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# Risk factors for recurrent vulvovaginal candidiasis

## Faktori rizika od nastanka rekurentne vulvovaginalne kandidijaze

**Slobodan Janković*, Dragica Bojović*, Dubravka Vukadinović*, Elmedina Daglar*, Marija Janković*, Dragomir Laudanović*, Vladan Lukić*, Vesna Mišković*, Zorica Potpara*, Ivana Projović*, Vesna Čokanović*, Nadežda Petrović*, Marko Folić*, Viktorija Savić†**

***University of Kragujevac, Medical Faculty, Kragujevac, Serbia;**
**†Clinical Center of Serbia, Belgrade, Serbia**

**Abstract**

**Background/Aim.** Recurrent vulvovaginal candidiasis is relatively frequent condition, and may have serious health consequences, like chronic vulvovaginal pain syndrome. The aim of our study was to determine possible risk factors for recurrent vulvovaginal candidiasis in non-pregnant females within the reproductive age. **Methods.** The design of our study was of a case-control type. Case and control patients were selected from the gynecological patients at six primary care facilities in Serbia and in Montenegro. The data on the patients' health condition, concomitant therapy and diseases were taken from their records, and the data on habits were obtained by unstructured interview. For potential risk factors crude odds ratios were calculated, and then adjusted by logistic regression. **Results.** A total of fifty-one patients had four or more episodes of vulvovaginal candidiasis during the last year (cases), and 132 patients with one to three episodes of vulvovaginal candidiasis were sampled as controls, matched by age. The only two significant associations were found between recurrent vulvovaginal candidiasis and continual wearing of panty liners during the last year (Odds ratio – $OR_{adjusted}$: 3.97; confidence interval – CI: 1.57–10.02; $p = 0.004$), and between recurrent vulvovaginal candidiasis and predominant use of vaginal tampons during menstruation in the last year ($OR_{adjusted}$: 4.25; CI: 1.11–16.27; $p = 0.035$). The synergistic effect was observed for the concurrent continual wearing of panty liners during the last year and self-medication with antimycotics. **Conclusions.** Local factors, like wearing of panty liners or use of tampons during menstruation, may promote recurrence of vulvovaginal candidiasis, especially in patients who practice self-medication with antimycotics.

**Key words:**
**candidiasis, vulvovaginal; recurrence; risk factors; risk; data interpretation, statistical.**

**Apstrakt**

**Uvod/Cilj.** Rekurentna vulvovaginalna kandidijaza je često zdravstveno stanje koje može da ima i ozbiljne posledice, kao što je sindrom hroničnog vulvovaginalnog bola. Cilj ove studije bio je da se utvrde faktori rizika od nastanka rekurentne vulvovaginalne kandidijaze kod negravidnih žena u reproduktivnom periodu. **Metode.** U našoj studiji tipa *case-control* učestvovale su ginekološke bolesnice iz šest ustanova primarne zdravstvene zaštite Republike Srbije i Republike Crne Gore. Podaci o zdravstvenom stanju, stanju bolesti i pratećoj terapiji bolesnica prikupljeni su iz njihovih zdravstvenih kartona, dok su podaci o navikama dobijeni nestrukturisanim intervjuom. Značaj potencijalnih faktora rizika prvo je pojedinačno procenjivan neprilagođenim unakrsnim odnosom, da bi zatim, uz pomoć binarne logističke regresije, unakrsni odnos bio prilagođen za istovremeno dejstvo više faktora. **Rezultati.** Grupa od 51 bolesnice imala je četiri ili više od četiri epizoda vulvovaginalne kandidijaze tokom protekle godine, dok su 132 bolesnice kontrolne grupe imale po jednu do tri epizode u istom periodu (grupe su bile usklađene po životnom dobu). Utvrđena je značajna povezanost između rekurentne vulvovaginalne kandidijaze i kontinuiranog nošenja dnevnih uložaka tokom proteklih godinu dana [*dds-ratio* $(OR)_{adjusted} = 3,97$; interval poverenja (CI) = 1,57–10,02; $p = 0,004$)], kao i između rekurentne vulvovaginalne kandidijaze i predominantne upotrebe vaginalnih tampona tokom menstruacije u proteklih godinu dana [$OR_{adjusted} = 4,25$; CI = 1,11–16,27; $p = 0,035$]. Zapaženo je da istovremeno kontinualno nošenje dnevnih uložaka tokom poslednjih godinu dana i samomedikacija antimikoticima dodatno povećavaju sklonost nastanku rekurentne vulvovaginalne kandidijaze. **Zakljak.** Lokalni faktori, kao što su nošenje dnevnih uložaka ili upotreba tampona tokom menstruacije, doprinose recidivu vulvovaginalne kandidijaze, pogotovo kod bolesnica koje praktikuju samomedikaciju antimikoticima.

