REVIEW ARTICLE

Prevalence of *Trichomoniasis* in Cervical Cancer Patients

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ABSTRACT

Background: *Trichomoniasis* is the most frequent non-viral sexually transmitted disease in the world, and it can lead to persistent HPV infection. *Trichomonas vaginalis* infection causes damage to the vaginal mucosa, activation of oncogenes and inactivation of tumor suppressor proteins, and production of non-specific oxidants that lead to cervical cancer. This study aims to determine the prevalence of *trichomoniasis* in cervical cancer patients.
Methods: This study uses systematic literature review method and uses 10 international journals obtained through machine learning and indexed in Scimago. Journals are screened through PRISMA and have gone through a critical appraisal process. This study took place from April to September 2021.
Results: The prevalence of *trichomoniasis* in cervical cancer patients ranged from 0.022% to 87.7%, according to the findings of this study. The prevalence results vary due to differences in demographics and diagnostic methods used. Statistical analysis of the association between *trichomoniasis* and cervical cancer varied between significant and insignificant. Differences in the association are influenced by the research design used, diagnostic methods, and sample of the research.
Conclusions: The conclusion of this study is that the prevalence of *trichomoniasis* in cervical cancer patients was discovered to be the highest in the study by Ghosh *et al.* in Kolkata, India (72.6% women with CIN 1, 71.0% women with CIN 2 or CIN 3, and 87.7% women with invasive cancer) and the lowest in the study by Su *et al.* in Taiwan (0.022%). The association between *trichomoniasis* and cervical cancer was found to be varied.

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Introduction

Trichomonasis is a protozoan infection caused by *Trichomonas vaginalis*. *Trichomoniasis* is the most frequent non-viral sexually transmitted disease in the world. This parasite can survive for 24 hours in a humid and warm environment.[1] The prevalence of *trichomoniasis* in the United States is 1.3%, while the prevalence of *trichomoniasis* in Bandung is 2%. People with multiple sexual partners have a higher risk of *trichomoniasis*. An increased risk was also seen in older women, black women, and people with limited knowledge and low socioeconomic status. [2–4]

Trichomoniasis generally does not cause symptoms, so screening is rarely done. This causes the available screening and diagnostic equipment to be inadequate.[5] *Trichomoniasis* can occur in men and women with equal frequency, but symptoms in men are milder and disappear within a few weeks. Meanwhile, in women, infection can occur for several years with some symptoms such as *pruritus* and smelly vaginal discharge.[6] If not treated properly, *trichomoniasis* can be associated with pelvic inflammatory disease, cervical cancer, and premature birth. In addition, individuals with *trichomoniasis are* more susceptible to HIV infection and *herpes virus*.[1]

