Recurrent vaginal discharge: a myth or a fact?

Corrimento vaginal recorrente: mito ou fato?

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ABSTRACT

Introduction: Vaginal discharge is a frequent gynecological complaint, and may represent a disease or not. A vaginal discharge is considered recurrent when it occurs four or more episodes per year. Among the aetiologies, physiological and infectious conditions are mentioned, being the infectious ones, particularly those caused by *Candida spp.* fungus, the most related to the symptom. Despite the diagnostic and therapeutic resources available, empirical clinical treatments and self-treatments are very frequent and related to ineffective therapeutic results, leading this population to question what the differences regarding women with no symptoms are. **Objective:** To identify sociodemographic, behavioral and microbiological differences between women with recurrent vaginal discharge and asymptomatic women. **Methods:** Cross-sectional study involving 126 women with recurrent discharge complaints (study group) and 155 (control group), totaling 281 evaluated women. The group included women in the menacme, sexually active, and those who fit in the criteria of recurrent vaginal discharge, without definite previous diagnosis, compared with asymptomatic women, who attended an annual routine examination. Pregnant, diabetic and immunosuppressed women were excluded. The study was based on the principle of the null hypothesis, when there are no differences between the two studied groups. **Results:** The average age was 29.95 years, predominantly single and without children. There was no significant difference in the analysis of relationship time with the current partner, numbers of partners throughout life, gender and contraceptive method. There was predominance of normal vaginal flora (type 1) in both groups, with average prevalence of 44.9%. The alkaline vaginal pH was predominant in the study group. **Conclusion:** The null hypothesis was confirmed. Biological, behavioral and sociodemographic differences in the studied populations were not identified. In women with recurrent discharge group, there were no infectious etiologic factors, suggesting that clinical diagnoses are not sufficient for the most efficient management of these situations, indicating laboratory evaluation for these cases in order to improve diagnostic accuracy.

Keywords: vulvovaginitis; vaginal discharge; leukorrhea; gynecological examination; vulvovaginal candidiasis; bacterial vaginosis.

RESUMO

Introdução: O corrimento vaginal é queixa ginecológica frequente, podendo ou não representar doença. Conceitua-se como corrimento vaginal recorrente aquele que ocorre em quatro ou mais episódios ao ano. Entre as etiologias, citam-se condições fisiológicas e infecciosas, sendo as infecciosas, particularmente as causadas por fungo *Candida spp.*, as mais relacionadas ao sintoma. Apesar dos recursos diagnósticos e terapêuticos disponíveis, tratamentos clínicos empíricos e autotratamentos são muito frequentes e associados a resultados terapêuticos pouco efetivos, levando essa população a questionamentos sobre quais diferenças elas teriam em relação a mulheres sem sintomas. **Objetivo:** Identificar diferenças sociodemográficas, comportamentais e microbiológicas entre mulheres com corrimento vaginal recorrente e mulheres assintomáticas. **Métodos:** Estudo transversal envolvendo 126 mulheres com queixa de corrimento recorrente (grupo de estudo) mais 155 controles, totalizando 281 mulheres avaliadas. Foram incluídas no grupo de estudo mulheres no menacme, sexualmente ativas e enquadradas nos critérios de corrimento vaginal recorrente, sem diagnóstico prévio definido, comparadas a mulheres assintomáticas, que compareciam a exame de rotina anual. Foram excluídas as gestantes, diabéticas e imunossuprimidas. Partiu-se de princípio da hipótese nula, em que não há diferenças entre os dois grupos estudados. **Resultados:** A média de idade foi de 29,95 anos, predominando solteiras e sem filhos. Não houve diferença significativa quando analisados: tempo de relacionamento com o atual parceiro, número de parceiros ao longo da vida, sexarca e método anticoncepcional. Houve predomínio da flora vaginal normal (tipo 1) em ambos os grupos, com prevalência média de 44,9%. O pH vaginal alcalino foi predominante no grupo de estudo. **Conclusão:** Confirmou-se a hipótese nula, não se identificando diferenças biológicas, comportamentais e sociodemográficas nas populações estudadas. Não se observaram, no grupo de mulheres com corrimento recorrente, fatores etiológicos infecciosos, sugerindo que diagnósticos clínicos não são suficientes para o manejo mais eficiente dessas situações, indicando-se avaliação laboratorial para esses casos com o objetivo de melhorar a acurácia diagnóstica.

Palavras-chave: vulvovaginite; descarga vaginal; leucorreia; exame ginecológico; candidíase vulvovaginal; vaginose bacteriana.