**Ključne reči:**
**kandidijaza, vulvovaginalna; recidiv; faktori rizika; rizik; statistička interpretacija podataka.**

**Correspondence to:** Slobodan Janković, University of Kragujevac, Svetozara Markovića 69, 34 000 Kragujevac, Serbia.
Phone.: +381 34 306 800. E-mail: slobnera@eunet.rs

## Introduction

Vulvovaginal candidiasis is an inflammation of the vagina and vulva caused by *Candida albicans* (46.9–75%), or one of other *Candida* species: *Candidia glabrata* (14–36.7%), *Candidia parapsilosis* (10.2%), *Candidia tropicalis* (2.8–7%), *Candidia krusei* (1.4–3.5%), and *Candidia kiefer* (1.9%)[1, 2]. Prevalence of symptomatic vulvovaginal candidiasis among the patients of gynecology clinics is around 8% [3], and vaginal carriers of these fungal species are encountered in as often as 27% of cases [4].

The patients who experience more than three attacks of vulvovaginitis caused by *Candida* species during the last year or have previous disease history longer than one year are classified as patients with recurrent vulvovaginal candidiasis [5, 6]. Recurrent vulvovaginal candidiasis is relatively frequent (around 8.5% in patients with symptomatic vulvovaginal candidiasis) [7], and may have serious health consequences, like chronic vulvovaginal pain syndrome [8].

There are many risk factors for development of vulvovaginal candidiasis [7], like advanced reproductive age, pregnancy, diabetes, hormonal contraception [9], recent antibiotic use, dietary practices, gastrointestinal colonization by the organism, clothing and sanitary protection practices, sexual communicability of the organism, and specific immunological defects [10]. However, risk factors for recurrent vulvovaginal candidiasis are somewhat different, and not yet established with certainty. Stress [11], use of panty liners or pantyhose, consumption of cranberry juice or acidophil-containing products, a history of bacterial vaginosis, steroid therapy, diabetes mellitus, age < 40 years and abnormal local host response to *Candida* [12] were positively associated with recurrent vulvovaginal candidiasis [13, 14], but this association was not confirmed in more than one study and the pathophysiology of chronic, recurrent vulvovaginal candidiasis remains unclear [15]. Some studies did not confirm these risk factors at all, but only pointed to the importance of hormonal contraception, frequency of sexual intercourses and technique of vulvovaginal hygiene [16].

The aim of our study was to determine association of previously investigated and some new risk factors with recurrent vulvovaginal candidiasis in non-pregnant females within the reproductive age, and therefore resolve controversies made by opposing results of previous studies.

## Methods

Our study was conducted in six primary care gynecological dispensaries in Serbia and Montenegro, located in six cities: Belgrade, Jagodina, Kragujevac, Novi Pazar, Uzice (in Serbia) and Podgorica (in Montenegro), covering population of approximately 800 000 inhabitants. The source population of our study consisted of all consecutive patients in reproductive age with vulvovaginal candidiasis (microbiologically proved) who visited gynecological dispensaries (n = 804) during one-month period, from March 1st, 2009, to March 31st, 2009. Data on drug prescription and (co)morbidity were obtained from medical records. Data on non-prescription drugs use and habits were obtained by unstructured interview with the patients. All data were kept anonymous, with previous consent of the patients, and the study protocol was approved by Ethics Committee of the School of Medicine, University of Kragujevac, empowered to make decisions on clinical studies in six primary care facilities.