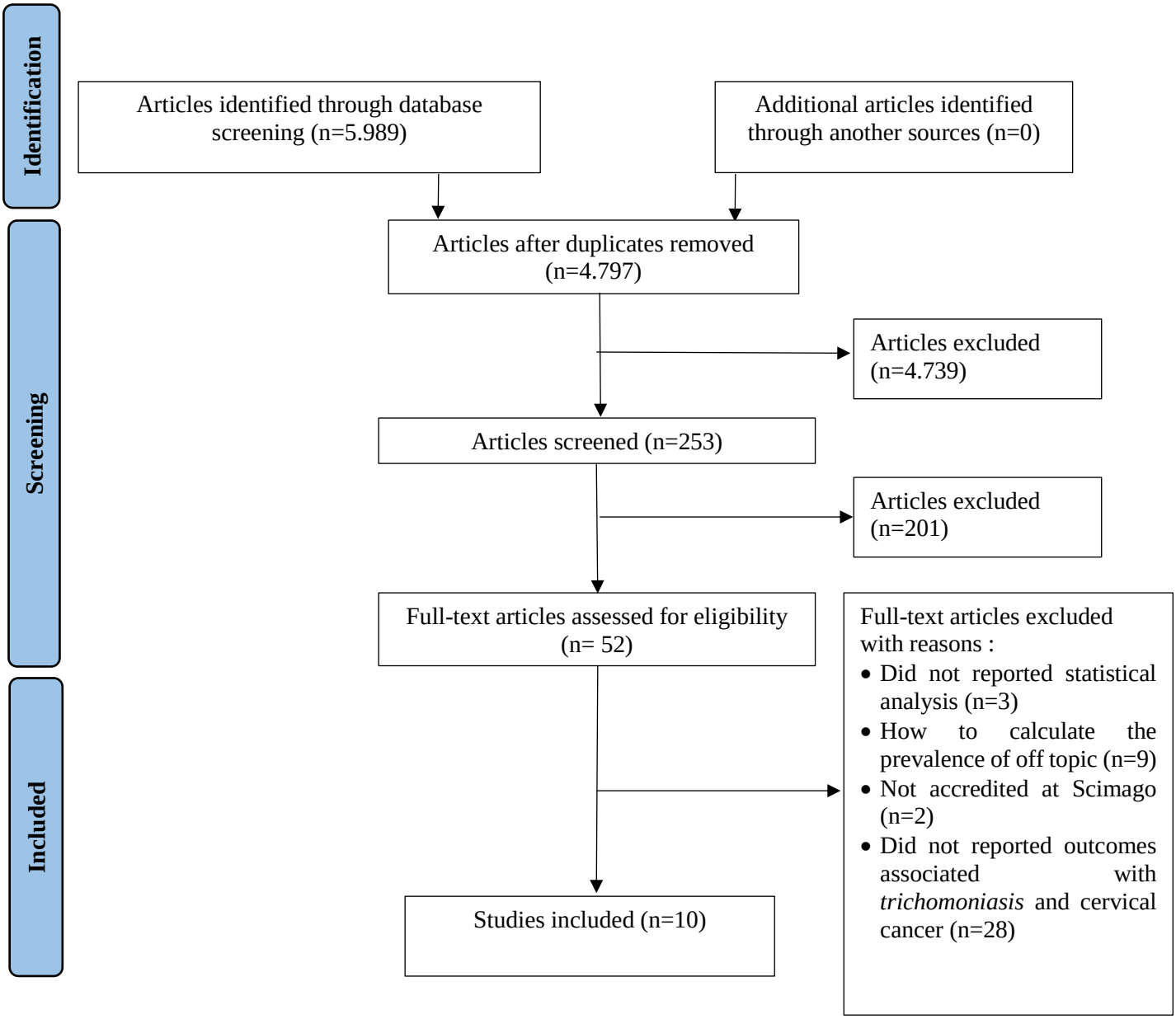
Cervical cancer is cancer that develops in a woman's cervix. Cervical cancer is caused by the *human papillomavirus* (HPV), which accounts for 99% of all cases. HPV is transmitted through sexual contact, resolves spontaneously, and generally causes no symptoms. A persistent HPV infection can cause cervical cancer. The fourth most frequent malignancy in women is cervical cancer. Cervical cancer was diagnosed in around 570,000 women worldwide in 2018, with approximately 311,000 women dying from the disease. Cervical cancer is a form of cancer that can be treated well if detected early in the disease and treated effectively. If detected at late stage, the disease can be controlled with appropriate treatment and palliative care.[7]

Trichomonas vaginalis infection causes damage to the vaginal mucosa and the release of lytic enzymes thereby increasing the virulence of HPV. This infection causes activation of oncogenes and inactivation of *tumor suppressor proteins* that lead to cervical epithelial mutations and tumor formation.[8] Chronic inflammation of *T. vaginalis* can lead to the production of nonspecific oxidants that can damage *host* DNA and lead to cervical cancer. This literature study will provide knowledge about the prevalence of *trichomoniasis* in cervical cancer patients and provide knowledge and awareness that *trichomoniasis* is an infection that must be treated properly.

Methods

This research uses systematic literature review method that aims to determine the prevalence of *trichomoniasis* in cervical cancer patients. The author searches for articles in the form of original articles on machine learning. Machine learning used include *Google Scholar, PubMed,* and *ScienceDirect*. The search for articles was carried out from April to September 2021. The author entered keywords related to this research, namely the prevalence of

trichomoniasis or *trichomoniasis* prevalence and cervical cancer or uterine cervical neoplasm or cervical neoplasm. The journals used are journals published from 2016 to 2021, in the form of *original articles*, and indexed at *Scimago*.



Results

Ten journals were used in this study. All journals are international journals indexed on *Scimago*. Three journals are research conducted in India, two journals are research conducted in Brazil, while the other journals are research conducted in Taiwan, China, Korea, Italy, and Rwanda. These journals used case-control, cross-sectional, and retrospective cohort study design. The journals used in this study reported the prevalence of *trichomoniasis* in cervical cancer patients differently. There are several journals that report the total prevalence in cervical cancer patients, or based on the stage or grade of cervical cancer. All journals also report statistical analyzes of *trichomoniasis* and cervical cancer.