INTRODUCTION

The normal vaginal microbiota is predominantly composed of *Lactobacilli* producing hydrogen peroxide (80 to 95%) and some bacteria. The physiological vaginal discharge, clear or whitish, variable throughout the menstrual cycles and composed by microbiota and cervical fluids, is one of the frequent gynecological complaints confused by women with infectious symptoms, especially those caused by fungi. There is a wide spectrum of differences between what is normal and a vaginal disease, despite the symptoms can be common to both situations[1-4].

Pathological symptoms include infectious causes, such as bacterial vaginosis, vulvovaginal candidiasis and trichomoniasis, corresponding to 90% of cases. These configure vaginal disease that presents, in addition to abnormal vaginal discharge, itching, dyspareunia, and/or odor change[5-7].

Amongst infectious symptoms, bacterial vaginosis is considered the most common lower genital tract infection, with prevalence of approximately 27.5%. It results from the imbalance of vaginal microbiota with excessive growth of normal anaerobic bacteria and reducing concentrations of *Lactobacilli*. It is characterized by a greyish-white, fluid and fetid odor discharge that becomes accentuated after intercourses and/or menstrual period[8-11].

Vulvovaginal candidiasis is present in 20 to 25% of cases of infectious discharge. The clinical symptom is primarily characterized by

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the intense itching. The discharge is white, crumbly, odorless and cheesy-looking, adhered to the vaginal walls. In recurrent cases, predisposing factors are investigated, particularly immunosuppression, and more connected to other species of *Candida albicans* (responsible for 80 to 90% of candidiasis cases)[8-13].

Trichomoniasis is caused by a flagellate protozoan, *Trichomonas vaginalis*, responsible for 10 to 35% of vulvovaginitis. It is characterized by a moderate to a large amount of discharge, yellow-green, pemphigoid, vulvar irritation and/or itching, dysuria and polyuria, hyperemia with reddish plaques in cervix (cervix in strawberry or tigroid aspect) and, less common, pelvic pain[9,11,14].

Symptoms of vaginal itching without pathological discharges should also be observed. These are mostly due to allergic or irritative causes (clothing, toiletries and beauty products), skin disorders and vaginal atrophy. Nonspecific discharges can still result in different concomitant infections[8].

Among adult sexually active women, about 75% have at least one episode of vulvovaginitis in life[3,15]. And to avoid complications, such as the extension to upper genital tract and infertility due to tubal damage, the priority becomes the quick vulvovaginitis recognition and prevention, in order to treat the pathological cases in the most specific way possible[16].

Approximately 5% of women with vulvovaginitis will evolve to recurrent symptoms[17], being defined as recurrent vulvovaginitis the properly diagnosed episodes, clinical and laboratory exams, repeated for at least four times in a period of one year[18,19].

In such cases, empirical treatments with medicinal associations result in low efficiency and frequent return of symptoms[6], aggravated by self-treatments, which in general also contribute to the perpetuation of the irritative symptoms[2,20]. Nyirjesy noted that only 28% of the female population using self-treatment for recurrent candidiasis — when evaluated in a reference service — was diagnosed with this pathology, and 15% presented contact dermatitis caused by the topical medications used[15,21].

Nowadays, the diagnosis and the indication of the appropriate treatment are considered challenges, requiring knowledge of physiology, normal and abnormal vaginal microbiota, and the implementation of a complete diagnosis guideline, especially in recurrent symptoms[1-4].

OBJECTIVE

To evaluate, in the study population composed of women complaining of recurrent vaginal discharge with previous unsatisfactory treatments referred to specialized ambulatory of gynecological infections, the presence of microbiological, etiologic, behavioral and sociodemographic factors that justifies this complaint, comparing the existence of the same factors in control population of asymptomatic women.

METHODS

A diagnosis cross-sectional analytical study was carried out to evaluate the prevalence of *Candida spp*., bacterial vaginosis, trichomoniasis, *Chlamydia* infection, and mycoplasma diagnosis. Study group patients had reported recurrent vaginal discharge (four or more episodes in one year) with various systemic or topical treatments considered unsatisfactory. The control group consisted of asymptomatic women, morbidities-free, who attended various clinics for tests considered annual checkup. The research project was approved by the Ethics Committee in research in Human Beings of the Hospital das Clínicas of the Universidade Federal do Paraná (UFPR), and all subjects of the survey agreed with the participation by signing a written informed consent form.