The design of the study was of a case-control type, with the aim to assess the relationship between potential risk factors and occurrence of recurrent vulvovaginal candidiasis (more than three episodes during the previous year) in patients within reproductive age. The case and control patients (study population) were selected from the gynecological examination records made during the study period, at the study primary care facilities. Pregnant and lactating patients, patients of pre-menarche and post-menopause age were excluded from the study.

The cases were chosen from the study population if they experienced more than three episodes of vulvovaginal candidiasis during the last year. Vulvovaginal candidiasis episode was defined as simultaneous existence of two out of three following criteria: 1) isolation of *Candida* species from culture of vaginal smear; 2) detection of *Candida* species on potassium hydroxide (KOH) preparation of vaginal smear; and 3) clinical diagnosis made by a gynecologist working in the study primary care facilities. Recurrent episodes were considered and calculated as new events if the patients were previously treated with appropriate antimycotics, and if at least 30 days elapsed from the achieved clinical resolution of symptoms in a previous episode. The case patients were counted only once, even if they had more than one visit to the gynecological dispensary during the study period.

For each case, at least two age-matched control patients were randomly selected from the source population. The control patients were defined as those patients with one to three episodes of vulvovaginal candidiasis during the last year.

In order to identify risk factors and potential confounders, the following data on status, habits, (co)medication and (co)morbidity were collected for each patient: age, body mass index, existence of diabetes mellitus type 1 or 2; antibiotic use during seven or more days within the last month; systemic use of corticosteroids for at least 15 days in the last 15 months; continual wearing of panty liners during the last year; wearing of tight clothes during 90% of time in the last year; predominant wearing of underwear made from synthetic fabric; predominant wearing of lace thong underwear during the last year; predominant use of vaginal tampons during menstruation in the last year; use of immunosuppressive drugs for at least one month during the last year; the presence of intrauterine contraceptive device during at least 6 months in the last year; the rate of sexual intercourses during the last year; the use of hormonal contraceptives during at least 6 months before enrollment to the study; exposure to training in vaginal irrigation offered by health workers; smoking (more than 5 cigarettes daily during the last year); bacteria in vaginal smear confirmed at least once during the last year; concomitant chronic non-contagious disease except diabetes mellitus; self-medication with antimycotics (without being prescribed by a physician) during the last year; serious event causing stress during the last year (divorce, death of a

first-line relative, loss of job or change of a place of living); concomitant hypothyreosis or hyperthyreosis; employment status; regular daily intake of coffee during the last year; previous hysterectomy; sedentary job during the last year; alcohol intake per week during the last year; average weekly intake of fermented milk products during the last year; level of education; number of irregular periods during the last year; average duration of menstrual bleeding and religion (Christian, Muslim or Atheist).

The prevalence of each characteristic during the last 3 years was determined for both cases and controls. The differences between cases and controls in the observed characteristics were assessed by a Student's *t* test for continuous variables and a $\chi^2$ test for frequencies. The differences were considered significant if probability of null hypothesis was less than 0.05. In order to estimate the association between independent variables and recurrent vulvovaginal candidiasis crude and adjusted odds ratios (OR) with 95% confidence intervals (95% CI) were calculated using logistic regression [17, 18].

## Results

A total number of patients with vulvovaginal candidiasis in the six gynecological dispensaries during the study period was 804. Fifty-one patients had four or more episodes of vulvovaginal candidiasis during the last year (cases), and 132 patients with one to three episodes of vulvovaginal candidiasis were sampled as controls, matched by age. Significant differences between cases and controls were observed in: antibiotic use during seven or more days within the last month ($\chi^2 = 3.877$; $p = 0.049$; OR = 1.97; CI = 0.98–3.94), continual wearing of panty liners during the last year ($\chi^2 = 13.131$; $p = 0.0001$; OR = 3.23; CI = 1.68–6.22), predominant use of vaginal tampons during menstruation in the last year ($\chi^2 = 6.467$; $p = 0.011$; OR = 3.25; CI = 1.24–8.50) and self-medication with antimycotics ($\chi^2 = 4.055$; $p = 0.044$; OR = 1.95; CI = 1.00–3.83) (Table 1).