1. Prevalence of *Trichomoniasis* in Cervical Cancer Patients

The prevalence of *trichomoniasis* in cervical cancer patients was discovered to be the highest in the study by Ghosh *et al.* in Kolkata, India (72.6% women with CIN 1, 71.0% women with CIN 2 or CIN 3, and 87.7% women with invasive cancer). According to study by Amorim *et al.*, 2017 in Brazil, *trichomoniasis was* found in 55.6% of women with CIN 1, 62.5% of women with CIN 2, and 64.3% of women with CIN 3 or carcinoma *in situ*. Study by Mukanyangezi *et al.*, 2018 in Rwanda reported that *trichomoniasis was* found in 7.7% in the HIV positive with LSIL, HSIL, and cancer group and as much as 22.2% in the HIV negative with LSIL, HSIL, or cancer group.[13] Study by Dey *et al.*, 2016 in Delhi, India reported the prevalence of *trichomoniasis* as much as 17.3% in women with ASCUS and 4.8% in women with LSIL. According to a study by Yang *et al.*, 2020 in China, 13.85% of women with CIN 1, 4.68% of women with CIN 2, 8.55% of women with CIN 3, and 1.22% of women with cancer had co-infection with *T. vaginalis* and HPV16. This study also reported a prevalence of co-infection with *T. vaginalis* and HPV18 as much as 12.38% in women with CIN 1, 2.86% in women with CIN 2, 0.95% in women with CIN 3, and 0.95% in women with cancer and the prevalence of coinfection with *T. vaginalis* and other types of hrHPV as much as 4.20% in women with CIN 1, 1.34% in women with CIN 2, 0.54% in women with CIN 3, and 0.09% in women with cancer.[8]

Trichomoniasis was found in 5.6% of women with ASCUS, 7.5% of women with LGSIL, 3.7% of women with ASC-H, and 2.8% of women with HGSIL in the study by Kassandra *et al.*, 2021 which was held in Maranhao, Brazil. Study by Gupta *et al.*, 2020 in India reported the prevalence of *trichomoniasis* as much as 7.8% in the group with CIN and 4.1% in the group with cervical cancer. Study by Raffone *et al.*, 2020 in Naples, Italy reported the prevalence of *trichomoniasis* as much as 2% in women with CIN 1 or LSIL. According to study by Kim *et al.*, 2016 conducted in Korea, *trichomoniasis was* found in 1.0% of women with ASCUS, 1.0% of women with LSIL, and 0.5% of women with HSIL. The prevalence of *trichomoniasis* in patients with cervical cancer was discovered to be the lowest in the study by Su *et al.*, 2020 in Taiwan. In this study, *trichomoniasis was* found in 0.022% of women with cervical lesions.[9-11]

Based on these data, the prevalence of *trichomoniasis* in cervical cancer patients ranged from 0.022% to 87.7%. The first factor that influences the difference in prevalence is demographic differences. In this study, the highest

prevalence was found in Kolkata, India and the lowest was found in Taiwan. Differences in race, poverty, and low levels of education also appear to have an effect on the prevalence of *trichomoniasis.*[12] Several studies in India show that the level of hygiene and use of gynecological services in Indian women is still very low. In addition, the Indian government is less aware of the importance of women's health in rural areas in India.[13] The second factor that influences the difference in prevalence is the difference in the diagnostic method used in the study reviewed. Each diagnostic methods used has a different level of sensitivity and specificity, so that the reported study results are also different.

2. The Relationship Between *Trichomoniasis* and Cervical Cancer

Trichomonas vaginalis infection causes cellular and immune changes in the female reproductive area, thus facilitating cell mutation and causing cervical cancer. *T. vaginalis* can produce lytic enzymes that induce vaginal mucosal damage, thereby causing microepithelial lesions, and integration of HPV DNA within host cells is induced.[14] Overexpression of E6 and E7 proteins occurs as a result of HPV DNA incorporation into host cells. This process inhibited the activity tumor suppressor protein and induce immunosuppression. Physiologically, tumor suppressor proteins have a role to trigger the process of apoptosis, repair DNA host damage, and inhibition of c-myc protein, a protein encoded by the c-myc gene. In the cell cycle, the c-myc protein is involved in cell proliferation, replication, and associated with its function to trigger tumor development (proto-oncogene).[15] Inhibition of the protein suppressor tumor's activity will trigger the development of cervical cancer.[16] Over-stimulation of E6 and E7 proteins also causes immunosuppression so that HPV infection can be persistent and cause the production of lytic enzymes and chronic inflammatory processes.[12] On the other hand, persistent infection of *T. vaginalis* will trigger an inflammatory response and oxidant production that causes host DNA damage. Damage to host DNA can also lead to the development of cervical cancer.[14]