Inclusion criteria were the following: women over 18 years of age in menacme who met the criteria for recurrent vulvovaginitis without a definite diagnosis submitted to any evaluation or treatment in the last six months for the presented symptoms and recurrent symptoms. Exclusion criteria were as follows: pregnant, diabetic, immunosuppressed, undergoing treatment for any sexually transmitted disease diagnosed in the last six months, menopausal and prepubescent women.

All patients were submitted to previous anamnesis for the collection of sociodemographic, behavioral and clinical information in an adequate instrument of data collection, and then referred to a gynecological examination associated with diagnostic procedures and biological materials collections for microbiological analysis.

The gynecological examination was conducted in accordance with the conventional technique. The complementary examinations and biological materials collections have been made systematically as described next:

1. measurement of vaginal pH with indicator tape in vaginal right wall;
2. collection of material with sterile swab from vaginal sac followed by sowing of culture medium for fungi and smear on blade for Gram and collection of material in test tube with saline for fresh examination;
3. removal of excess of mucus, if necessary, and collection of endocervical secretions with sterile swab in appropriate lamina for direct immunofluorescence for *Chlamydia* followed by sowing in culture medium suitable for mycoplasma;
4. collection of cervical ectocervix smear with Ayre's spatula and with endocervical brush on a lamina and preserved with appropriate fixative;
5. collection of secretion in vaginal sac with the same Ayre's spatula in lamina for amines test.

The vaginal environment pH was determined by placing a universal indicator tape with four turns on the right vaginal wall and interpreted after 10 seconds of contact, according to changes in color, and compared to the standard colorations at the time of collection by the observer. The fresh examination made the quantitative evaluation of epithelial cells, leukocytes, hyphae and trichomonas, with standardized reading by the laboratory. Gram staining was performed using a Gram staining set (set of dyes for differential staining in bacteriology with staining technique, reading and interpretation of standardized results according to international techniques).

The evaluation of mycoplasmas used the mycoplasma kit composed of one tube containing 2 mL of A3XB broth; one tube with 2 mL of MLA broth; one tube with 2 mL of U 10 broth and plates with 10 mL of A7 medium for the isolation, identification and

quantification of urogenital mycoplasmas (*Ureaplasma urealyticum* and *Mycoplasma hominis*).

Chlamydia was evaluated by direct immunofluorescence method after direct staining agent with marked antibodies, using the Biomed Pathfinder *Chlamydia Trachomatis* Direct Antigen Detection System Kit.

The evaluation of fungi was performed in selective culture medium for isolation of pathogenic fungi, mycosel agar, which contains two antimicrobials (cycloheximide and chloramphenicol), and can be used for the selective isolation of pathogenic fungi samples from biological samples potentially contaminated with bacteria and saprophytic fungi. The sample was also seeded by striking the inclined surface of several mycosel agar tubes with a bacteriological ring followed by incubation for up to two weeks at 20 to 25ºC and also at 35ºC. The reading and interpretation depends on the characteristics of the main fungi isolated from clinical materials in mycosel. *Candida albicans* showed good growth of white creamy colonies[22-24].

Cytology criteria based on oncotic Bethesda System were used for cytological diagnostics of normality, Atypical Squamous Cells of Uncertain Significance (ASCUS) and Squamous Intraepithelial Lesions (SIL).

The collected materials were sent on the same day to the laboratory where the analysis was performed, following universal standard techniques.

Statistical analysis occurred through the groups' comparison in relation to the dichotomous variables using Fisher's exact test, and χ^2 test was considered concerning the polytomous variables. The Student's t-test for continuous variables was considered, taking into account the homogeneity of variances. P values less than 0.05 indicated statistical significance. The evaluation was performed by a professional of the Statistics Department of the UFPR.

RESULTS

The results were based on the null hypothesis, *i.e.*, inferred there is no statistically significant difference in the analyzed variables (sociodemographic, behavioral and microbiological ones) among women with recurrent vaginal discharge and the asymptomatic control group.

Sociodemographic information analyzed were age, marital status, number of children and occupation. Among age average, despite a little difference in numeric absolute terms, there was statistical difference between the study and control groups (p=0.0258). Regarding marital status, there was significant prevalence of unmarried women in relation to married women in both groups, with significant predominance of married women in the study group (p=0.0258). In reference to the number of children, women without children were prevalent in both groups. There was no significant difference between the study group and the control group (p=0.5249). Concerning occupation, women who work outside home predominated in both groups. There was no significant difference between the study group and the control group (p=0.6670). **Table 1** describes the sociodemographic information.