**Table 1**

**Baseline characteristics of cases and controls**

| Variable | Cases (n = 51) | Controls (n = 132) | Test value and significance of null hypothesis | Crude odds ratios with confidence intervals (1.96 SE) |
|---|---|---|---|---|
| Age (years) | 32.7 ± 7.0 | 34.5 ± 9.4 | T = -1.376, $p = 0.171$ | N/A |
| BMI (kg/m$^2$) | 22.3 ± 3.1 | 23.2 ± 3.7 | T = -1.684, $p = 0.095$ | N/A |
| Concomitant diabetes | 2 (4%) | 2 (2%) | $\chi^2 = 0.189$, $p = 0.664$ | 2.60 (0.36–18.92) |
| Antibiotic use, 7 days in the last month | 18 (35%) | 28 (21%) | $\chi^2 = 3.877$, $p = 0.049$* | 1.97 (0.98–3.94) |
| Corticosteroids use | 5 (10%) | 6 (5%) | $\chi^2 = 0.990$, $p = 0.320$ | 2.23 (0.65–7.64) |
| Panty liners | 28 (54%) | 35 (27%) | $\chi^2 = 13.131$, $p = 0.000$* | 3.23 (1.68–6.22) |
| Tight clothes | 24 (46%) | 45 (34%) | $\chi^2 = 2.634$, $p = 0.105$ | 1.66 (0.88-3.13) |
| Synthetic underwear | 11 (21%) | 27 (20%) | $\chi^2 = 0.028$, $p = 0.868$ | 1.04 (0.48–2.27) |
| Lace thong underwear | 8 (16%) | 15 (11%) | $\chi^2 = 0.626$, $p = 0.429$ | 1.42 (0.57–3.55) |
| Vaginal tampons | 10 (20%) | 9 (7%) | $\chi^2 = 6.467$, $p = 0.011$* | 3.25 (1.24–8.50) |
| Immunosuppressive drugs | 1 (2%) | 6 (5%) | $\chi^2 = 0.150$, $p = 0.698$ | 0.41 (0.05–3.50) |
| Intrauterine contraceptive device | 1 (2%) | 6 (5%) | $\chi^2 = 0.150$, $p = 0.698$ | 0.41 (0.05–3.50) |
| Rate of sexual intercourses *per* week | 1.4 ± 1.2 | 1.5 ± 1.4 | T = -0.567, $p = 0.571$ | N/A |
| Oral contraceptives | 5 (10%) | 3 (2%) | $\chi^2 = 3.352$, $p = 0.067$ | 3.58 (0.78–16.55) |
| Vaginal irrigation training | 14 (27%) | 38 (29%) | $\chi^2 = 0.032$, $p = 0.857$ | 0.91 (0.45–1.84) |
| Smoking | 21 (41%) | 52 (39%) | $\chi^2 = 0.049$, $p = 0.825$ | 0.89 (0.47–1.68) |
| Bacterial vaginosis | 21 (41%) | 45 (34%) | $\chi^2 = 0.801$, $p = 0.371$ | 1.31 (0.70–2.49) |
| Chronic disease | 6 (12%) | 13 (10%) | $\chi^2 = 0.145$, $p = 0.703$ | 1.19 (0.43–3.31) |
| Self-medication with antimycotics | 20 (39%) | 32 (24%) | $\chi^2 = 4.055$, $p = 0.044$* | 1.95 (1.00–3.83) |
| Stressful event | 17 (33%) | 31 (23%) | $\chi^2 = 1.844$, $p = 0.174$ | 1.52 (0.76–3.03) |
| Thyroid dysfunction | 2 (4%) | 4 (3%) | $\chi^2 = 0.092$, $p = 0.761$ | 1.28 (0.23–7.19) |
| Unemployed | 29 (57%) | 73 (55%) | $\chi^2 = 0.036$, $p = 0.849$ | 1.02 (0.55–1.88) |
| Regular daily intake of coffee | 47 (92%) | 122 (92%) | $\chi^2 = 0.004$, $p = 0.951$ | 0.98 (0.35–2.80) |
| Hysterectomy | 0 (0%) | 2 (2%) | $\chi^2 = 0.008$, $p = 0.928$ | 1.25 (0.11–14.06) |
| Sedentary job | 15 (29%) | 41 (31%) | $\chi^2 = 0.047$, $p = 0.828$ | 0.90 (0.45–1.79) |
| Average alcohol intake per week (mL of pure ethanol) | 4.97 ± 14.95 | 1.71 ± 10.04 | $t = 1.703$, $p = 0.090$ | N/A |
| Average weekly intake of fermented milk products (mL) | 1 793.92 ± 1 249.51 | 1 702.65 ± 3 141.97 | $t = 0.003$, $p = 0.998$ | N/A |
| Level of education ($\bar{x}$ ± SD) | | | | |
| high | 3 (6%) | 17 (13%) | | |
| middle | 32 (63%) | 79 (60%) | $\chi^2 = 1.916$, $p = 0.384$ | N/A |
| low | 16 (31%) | 36 (27%) | | |
| No of irregular menstrual cycles *per* year | 1.6 ± 3.6 | 1.0 ± 2.4 | $t = 1.265$, $p = 0.207$ | N/A |
| Average duration of menstrual bleeding ($\bar{x}$ ± SD) | 5.04 ± 1.38 | 4.96 ± 1.75 | $t = 0.315$, $p = 0.754$ | N/A |
| Religion, n (%) | | | | |
| Christan | 35 (69%) | 94 (71%) | $\chi^2 = 3.490$, $p = 0.479$ | N/A |
| Muslim | 2 (4%) | 3 (2%) | | |
| Atheist | 14 (27%) | 14 (27%) | | |

