante seis anos no estado do Rio Grande do Sul, Brasil

Candidíase Vulvovaginal (CVV) é uma infecção vaginal comum. O constante aumento da incidência da doença pode estar associado a fatores como idade, infecção por HIV, diabetes, uso de métodos hormonais de contracepção e alterações citopatológicas. O objetivo deste estudo foi avaliar a prevalência de *Candida* sp. em amostras de secreção vaginal no estado do Rio Grande

Corresponding author: Alexandre M. Fuentefria. Faculty of Pharmacy, Federal University of Rio Grande do Sul. Address: Av. Ipiranga n. 2752, Zip code: 90610-000, Porto Alegre, RS, Brazil. E-mail: alexmf77@gmail.com

Received for publication in: 29/12/2011. Reviewed in: 14/2/2012. Accepted in: 7/5/2012.

¹ Grupo de Pesquisa em Micologia Aplicada. Departamento de Análises. Faculdade de Farmácia. Universidade Federal do Rio Grande do Sul. Porto Alegre, RS, Brasil.

² Laboratório de Doenças Infecciosas e Auto-Imunes. Hospital de Clínicas de Porto Alegre. Porto Alegre, RS, Brasil.

³ Medicina Diagnóstica LTDA. Erechim, RS, Brasil

so Sul, no período de 2005 a 2010. Trata-se de um estudo retrospectivo e observacional, por meio do qual foram avaliados 121.328 relatórios médicos de citopatologia num período de seis anos. Foram constatados 8.582 (7,1%) casos positivos de *Candida* sp.. A idade média das pacientes era de 35 anos. Mais da metade das pacientes (53%) usavam anticoncepcional oral e, em 49% dos casos, verificou-se a existência de alterações no colo do útero. A continuidade da investigação epidemiológica é necessária para o acompanhamento das tendências ao longo dos anos e para uma melhor compreensão dos fatores que predispõem à CVV no Brasil.

DESCRITORES: Candida. Candidíase vulvovaginal. Epidemiologia.

INTRODUCTION

Candida species is responsible for a wide spectrum of conditions (1), that ranges from life-threatening invasive to non-life-threatening mucocutaneous diseases. This dimorphic yeast is a commensal agent that colonizes skin and mucosa from the gastrointestinal and the reproductive tracts. Among the many causes of vaginitis, vulvovaginal candidiasis (VVC) is the second most common cause, after bacterial vaginosis, and is diagnosed in up to 40% of women with vaginal complaints in the primary care setting (3, 12).

VVC is an inflammatory condition caused predominately by *C. albicans*, resulting in severe genital itching, intense polymorphonuclear leukocytic infiltrate and abnormal discharge. *Candida* spp., mostly *C. albicans*, may be isolated in the vaginal tract of 20 to 30% of healthy asymptomatic not pregnant women at any single point in time and in up to 70% if followed longitudinally over a 1-year period (4, 5). Although *C. albicans* is the most common species in candidiasis, we should stress the importance of performing culture techniques for better diagnosis. The emergence of non-*albicans* species, especially *C. krusei* and *C. glabrata* as resistant species to antifungal agents classically used, has the effect of selecting more resistant isolates as well as modification of patients conditions (10, 11).

If the balance between colonization and the host is temporarily disturbed, *Candida* can cause diseases such as VVC, which is associated with clinical signs of inflammation. Such episodes may happen sporadically or often and are usually attributed to the presence of a known risk factor, for example, previous history of VVC, broad spectrum antibiotic treatment, chronic corticosteroid therapy, diabetes, pregnancy, oral contraceptive pills and contraception devices (diaphragm, vaginal contraceptive sponge, intrauterine device). This opportunist yeast infection is not a reportable disease and is often diagnosed without confirmatory tests and treated with over-the-counter (OTC) medications, and thus the exact incidence is unknown. Limited data addressing the incidence of VVC suggest approximately two-thirds of women experience at least one episode during their lifetime and nearly 50% of women have multiple episodes (6, 8, 14).

The purpose of this observational study was to study the prevalence of *Candida* sp. causing VVC in cytopathology reports of a reference laboratory of the national health system of Rio Grande do Sul State, in a six year (2005-2010) period.

MATERIAL AND METHODS

The following variables were analyzed retrospectively: age, contraceptive use, presence of *Candida* sp. and alterations in the cervix. Retrospective chart review was performed to determine by cytopathology reports the VVC epidemiology in southern Brazil.

The volunteers were referred by physicians of the national health system to undergo laboratory tests of the vaginal and cervix secretions and all the women who attended this laboratory examination were invited to participate in this study. We included only the first episode of *Candida* sp. for each patient. A database was created with the following variables: age, use of oral contraceptives and presence of alterations in the cervix. Collection of material from the squamocolumnar junction with an special brush was done and the smear was fixed in alcohol 97%. The glass slide was used to perform cytology stained by the Papanicolaou method. Records from the laboratory were used to identify patients positive for *Candida* sp. from 2005 to 2010. The criteria used to validate the diagnosis of vaginal candidiasis was the presence of vaginal discharge on physical examination and the presence of filamentous forms (pseudohyphae) or yeast by microscope examination.