From a behavioral standpoint, the following information were evaluated: number of partners by the time of the examination, sexarche age, time of sexual relationship with the current partner, smoking and use of contraceptive methods.

When assessing the number of partners, there was predominance of women with two to five partners over a lifetime and those who have had a unique partner in both groups. There was no significant difference between the study group and the control group (p=0.4361).

Regarding the age of sexual activity onset, the average age was 17.95 years old in the study group and 18.34 years old in the control group. There was no significant difference between the study group and the control group. The statistical test result indicated the non-rejection of the null hypothesis at 5% significance level (p=0.2044).

When evaluating the time of sexual relationship with the current partner, the percentage of women who were stable with the same partner for more than one year was prevalent in both study and control groups. There was no significant difference between the study group and the control group (p=0.4119).

The use of contraceptives showed predominance of hormonal methods, followed by not using any method. There was no significant difference between the study group and the control group (p=0.6097). Smoking was also prevalent in both groups, with no significant

Table 1 – Sociodemographic information of study group and control group in absolute and relative values.

	Study group (n=126)		Control group (n=155)		p
Average age	**28.86 years old**		**30.84 years old**		**0.0258**
	n	**%**	**n**	**%**	
Marital status					
Married or common-law	56	44.4	36	23.2	0.0258
Single ou divorced	70	55.6	119	76.8	
Children					
No children	63	50.0	64	41.9	
1 child	37	29.4	51	32.9	0.5249
2 or more children	26	20.6	40	25.2	
Occupation					
No	30	23.8	33	21.3	0.6670
Yes	96	76.2	122	78.8	
Number of partners					
1	45	35.7	61	39.3	
2 to 5	66	52.4	71	45.8	0.4361
6 to 10	9	7.1	18	11.6	
More than 10	6	4.8	5	3.2	
Time of relationship					
Up to one year	8	6.4	6	3.9	
More than one year	108	85.7	137	88.4	0.4119
No partner	10	7.9	12	7.7	
Contraceptive method					
Hormonal	71	56.3	80	51.6	
Non-hormonal	17	13.5	27	17.4	0.6097
None	38	30.2	48	31.0	
Smoker					
No	113	89.7	144	92.9	0.3933
Yes	13	10.3	11	7.1	

difference between the study group and the control group (p=0.3933). The data of the behavioral variables were mentioned in **Table 1**.

As for the microbiological profile, the analyzed data are described in **Table 2**. They are: the type of flora, the presence of fungi, the presence of infection by *Chlamydia*, trichomoniasis infection and mycoplasma infection.

The type of vaginal flora prevalent in both groups was type I (normal), according to Spiegel et al.[25]. There was no statistically significant difference between the types of flora when the study group and the control group were compared (p=0.6140), confirming the null hypothesis.

The prevalence of bacterial vaginosis was similar in both groups (16.67% in the study group and 15.48% in the control group), with no significant difference between the two groups (p=0.8704), confirming the hypothesis of nullity.

Concerning the presence of fungi in culture, there had been higher positivity in the study group with tendency towards statistical significance, which shows a difference between the two populations (p=0.0572).

The presence of endocervical *Chlamydia* presented low prevalence in both groups, with no statistical significance between them (p=0.5890).

The vaginal trichomoniasis presented very low prevalence in both groups, with no significant difference between them (p=0.4484).

In the control group, there was a discreetly higher prevalence of mycoplasmas. However, there was no statistical significance between the groups (p=0.5890).

The alkaline vaginal pH (above 4.5) proved to be the most prevalent in both study and control groups, followed by the normal vaginal pH (between 3.5 and 4.5). No significant difference was observed between the groups (p=0.7301).

Table 2 – Microbiological profile information analyzed in the study and control groups in absolute and relative values.

	Study group (n=126)		Control group (n=155)		p
	n	%	n	%	
Flora					
Normal	53	42.1	74	47.7	
Intermediate	39	30.9	45	29.0	0.6140
Abnormal	34	27.0	36	23.3	
Fungi					
Negative	110	87.3	146	94.2	0.0572
Positive	16	12.7	9	5.8	
Chlamydia					
Negative	124	98.41	154	99.4	0.5890
Positive	2	1.59	1	0.6	
Trichomonas					
Negative	125	99.2	155	100	0.4484
Positive	1	0.8	0	0	
Mycoplasma					
Negative	113	89.69	131	89.5	0.5890
Positive	13	10.31	24	10.5	
pH					
<3.0	2	1.6	2	1.3	
3.5 to 4.5	59	46.8	72	46.4	0.7301
>4.5	65	51.6	81	52.2	

DISCUSSION

The present study examined 281 women attended in ambulatory with gynecological infections. Among them, 126 belonged to the study group, as had previously presented clinical diagnosis of recurrent pathological discharge, while women of the control group were asymptomatic.