**Results are presented as $\bar{x}$ ± SD, or n(%); *Significant difference; SE – standard error; N/A –not available**

There were no significant differences between the cases and controls in: age; body mass index; existence of diabetes mellitus type 1 or 2; systemic use of corticosteroids for at least 15 days in the last 15 months; wearing of tight clothes during 90% of time in the last year; predominant wearing of underwear made from synthetic fabric; predominant wearing of lace thong underwear during the last year; the use of immunosuppressive drugs for at least one month during the last year; the presence of intrauterine contraceptive device during at least 6 months in the last year; the rate of sexual intercourses during the last year; the use of hormonal contraceptives during at least 6 months before enrollment to the study; exposure to training in vaginal irrigation offered by health workers; smoking (more than 5 cigarettes daily during the last year); bacteria in vaginal smear confirmed at least once during the last year; concomitant chronic non-contagious disease except for diabetes mellitus; serious event causing stress during the last year (divorce, death of a first-line relative, loss of job or change of a city); concomitant hypothyreosis or hyperthyreosis; employment status; regular daily intake of coffee during the last year; previous hysterectomy; sedentary job during the last year; alcohol intake per week during the last year; average weekly intake of fermented milk products during the last year; the level of education; number of irregular periods during the last year; average duration of menstrual bleeding and religion (Christian, Muslim or atheist).

The results of the logistic regression analysis with the adjustment for potential confounders are shown in Table 2. The only two significant associations were between recurrent vulvovaginal candidiasis and continual wearing of panty liners during the last year ($OR_{adjusted}$ = 3.97; CI = 1.57–10.02; $p$ = 0.004), and between recurrent vulvovaginal candidiasis and predominant use of vaginal tampons during menstruation in the last year ($OR_{adjusted}$ = 4.25; CI = 1.11–16.27; $p$ = 0.035). Although the crude odds ratios for antibiotic use during seven or more days within the last month (OR = 1.97; CI = 0.98–3.94) and self-medication with antimycotics (OR = 1.95; CI = 1.00–3.83) were above one, and the difference was significant ($p$ = 0,049 and 0.044, respectively), after adjustment these odds ratios dropped to values close to one, their CIs included 1, and the differences became statistically not significant ($p$ = 0.778 and 0.309, respectively).

