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## ORIGINAL ARTICLE

# A Little-Known Vaginitis-Like Picture: Cytolytic Vaginosis

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### SUMMARY

***Background:*** **Cytolytic vaginosis (CV) is a condition characterized by an increase in lactobacilli in the vaginal flora, causing complaints of discharge, itching, dyspareunia, and dysuria. Since there are no antimicrobials in the treatment protocols of CV, the diagnostic and therapeutic criteria of which were first defined by Cibley, differential diagnosis of CV from other vaginitis agents will prevent unnecessary use of antimicrobials and recurrent complaints. In our study, we aimed to determine the frequency of CV in patients presenting with vaginitis complaints and the diagnostic accuracy of the diagnostic criteria.**
***Methods:*** **In total, 140 women, 103 with vaginitis complaints and 37 without vaginitis complaints, were examined for bacterial vaginosis (BV), vulvovaginal candidiasis (VVC), Trichomonas vaginalis (Tv), and CV. For the diagnosis of CV, vaginal pH ≤ 4.5, the presence of a large number of lactobacilli in Gram staining, the presence of false clue cells, cytolysis in vaginal epithelial cells, leukocyte deficiency or absence, absence of Tv, BV, or VVC were used.**
***Results:*** **Out of 103 patients, 30 (29.1%) had BV, 20 (19.4%) had VVC, 20 (19.4%) had CV, 5 (4.9%) had BV and VVC, and 4 (3.9%) had Tv. The sensitivity and specificity of the diagnostic criteria were 80% and 99% for epithelial cytolysis, 70% and 99% for false clue cells, 100% and 86% for pH ≤ 4.5, and 100% and 56% for numerous lactobacilli, respectively.**
***Conclusions:*** **In Turkey and worldwide, CV is not considered in vaginitis cases. In our study, the high rate of 19.4% in vaginitis cases shows the need for comprehensive research on this subject.**
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**KEYWORDS**

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## INTRODUCTION

Vaginitis, an inflammatory reaction of the vagina, is characterized by discharge, foul odor, and/or itching. Most cases of vaginitis are of microbial origin, and the most common causes are bacterial vaginosis (BV), vulvovaginal candidiasis (VVC), and trichomoniasis. In vaginosis with similar symptoms, there is an imbalance in the normal microbiota of the vagina [1].
Although evidence related to cytolytic vaginitis (CV) emerged in 1961, its clarification came in 1991 when Cibley [2] identified CV in women with VVC symptoms. This study proposes diagnostic criteria and treatment for these patients, in whom the pathophysiology

and treatment are markedly different, although the symptoms of VVC (cheesy discharge, irritation, and pruritus) are seen. However, the article did not present quantitative patient data, including demographics, symptoms, diagnosis, and treatment outcomes. Since then, CV has remained a controversial and underresearched condition. CV is characterized by the presence of large numbers of lactobacilli, which can cause cytolysis of the vaginal epithelium, hence the name CV [3]. Lactobacilli are the most prevalent bacteria found in the vaginal microbiota of women who are of reproductive age. They play a crucial role in maintaining the balance of the vaginal ecosystem by producing antimicrobial substances like hydrogen peroxide and bacteriocin. Additionally, they produce lactic acid that helps to keep the normal vaginal pH at a slightly acidic level, ranging between 3.8 and 4.2 [4]. A shift in this balance in favor of lactobacilli can lead to symptoms similar to those of a fungal infection, such as white cheesy discharge, itching, vulvar dysuria, and dyspareunia [5]. The symptoms are cyclical and more pronounced during the luteal phase [2]. Since the management of CV differs from other types of vaginitis, failure to consider CV in vaginitis cases may lead to treatment failure. As a result, patients with persistent symptoms may have repeated visits to the doctor.

Studies on CV are limited; 67% of the 43 publications between 1961 and 2021 were conducted since 2007, and 28% of these were reported from the United States [6]. The prevalence of CV has been observed between 1.7% and 26.7% in the publications written after it was defined by Cibley [1,5,7-12].

Our study aimed to investigate two key aspects: the specificity of the criteria used to diagnose CV and the incidence of CV in patients with vaginitis. By addressing these objectives, we hope to provide valuable insights into the diagnosis and prevalence of CV.