This literature study showed that four selected journals found significant associations among *trichomoniasis* and cervical cancer based on statistical analysis. Study by Amorim *et al.*, 2017 reported that *T. vaginalis* is a risk factor for cervical lesions. Study by Dey *et al.*, 2016, found that *T. vaginalis* had a significant association with ASCUS, LSIL, and all *premalignant* cervical lesion. According to a study published in 2021 by Kassandra *et al.*, women with LGSIL and ASCH had a 3,179-fold and 12,047-fold increased risk of *T. vaginalis* infection, respectively. Study by Su *et al.*, 2020 reports cervical cancer risk was 3.684 times higher in those who had *T. vaginalis* infection compared to women who do not have *T. vaginalis* infection.

Study by Mukanyangezi *et al.*, 2018 reported that *trichomoniasis* is a risk factor for SIL and cancer in the HIV negative group, but the results of statistical analysis showed a non-significant relationship in the HIV positive group.[17] Study by Yang *et al.*, 2020 reported that coinfection of *T. vaginalis* with hrHPV increased the risk of CIN 1, but did not increase the risk of CIN 2-3. Study by Raffone *et al.*, 2020 stated that patients co-infected with *T. vaginalis* and

Gardnerella vaginalis had an 8-fold risk of cervical lesion progression, but *T. vaginalis* infection without co-infection with *Gardnerella vaginalis* did not significantly affect the risk of lesion persistence or progression.[10]

Three other journals reported non-significant association between *trichomoniasis* and cervical cancer in statistical analysis. Study by Ghosh *et al.*, 2017 reported that HPV coinfection with *T. vaginalis* did not significantly affect CIN. Invasive cancer risk was higher in women who were co-infected with HPV and *T. vaginalis* than in those who were not, although there was no statistically significance difference. The prevalence of *trichomoniasis* was higher in the group with pre-invasive lesions than in the group with normal cytology or invasive lesions. However the difference was not statistically significant. Study by Tompkins *et al.*, 2020 reported that statistical analysis showed insignificant results between *T. vaginalis* and cervical abnormalities.[18]

The correlation between the prevalence of *trichomoniasis* and the severity *grade* of cervical cancer appears to be variable. The prevalence of *trichomoniasis* was higher in the group with pre-invasive lesions than in the group with normal cytology or invasive lesions, according to a study by Gupta *et al.*, 2020, however the difference was not statistically significant. Study by Yang *et al.*, 2020 reported that co-infection of *T. vaginalis* with hrHPV increased the risk of CIN 1, but did not increase the risk of CIN 2-3. There are no journals that can explain the cause of the higher prevalence of *trichomoniasis* in lower grade cancer. According to a 2017 study by Ghosh *et al.*, the prevalence of *trichomoniasis* in cervical cancer was greater than CIN, which was 87.7%. The prevalence of *trichomoniasis* in patients with the higher grade of cervical lesions can be caused by secondary infection due to tumor necrosis.

Differences in the correlation of *trichomoniasis* and cervical cancer may be influenced by the study design used in the study being reviewed. Most of the research reviewed is not a longitudinal study with a long observation period, so the data displayed is data in a short time, whereas the development of cervical cancer takes a long time (years) until abnormalities appear and can be detected in cells and tissues. Another factor that may influence the difference in results between one study and another is the difference in the number of samples used. The limited number of samples cannot describe the true correlation in the population. Differences in diagnostic tools can also affect research results because the sensitivity and specificity of a diagnostic tool will determine whether a respondent's examination result is positive or negative. Research on the prevalence of *trichomoniasis* in cervical cancer patients is still very limited, so there are only few journals that can be reviewed in this study. Further research with a prospective design regarding *trichomoniasis* in cervical cancer patients needs to be done in the future.

Conclusion

Based on ten articles discussed in this study, the prevalence of *trichomoniasis* in cervical cancer patients was discovered to be the highest in the study by Ghosh *et al.* in Kolkata, India (72.6% women with CIN 1, 71.0% women with CIN 2 or CIN 3, and 87.7% women with invasive cancer) and the lowest in the study by Su *et al.* in Taiwan

(0.022%). The association between *trichomoniasis* and cervical cancer was found to be varied. Some journals report statistically significant analyzes, while other journals report non-significant statistical analysis results.