The interactions between risk factors which are likely to have an additive risk for recurrent vulvovaginal candidiasis were investigated (Table 3). The analysis did not show a syn-

**Table 2**

**Crude and adjusted odds ratios (OR) of the risk factors for recurrent vulvovaginal candidiasis**

| Risk factors | Crude OR (95% CI) | Adjusted* OR (95% CI) |
|---|---|---|
| Antibiotic use during seven or more days within the last month | 1.97 (0.98–3.94) | 1.17 (0.39–3.47) |
| Continual wearing of panty liners during the last year | 3.23 (1.68–6.22) | 3.97 (1.57–10.02) |
| Predominant use of vaginal tampons during menstruation in the last year | 3.25 (1.24–8.50) | 4.25 (1.11–16.27) |
| Self-medication with antimycotics | 1.95 (1.00–3.83) | 1.76 (0.59–5.23) |

***Adjusted for age, body mass index, existence of diabetes mellitus type 1 or 2; antibiotic use during seven or more days within the last month; systemic use of corticosteroids for at least 15 days in the last 15 months; continual wearing of panty liners during the last year; wearing of tight clothes during 90% of time in the last year; predominant wearing of underwear made from synthetic fabric; predominant wearing of lace thong underwear during the last year; predominant use of vaginal tampons during menstruation in the last year; use of immunosuppressive drugs for at least one month during the last year; presence of intrauterine contraceptive device during at least 6 months in the last year; rate of sexual intercourses during the last year; use of hormonal contraceptives during at least 6 months before enrollment to the study; exposure to training in vaginal irrigation offered by health workers; smoking; bacteria in vaginal smear confirmed at least once during the last year; concomitant chronic non-contagious disease except diabetes mellitus; self-medication with antimycotics (without being prescribed by a physician) during the last year; serious event causing stress during the last year; concomitant hypothyreosis or hyperthyreosis; employment status; regular daily intake of coffee during the last year; previous hysterectomy; sedentary job during the last year; alcohol intake per week during the last year; average weekly intake of fermented milk products during the last year; level of education; number of irregular periods during the last year; average duration of menstrual bleeding and religion.**
**CI – confidence interval.**

**Table 3**

**Interactions between the concurrent continual wearing of panty liners during the last year, predominant use of vaginal tampons during menstruation in the last year, antibiotic use during seven or more days within the last month and self-medication with antimycotics**

| Risk factors | Crude odds ratio (95% CI) | Adjusted* odds ratio (95% CI) |
|---|---|---|
| Only antibiotic use during seven or more days within the last month (A) | 1.97 (0.98–3.94) | 1.17 (0.39–3.47) |
| Only continual wearing of panty liners during the last year (B) | 3.23 (1.68–6.22) | 3.97 (1.57–10.02) |
| Only predominant use of vaginal tampons during menstruation in the last year (C) | 3.25 (1.24–8.50) | 4.25 (1.11–16.27) |
| Only self-medication with antimycotics (D) | 1.95 (1.00–3.83) | 1.76 (0.59–5.23) |
| Both A and B | 3.08 (1.32–7.16) | 2.59 (0.74–9.07) |
| Both A and C | 3.65 (0.79–16.91) | 3.03 (0.35–26.23) |
| Both A and D | 2.59 (1.11–6.04) | 2.61 (0.83–8.21) |
| Both B and C | 4.27 (1.16–15.75) | 3.97 (0.78–20.17) |
| Both B and D† | 3.13 (1.35–7.28) | 5.35 (1.57–18.28) |
| Both C and D | 5.73 (1.38–23.80) | 6.10 (0.90–41.40) |

***Adjusted for age, body mass index, existence of diabetes mellitus type 1 or 2; antibiotic use during seven or more days within the last month; systemic use of corticosteroids for at least 15 days in the last 15 months; continual wearing of panty liners during the last year; wearing of tight clothes during 90% of time in the last year; predominant wearing of underwear made from synthetic fabric; predominant wearing of lace thong underwear during the last year; predominant use of vaginal tampons during menstruation in the last year; use of immunosuppressive drugs for at least one month during the last year; presence of intrauterine contraceptive device during at least 6 months in the last year; rate of sexual intercourses during the last year; use of hormonal contraceptives during at least 6 months before enrollment to the study; exposure to training in vaginal irrigation offered by health workers; smoking; bacteria in vaginal smear confirmed at least once during the last year; concomitant chronic non-contagious disease except diabetes mellitus; self-medication with antimycotics (without being prescribed by a physician) during the last year; serious event causing stress during the last year; concomitant hypothyreosis or hyperthyreosis; employment status; regular daily intake of coffee during the last year; previous hysterectomy; sedentary job during the last year; alcohol intake per week during the last year; average weekly intake of fermented milk products during the last year; level of education; number of irregular periods during the last year; average duration of menstrual bleeding and religion.**
**†Synergistic combination; CI – confidence interval.**