## MATERIALS AND METHODS

A total of 103 patients (aged 16 - 50 years) presented to the gynecology and obstetrics outpatient clinic with complaints of vaginal discharge (with or without accompanying complaints of itching and/or foul odor), no menstrual bleeding, and no use of antibiotics in the previous week were included in the study. Additionally, 37 controls (aged 16 - 50 years) without complaints of vaginal discharge, itching, foul odor, or menstrual bleeding, and no use of antibiotics in the previous week were included. Patients' complaints of vaginitis and the characteristics of the discharge were also recorded in the study records.

Samples were collected from the vaginal sidewalls or posterior fornix using an Amies transport medium and two dry sterile swabs. The patients' vaginal pH was measured from the vaginal sidewalls or posterior fornix using pH strips with 0.5 intervals (Merck) [13].

The first dry swab was mixed with two drops of 10% KOH on the slide and examined for the presence of an amine odor. The second dry swab was suspended in 1.5 mL of 0.85% sodium chloride solution and divided into sterile tubes. A slide preparation was made from this liquid at the patients' bedside and examined under a light microscope at x 10 and x 40 magnifications. The remaining fluid was stored at room temperature as preparation for Gram staining and T. vaginalis culture within three hours. The Amies transport medium was reserved for yeast culture and as preparation of a second Gram staining and was again kept at room temperature for a maximum of three hours.

**The following criteria were used for diagnosis:**

BV - presence of at least three of the following criteria: white-grey thin homogeneous discharge, amine odor, presence of clue-cells, and vaginal pH $\geq$ 4.5 [14].

VVC - presence of yeast cells and hyphae by microscopic examination or growth on SDA [14].

Tv - Presence of parasite by microscopic examination and/or growth in culture (CPLM and Trichomonas medium) [14].

CV - Gram stain; numerous lactobacilli, few or no leucocytes, cytolysis in vaginal epithelium (overgrowth of lactobacilli produces hyperacidity and low pH. This over-acidification results in damage to vaginal epithelium and causes lysis of epithelial cells) [15], presence of false clue cells (epithelial cells coated with Gram-positive bacilli), vaginal pH < 4.5, absence of Tv, BV, or VVK [2].

## RESULTS

Out of the 103 patients, 30 (29.1%) had BV, 20 (19.4%) had VVC, 20 (19.4%) had CV, five (4.9%) had BV and VVC, and four (3.9%) had trichomoniasis. In seven patients (6.8%), the investigated vaginitis pathogens could not be identified. Eight patients (7.8%) were grouped as CV with an increased number of leucocytes (CV + PNL) and nine patients (8.7%) as CV + VVC. The findings in the control group were: yeast growth in six patients (16.2%), amine odor in one patient, clue cells in four patients, false clue cells in one patient, and cytolysis in epithelial cells in one patient. Gram staining images are shown in Figure 1. Discharge was the most common complaint in patients with BV and CV, while discharge and itching were the most common complaints in patients with VVC. Table 1 details the complaints of the patients who consulted a physician.

Discharge characteristics were divided into two groups, cheesy and homogeneous, and the distribution of discharge in vaginitis is shown in Table 2. The relationship between cheesy and homogeneous discharge with BV, CV, and VVC was analyzed by the Pearson chi-squared test. A significant correlation was found between cheesy discharge and VVC ($p = 0.0005$) and between homogeneous discharge and BV ($p = 0.0005$). No significant correlation was found between cheesy discharge and

**Table 1. Patients' complaints for consulting a doctor.**

| | Discharge n (%) | Discharge + itching n (%) | Discharge + itching + dyspareunia n (%) | Discharge + itching + dysuria n (%) | Discharge + dyspareunia n (%) | Discharge + foul odor n (%) | Discharge+ dyspareunia + foul odor n (%) | Discharge + itching + dyspareunia + dysuria n (%) |
|---|---|---|---|---|---|---|---|---|
| **BV** | 12 (63.2) | 4 (21.1) | - | - | 5 (26.3) | 6 (31.6) | 2 (10.5) | - |
| **CV** | 13 (65) | 3 (15) | 3 (15) | - | - | - | - | 1 (5) |
| **VVC** | 5 (25) | 11 (55) | 4 (20) | - | - | - | - | - |
| **BV + VVC** | 4 (80) | 1 (20) | - | - | - | - | - | - |
| **CV + VVC** | 1 (11.1) | 6 (66.7) | 2 (22.2) | - | - | - | - | - |
| **CV + PNL** | 3 (42.9) | 3 (42.9) | - | - | 1 (14.3) | - | - | - |
| **Tv** | - | - | 2 (50) | 1 (25) | 1 (25) | - | - | - |