RESULTS

A total of 121,328 medical reports of cytopathology Laboratory from 2005 to 2010 were assessed. The mean age of patients ranged from 34-37 years during the study period. The results of this study showed a prevalence of 8,582 (7.1%) of positive cases for *Candida* sp. causing vulvovaginal candidiasis in the population studied during the period of six years. According to annual distribution, major incidence of positive cases for *Candida* sp. was observed in 2008 (8.5%), followed by 2010 (8.4%), 2009 (6.5%), 2006 (6.2%), 2005 (6.1%) and 2007, with the lowest incidence of *Candida* sp. in the population studied being 1,118 cases (5.5%).

The data in Table 1 represents the annual percentage rate of *Candida* sp.. An increase in positive cases was observed in the 2 last years of the survey. In 2010 the number of *Candida* sp. reported was 1.74% greater than what was observed in the same period of 2009. More than half of patients (53%) were using contraception and changes in the cervix were present in 49% of the cases. From 2005 to 2009, the average percentage of positive samples for VVC with cervical abnormalities was 43.6%. In the same period, the average percentage of women using oral contraceptives and positive for VVC was 44.8%, similar to the average percentage of women using oral contraceptives without fungal disease (49.33%) (Table 1).

Table 1. Number and annual percentage of samples positive from reference laboratory to the national health system, in Southern Brazil, during the period of January 2005 to December 2010.

Year	Number of cytopathology reports	Number and percentage of positive samples	Number and percentage of positive samples to VVC with cervical alterations	Number and percentage of women using oral contraceptives with VVC	Number and percentage of women using oral contraceptives without VVC	Number and percentage of cervical alterations in women without VVC
2005	14,788	889 (6.1%)	435 (48.9%)	471 (53%)	7366 (49.8%)	6810 (46%)
2006	12,485	769 (6.2%)	230 (29.9%)	201 (26.1%)	6209 (49.7%)	5740 (46%)
2007	20,438	1,118 (5.5%)	458 (40.9%)	408 (36.5%)	10239 (50.1%)	9466 (46.3%)
2008	22,770	1,939 (8.5%)	911 (47%)	1058 (54.5%)	10104 (48.4%)	10207 (44.8%)
2009	20,848	1,359 (6.5%)	584 (43%)	557 (41%)	10329 (49.5%)	9549 (45.8%)
2010	29,999	2,508 (8.4%)	1304 (52%)	1454 (58%)	14570 (48.5%)	13460 (44.8%)

DISCUSSION

Vulvovaginal candidiasis is a common disease and the majority of cases are caused by *C. albicans*, but in recent years an increase has been observed in the frequency of non-albicans species, especially due to *C. glabrata* and *C. tropicalis*. Although VVC is a common disease, little is known about the epidemiology of this disease and data concerning about the epidemiology of *Candida* spp. in Brazilian population are rare. In this study all women who attended the laboratory for routine laboratory tests in the period from 2005 to 2010 were included in this study, regardless of presenting symptoms of VVC. In our study we found 7.1% of *Candida* spp. during the period of six years of research (2005-2010).

The increase in positive cases observed in the last two years could be explained by the number of patients that also increased from 2010 compared to 2009 (8000 - 41%), due to the action of social awareness programs for preventive exams during this period.

Comparing our results with those of some studies realized in southern Brazil, Camargo et al. (7) observed a frequency of 18.2% and Ferraza et al. (9) made investigations in two cities in different regions of southern Brazil, evaluating a total of 130 samples and obtaining approximately 24% of *Candida* spp. in the population studied. The results of Linares et al. (13) were more similar to our data. In this study, a total of 702 samples of vaginal secretions from symptomatic and asymptomatic patients were analyzed and they observed a frequency of 5.8% of *Candida* spp. during a year of observation (2004 to 2005). In this case, the majority of patients with *Candida* sp. had age ranging from 21 to 30 years, similar to our data. A similar study has demonstrated that the prevalence of vulvovaginal candidiasis occurs more frequently in fertile women aged between 20 and 30 years (15).

Other comparable study was conducted in Mubarak Al-Kabeer Hospital (Kuwait) (2) over a 6-year period (2002-2007) with 42,294 cytopathology reports, a specific infection was identified in 2,679 (15.2%) cases. In 42,294 cytopathology reports, *Candida* sp. was the most detectable infectious agent with a prevalence of 4.69%, followed by *T. vaginalis* and HPV, corroborating with our percentage of 7.1%.