ergistic effect for: 1) the concurrent continual wearing of panty liners during the last year and predominant use of vaginal tampons during menstruation in the last year; 2) antibiotic use during seven or more days within the last month and self-medication with antimycotics; 3) predominant use of vaginal tampons during menstruation in the last year and antibiotic use during seven or more days within the last month; 4) predominant use of vaginal tampons during menstruation in the last year and self-medication with antimycotics; 5) the concurrent continual wearing of panty liners during the last year and antibiotic use during seven or more days within the last month. After adjustment, the odds ratios either dropped down or their confidence intervals included 1, and were not statistically significant ($p > 0.05$). However, the synergistic effect was observed for the concurrent continual wearing of panty liners during the last year and self-medication with antimycotics: the odds ratio increased to 5.35 (CI = 1.57–18.28), and was highly statistically significant ($p = 0.007$).

## Discussion

The results of our study did not confirm the results of previous studies which identified factors like stress [11], consumption of acidophil-containing products, a history of bacterial vaginosis, steroid therapy, diabetes mellitus, age < 40 years [12], hormonal contraception, frequency of sexual intercourses and technique of vulvovaginal hygiene [16] as predisposing for recurrent vulvovaginal candidiasis. However, continual wearing of panty liners during the last year emerged as significant risk factor in our study, which is in accordance with studies described by Sheary and Dayan [12]. Both this factor and predominant use of vaginal tampons during menstruation (which also has been significantly associated with recurrent candidiasis in our study) could somehow promote growth of *Candida* or break normal protective mechanisms of vaginal mucosa, allowing invasion of the yeast and inflammation. According to the vaginal relapse theory [19], female vagina is often colonized with small numbers of yeast. If predisposing factors are present, the yeast increases in number, invades mucosa and causes a new clinical episode of vulvovaginal candidiasis. The exact mechanism how these two local factors promote growth or mucosal invasion of the yeast remains unclear, and needs to be investigated.

It seems that systemic factors that decrease a host immune defense are not important in pathogenesis of recurrent vulvovaginal candidiasis: neither diabetes mellitus, systemic use of corticosteroids, the use of immunosuppressants, smoking, concomitant chronic non-contagious disease except diabetes mellitus, serious event causing stress during the last year nor concomitant hypothyreosis or hyperthyreosis were associated with recurrent candidiasis in our study. Other studies also did not find straightforward connection between these systemic factors and recurrence of vulvovaginal disease [20]. At most, the systemic factors may assist to local risk factors to break vaginal mucosal defense.

Although the emergence of increasingly resistant *Candida* species does not seem to play a major part in recurrent vulvovaginal candidiasis, women with recurrent disease do have higher prevalence (10–15%) of *Candida glabrata*, which is inherently less sensitive to the imidazole group of drugs [20, 21]. In our study, self-medication with antimycotics, as one of the causes of selection of resistant *Candida* species [19, 20], was not associated by itself with recurrent vulvovaginal candidiasis. However, it interacts with the local risk factor (wearing of panty liners), and increases likelihood of recurrence in women who already have this local risk factor (significant increase in odds ratio – see Table 3). This means that women who wear panty liners increase their chances to have recurrent vulvovaginal candidiasis if they simultaneously practice selfmedication with antimycotics. This interaction suggests that clusters of risk factors could be more important for the development of recurrent vulvovaginal candidiasis than individual risk factors itself, which should be clarified by further research.

## Conclusion

Our study confirmed only two local factors identified by previous studies (wearing of panty liners and the use of tampons during menstruation) as important for recurrence of vulvovaginal candidiasis, and showed that recurrence-promoting effect of one of them (wearing of panty liners) is augmented by the practice of self-medication with antimycotics.

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