**BV - bacterial vaginosis, CV - cytolytic vaginosis, VVC - vulvovaginal candidiasis, PNL - increased number of leucocytes, Tv - T. vaginalis.**

**Table 2. Distribution of discharge according to vaginitis.**

| | Discharge n (%) | | | Total |
|---|---|---|---|---|
| | Cheesy | Homogenous | None | |
| **BV** | 1 (3.3) | 28 (93.3) | 1 (3.3) | 30 |
| **BV + VVC** | 2 (40) | 3 (60) | - | 5 |
| **VVC** | 13 (65) | 7 (35) | - | 20 |
| **CV** | 11 (39.3) | 17 (60.7) | - | 28 |
| **CV + VVC** | 3 (33.3) | 6 (66.7) | - | 9 |
| **Tv** | - | 4 (100) | - | 4 |
| **Total** | 30 (31.3) | 65 (67.7) | 1 (1) | 96 |

**BV - bacterial vaginosis, CV - cytolytic vaginosis, VVC - vulvovaginal candidiasis, Tv - T. vaginalis.**

**Table 3. Sensitivity, specificity, and positive and negative predictive values (%) of diagnostic criteria in CV.**

| | Sensitivity | Specificity | PPV * | NPV ** |
|---|---|---|---|---|
| **Cytolysis of the epithelial cell** | 80 | 99 | 94 | 96 |
| **False clue cell** | 70 | 99 | 93 | 94 |
| **pH ≤ 4.5** | 100 | 86 | 59 | 100 |
| **Increase in lactobacillus number** | 100 | 56 | 31 | 100 |

*** - positive predictive value, ** - negative predictive value.**

CV (p = 0.615). Cheesy discharge was not specific for CV or VVC (p = 0.118) (cheesy discharge was found in 40% of CV and 65% of VVC).

For CV, the sensitivity of cytolysis in epithelial cells was 80% and specificity was 99%; the sensitivity of false clue cell was 70% and specificity was 99%; the sensitivity of pH ≤ 4.5 was 100% and specificity was 86%; and the sensitivity of increase in lactobacillus number in Gram-stained preparations was 100% and specificity was 56%. Table 3 shows the CV diagnostic criteria's sensitivity, specificity, and positive and negative predictive values. Table 4 also shows the rates of

**Table 4. Rates of coexistence of diagnostic criteria in CV, CV + VVC, and CV + PNL.**

| | Homogeneous discharge, cytolysis, fcc n (%) | Cheesy discharge, cytolysis, fcc, n (%) | Homogeneous discharge, cytolysis, n (%) | Homogeneous discharge, fcc n (%) | Cheesy discharge, cytolysis n (%) | Cheesy discharge, fcc n (%) | Homogeneous discharge n (%) | Cheesy discharge n (%) |
|---|---|---|---|---|---|---|---|---|
| **CV** | **9 (24.3)** | **3 (8.1)** | **-** | **1 (2.7)** | **3 (8.1)** | **1 (2.7)** | **2 (5.4)** | **1 (2.7)** |
| **CV + VVC** | **7 (18.9)** | **1 (2.7)** | **-** | **-** | **1 (2.7)** | **-** | **-** | **-** |
| **CV + PNL** | **3 (8.1)** | **1 (2.7)** | **2 (5.4)** | **-** | **1 (2.7)** | **-** | **-** | **1 (2.7)** |