The sociodemographic profile of both groups (with and without recurrent vaginal discharge) was similar, showing that women with recurrent vaginal discharge are young, unmarried, without children, non-smoker, in use of hormonal contraceptive, with remunerated activities out of home, which is compliant with the literature, representing the modern woman starting an independent adult life[8,26].

The sexual behavior, evaluated by the start of sexual activity, the number of previous partners and the time of the last relationship, was also similar between groups and remained according to studies already described. No behavioral habit was inconsistent between the populations[20].

The microbiological analysis showed minimal alteration in both groups, contrary to the expected, especially in the study group. Regardless of the presence of recurrent vaginal discharge, the normal flora (type 1) was predominant. The incidence of abnormal vaginal flora in the study group (27%) was slightly lower than that one showed by Camargo et al. (34% of abnormal flora), and was slightly higher than the control group of this study, 23.2%[6], but without statistical difference between the asymptomatic control group, showing no differences in the composition of the vaginal microbiota[10,14,21].

The presence of fungi in vaginal secretion was higher in the study group (12.7%) than in the control group (5.81%), with tendency to statistical significance (p=0.0572), reinforcing greater colonization by *Candida spp.* fungi in the recurrent discharge group, in which this agent has been the most prevalent representative. This analysis suggests a more detailed investigation in the involvement of fungus in the genesis of recurrent vaginal discharge.

The presence of mycoplasmas, *Chlamydia* and trichomonas was much lower than the expected in both groups, suggesting low prevalence or low accuracy of previous clinical diagnoses[6,26]. The same pattern found by Di Bartolomeo et al. reports similar results, demonstrating that approximately half the women with recurrent vaginal discharge did not confirm pathogenic microbiota for fungal, bacterial and trichomoniasis infections[27]. Microbiological findings recommend new prevalence studies and also consider the non-utilization of molecular biology tests as a limitation factor for this sensitivity.

The cytopathological examination can be an accessory tool and with relative specificity for the recognition of alterations in the vaginal flora, indicating that it is an acceptable diagnostic criterion in the analysis of this symptom, being validated when it shows descriptive alterations in the microflora pattern[28-30].

The normal vaginal pH, between 3.5 and 4.5, produced by *Lactobacilli* protects against infections by pathogenic microbiota, being its verification an integral part of Amsel clinical criteria for the evaluation of vaginal discharge and diagnosis of vaginitis and infectious vaginoses[1]. The prevalence found was pH above 5 in both groups, which did not show any relation with increased prevalence of bacterial vaginosis and other vaginal infections.

As limitations of the diagnosis, we considered the non-utilization of molecular biology tests, a fact that could possibly be

associated with the underdiagnoses of some agents, especially *Chlamydia* and mycoplasma.

As perspectives, we observed that, although some syndromic approaches took into account the epidemiological data as a diagnostic key, in the studied population these epidemiological differences were not demonstrated, guiding the eventual revision of this type of approach.

CONCLUSION

Recurrent vaginal discharge is a frequent complaint in gynecological practice. Women in this condition do not generally present biological, behavioral and sociodemographic differences in relation to asymptomatic women, and might have been considered carriers of recurrent infections by *Candida* or other infections in clinical assessments of low accuracy.

Women with this symptom are labeled as carrying an abnormal recurrent infectious discharge, such as recurrent vaginal candidiasis, making difficult to understand their individual, physiological and pathological vaginal nature, leading to inappropriate treatments and self-treatments with the use of topical and systemic anti-infective medications.

Due to the way that recurrent vaginal discharge is often handled, the diagnosis of recurrent vulvovaginitis is still a myth that should be better explored by both clinical and scientific assistance.

In view of these results, it can be recommended the most detailed and objective clinical and laboratorial evaluation for the clinical management of these cases, involving detailed complete anamnesis and vaginal microbiological evaluation, preferentially through molecular biology methods. Similarly, detailed explanations about the vaginal microbiota and its physiological and pathological behavior and recommendations regarding drug management should be intensified by the clinical assistance to these women.

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Conflict of interests

The authors declare no conflict of interests.

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