Nevertheless, it will be important to compare our data with epidemiological data from different regions in Brazil. Our results show that it is necessary to undertake further researchers in the field of VVC, because many women are affected from these infections. It is important to perform species identification to obtain more epidemiological information in the increase or decrease of a particular species causing VVC, above all, because of the higher resistance to antifungal drugs of some of them.

Many potential risk factors for vulvovaginal candidiasis have been described, although there is no consensus in the literature, including the recent use of antibiotics, oral contraceptives, diabetes mellitus, pregnancy, use of pantyhose, absorbing clothes and specific immune deficiencies. It is speculated that inadequate hygiene habits may be predisposing factors of vaginal contamination, including anal hygiene performed from the anus to the vagina, and residues of faeces in underwear could be the origin of the yeasts in the development of candidiasis vulvovaginal.

We observed in table 1 that, in population-based studies, where there is potentially more sample variability, one can detect some trends different from those expected, as in the case of patients using hormones who might have more frequent episodes of candidiasis. In addition, other factors may be influencing, as changes in vaginal pH, the use of medicines and immunosuppression.

Continued epidemiological surveillance should be performed to monitor the trends over the years whilst specific studies in subgroups of complicated patients should be conducted to better understand the correlation between patients profile, pathogens and response to treatment.

ACKNOWLEDGMENTS

The study was supported by a grant from the Federal University of Rio Grande do Sul and Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq).

REFERENCES

- Achkar JM, Fries BC. Candida Infections of the genitourinary tract. Clin Microbiol Rev 23: 253-273, 2010.
- Al-Awadhi R, Al-Ramadan BA, George SS, Sharma PN, Kapila K. Gynecologic infections seen in cervical smears in Kuwait. *Acta Cytol* 54: 50-54, 2010.
- Anderson MR, Klink K, Cohrssen A. Evaluation of vaginal complaints. JAMA 291: 1368-1379, 2004
- Bauters TG, Dhont MA, Temmerman MI, Nelis HJ. Prevalence of vulvovaginal candidiasis and susceptibility to fluconazol in women. Am J Obstet Gynecol 187: 569-574, 2002.

- Beigi RH, Meyn LA, Moore DM, Krohn MA, Hillier SL. Vaginal yeast colonization in nonpregnant women: A longitudinal study. Obstet Gynecol 104: 926-930, 2004.
- Berg AO, Heidrich FE, Fihn SD, Bergman JJ, Wood RW, Stamm WE, Holmes KK. Establishing the cause of genitourinary symptoms in women in a family practice: comparison of clinical examination and comprehensive microbiology. *JAMA 251*: 620-625, 1984.
- Camargo FP, Alves IA, Parlow MS, Goulart LS. Isolamento de *Candida* sp. da Mucosa Vaginal de Mulheres Atendidas em um Serviço de Ginecologia do Município de Santo Ângelo – RS. *NewsLab* 87: 96-104. 2008.
- Eckert LO, Hawes SE, Stevens CE, Koutsy LA, Eschenbach DA, Holmes KK. Vulvovaginal candidiasis: clinical manifestations, risk factors, management algorithm. *Obstet Gynecol* 92: 757-765, 1998.
- Ferrazza MHSA, Ferrarezi ML, Consolaro MEL, Shinobu CS, Svidzinski TIE, Batista MR. Characterization of yeasts isolated from the vagina and their association with vulvovaginal candidíasis in two cities of the South of Brazil. Rev Bras Ginecol Obstet 27: 58-63, 2005.
- Garcia HM, Garcia SD, Copolillo EF, Cora EM, Barata AD, Vay CA. Prevalence of vaginal candidiasis in pregnant women. Identification of yeasts and susceptibility antifungal agents. Rev Argent Microbiol 38: 9-12, 2006.
- Ilkit M, Guzel AB. The epidemiology, pathogenesis, and diagnosis of vulvovaginal candidosis: a mycological perspective. Crit Rev Microbiol 37: 250-261, 2011.
- Leite MCA, Santos SMJ, Lima EQ, Rodrigues OG, Filho EQ. Prevalência dos agentes etiológicos das vulvovaginites através de resultados de exames citopatológicos: um estudo na Unidade de Saúde da Família em Patos – PB. NewsLab 104: 86-96, 2011.
- Linares CEB, Dagios G, Carati MR, Gasparin MP, Neto AT, Scheid LA, Schubert A. Epidemiologic and susceptibility study of Candida isolated from women with vulvovaginal candidiasis in Frederico Westphalen – RS. Saúde 31: 42-46, 2005.
- 14. Mccormack WM, Zinner SH. The incidence of genitourinary infections in a cohort of healthy women. Sex Transm Dis 21: 63-64, 1994.
- Sojakova M, Liptajova D, Simoncicova M, Borovsky M, Subik J. Vulvovaginal candidiasis and sensitivity of pathogens to antimycotics. Ceska Gynekol 68: 24-29, 2003.