**CV - cytolytic vaginosis, fcc - false clue cell, PNL - increased number of leucocytes.**

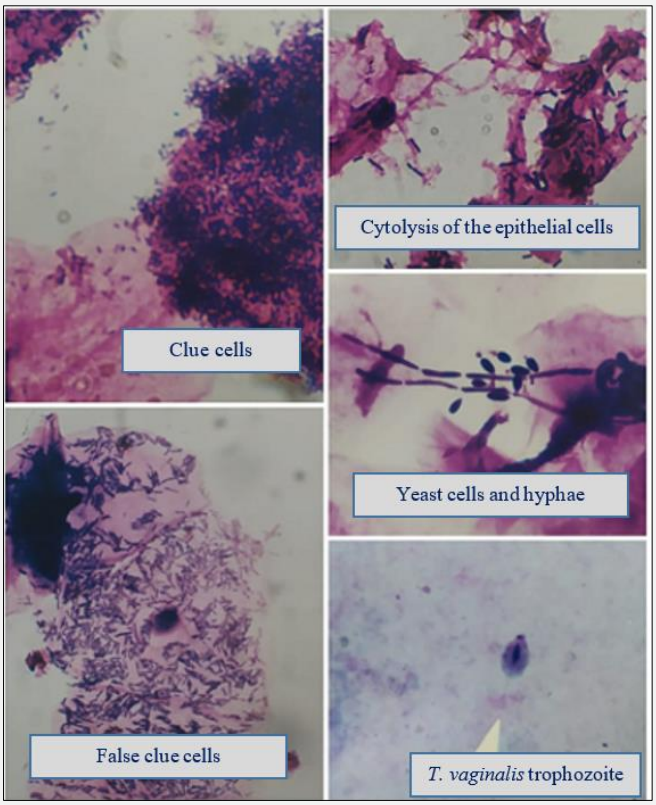


**Figure 1. Microscopic views of vaginitis.**

**Clue cells - Gram-labile coccobacilli accumulation on epithelial cells, False clue cell - lactobacilli accumulation on epithelial cells, Cytolysis of epithelial cells - lysis of epithelial cells because of low pH, Yeast cells and hyphae - branched pseudo-hyphae and yeast cells, T. vaginalis - Trophozoite, growth in culture with Giemsa stain.**

coexistence of diagnostic criteria in CV, CV + VVC, and CV + PNL.

## DISCUSSION

Most women experience vaginitis at least once in their lifetime, making it the most common gynecological diagnosis in patients admitted to primary care. Studies

have shown that vaginitis has a negative impact on women's quality of life; anxiety, embarrassment, and hygiene concerns are prevalent in those with especially recurrent symptoms [16]. CV is an unrecognized presentation of vaginitis in Turkey and worldwide. Cibley and Cibley stated that suspicion is the first step in the diagnostic criteria [2].

There is a paucity of studies on CV compared to the studies that have been published on vaginitis; Kraut et al. [6] ask "is it because CV is unknown to the medical community or because it is a variant of the normal vaginal microbiome?" However, studies of CV span 3 continents, are from diverse countries, and are published in a broad spectrum of journals; it is more suggestive that CV is a true condition. To inform clinicians whether and how much CV should be considered, further studies on prevalence using gold-standard diagnostic criteria in symptomatic women and asymptomatic women in various geographic locations are needed [6]. From this perspective, we believe that our study can address this gap by assessing the specificity of diagnostic criteria using samples obtained from both symptomatic and asymptomatic patients.

In some publications, CV was screened only in patients with clinically diagnosed VVC, and it was shown that the diagnosis of VVC was incorrectly given instead of CV. Cerikcioglu et al. [8] found CV at a rate of 7.1% in 210 patients with clinically similar complaints to VVC. Batashki et al. [7] found CV frequency of 3.9% in 1,152 patients with clinically VVC-like complaints. Some publications questioned CV criteria in a group of PAP smears without the presence of vaginitis picture. Demirezen [9] analyzed 2,947 PAP smears and found CV rate of 1.8%. Hacisalihoglu and Acet [1] found CV rate of 1.7% in their study with 2,932 PAP smears. The lower CV rates found in the four studies mentioned above compared to the rate of 19.42% in our study may be attributed to the fact that in these studies, CV investigation was performed only in patients who underwent general PAP smear screening or had a VVC-like clinical presentation.

In some publications, as in our study, CV has been investigated in patients with vaginitis complaints and is one of the top four causes of vaginitis. Wathne et al. [11] found CV rate of 4.9% in 101 patients with vaginitis, Raykova et al. [5] found CV rate of 5.1% in 468 patients with vaginal discharge, and Puri et al. [10] found CV rate of 16.3% among 190 smears showing inflammation from 308 PAP smears. Yang et al. [12] found CV rate of 26.7% in 484 patients with recurrent vaginitis. Puri et al. examined CV in patients with inflammation on PAP smears and Yang et al. examined CV in cases of recurrent vaginitis, and they found higher rates than other studies. In our study, 82.5% of the patients presenting with vaginitis to the outpatient clinic had been admitted to the hospital with the same complaints at least once before. The similar rates in Puri, Yang, and our study may be due to the similar characteristics of the patient groups.

Cibley mentioned in their publication the use of a sitz bath with sodium bicarbonate for CV treatment but did not provide any statistical studies or data to support this treatment. Although CV treatment is mentioned in some publications, no study has been done on it [3,12]. Treatment efficacy has been mentioned in two publications published in English. While Cerikcioglu [8] stated that two patients benefited from sodium bicarbonate sitz bath in their publications, an essential feature of the study by Hacisalihoglu and Acet [1] is that they performed a statistical study for the first time regarding the treatment (a course of treatment: sitting in a solution containing one tablespoon of NaHCO3 dissolved in 4 L of warm tap water every two days for ten days) results. The researchers gave sodium bicarbonate sitz baths to treat patients diagnosed with CV and found a decrease in the vaginitis complaints of 81% of the patients after one course of therapy. Hacisalihoglu and Acet's [1] study also found that 85% of the patients diagnosed with CV had previously used antifungal treatment. In our study, 85 (82.5%) of 103 patients who were admitted to the outpatient clinic with the complaint of vaginitis had consulted a physician with the complaint of discharge and/or itching at least once before. Also, the detection of CV in a patient who had been struggling with vaginitis for six years underscores the fact that CV must be thought of in the differential diagnosis of non-responding vaginal discharge [17]. These findings suggest that, due to a lack of proper diagnosis and treatment, patients admitted to outpatient clinics with recurrent vaginitis more than once.

The etiology of CV still needs to be fully understood. In a study, Lactobacillus crispatus was found at a high rate in patients with CV, while Lactobacillus spp. L-YJ was found at a high rate in the vaginal flora of the healthy group, and it was thought that some lactobacillus species may predispose to CV development. The vaginal microbiome is kept in a complex balance. Internal and external factors that affect this balance and change the composition of the vaginal microbiome may cause CV development. According to them, two suitable biomarkers, L. crispatus and Lactobacillus sp. L-YJ, were identified and would be helpful in identifying women at risk of serious illness before developing symptoms and may help reduce the incidence of CV [18].

In our study, the CV rate was found to be 19.4%, which was the second most common rate, along with VVC. This rate, which is higher than many studies, is thought to be the effect of the fact that CV was left untreated while other vaginitis was treated; 82.5% of our patient group had previously been admitted to hospital with vaginitis complaints. As sodium bicarbonate sitz baths are recommended in the treatment, CV should be considered in the differential diagnosis. With the correct diagnosis, unnecessary antimicrobial use will be avoided. In this way, patients will not burden the health care system with repeated visits to the doctor because they cannot be treated. The high rate of CV, particularly in patients with recurrent vulvovaginitis, highlights the im-

portance of correct diagnosis and treatment. In the presence of cheesy discharge, patients with CV may receive antifungal treatment because VVC comes to mind first. Our study concluded that cheesy discharge alone cannot be used to diagnose CV or VVC. Since Cibley's article in 1991, only about 20 articles have been published about CV, suggesting that gynecologists and laboratories have not given the situation enough attention. Recent studies also appear as a compilation of previous studies [6,15,19]. In particular, the number of studies with treatment follow-up is minimal (n = 4) [6]. It is essential to plan future studies on CV in terms of prevalence, diagnostic criteria, and treatment efficacy.

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**Ethical Approval:**
This study was approved by the Ethics Committee of Istanbul Provincial Health Directorate Bakirkoy Dr. Sadi Konuk Training and Research Hospital (date/number: 2023/512).

**Declaration of Interest:**
No conflict of interest was declared by the authors.

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