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Conflicts of Interest

There are no conflicts of interest declared by the author.

References

1. Stebut EV. Leishmaniasis and Other Protozoan Infection. In: Sewon K, Amagai M, Bruckner AL, et al. (eds) *Fitzpatrick's Dermatology in General Medicine*. New York: McGraw-Hill Education, 2019, p. 3243.
2. CDC. Parasites - Neglected Parasitic Infections (NPIs). *Centers for Disease Control and Prevention* 2017; 1.
3. Achdiat PA, Dwiyana RF, Feriza V, et al. Prevalence Of Trichomoniasis In Asymptomatic Pregnant Women Population In Bandung, West Java, Indonesia. *Indones J Trop Infect Dis* 2019; 7: 59.
4. Flagg EW, Meites E, Phillips C, et al. Prevalence of Trichomonas vaginalis Among Civilian, Noninstitutionalized Male and Female Population Aged 14 to 59 Years: United States, 2013 to 2016. *Sex Transm Dis* 2019; 46: 2–3.
5. Van Der Pol B. Trichomonas vaginalis. In: Singh SK (ed) *Diagnostics to Pathogenomics of Sexually Transmitted Infections*. 2018, p. 342.
6. Leitsch D. Recent Advances in the Trichomonas vaginalis Field. *F1000Research* 2016; 5: 2.
7. World Health Organization. Cervical Cancer. 2018; 1. [cited 2021 May 29]. Available from: https://www.who.int/health-topics/cervical-cancer#tab=tab_1
8. Yang, M., Li, L., Jiang, C. *et al.* Co infection with trichomonas vaginalis increases the risk of cervical intraepithelial neoplasia grade 2–3 among HPV16 positive female: a large population-based study. *BMC Infect Dis* 20, 642 (2020). https://doi.org/10.1186/s12879-020-05349-0
9. Belfort, I., Cunha, A., Mendes, F., Galvão-Moreira, L. V., Lemos, R. G., de Lima Costa, L. H., Monteiro, P., Ferreira, M. B., Dos Santos, G., Costa, J. L., de Sá Ferreira, A., Brito, L., Brito, L., Vidal, F., & Monteiro, S. (2021). Trichomonas vaginalis as a risk factor for human papillomavirus: a study with women undergoing cervical cancer screening in a northeast region of Brazil. *BMC women's health*, *21*(1), 174. https://doi.org/10.1186/s12905-021-01320-6
10. Raffone, A., Travaglino, A., Mascolo, M., Carotenuto, C., Guida, M., Mollo, A., Insabato, L., & Zullo, F. (2020). Histopathological characterization of ProMisE molecular groups of endometrial cancer. *Gynecologic oncology*, *157*(1),

252–259.

11. Su, R. Y., Ho, L. J., Yang, H. Y., Chung, C. H., Yang, S. S., Cheng, C. Y., Chien, W. C., & Lin, H. C. (2020). Association between Trichomonas vaginalis infection and cervical lesions: a population-based, nested case-control study in Taiwan. *Parasitology research*, *119*(8), 2649–2657. https://doi.org/10.1007/s00436-020-06759-4

12. Cunha APA, Belfort IKP, Mendes FPB, et al. Human papillomavirus and Its Association with Other Sexually Transmitted Coinfection among Sexually Active Women from the Northeast of Brazil. *Interdiscip Perspect Infect Dis* 2020; 2020: 2.

13. Tompkins EL, Beltran TA, Gelner EJ, et al. Prevalence and risk factors for Trichomonas vaginalis infection among adults in the U.S., 2013–2014. *PLoS One* 2020; 15: 7.

14. Dey S, Pahwa P, Mishra A, et al. Reproductive Tract infections and Premalignant Lesions of Cervix: Evidence from Women Presenting at the Cancer Detection Centre of the Indian Cancer Society, Delhi, 2000–2012. *J Obstet Gynecol India* 2016; 66: 441–451.

15. Kassandra I, Belfort P, Paula A, et al. Trichomonas vaginalis as a risk factor for human papillomavirus : a study with women undergoing cervical cancer screening in a northeast region of Brazil. *BMC Womens Health* 2021; 21: 1–8.

16. Evriarti PR, Yasmon A. Patogenesis Human Papillomavirus (HPV) pada Kanker Serviks. *J Biotek Medisiana Indones* 2019; 8: 23–32.

17. Mukanyangezi, M. F., Sengpiel, V., Manzi, O., Tobin, G., Rulisa, S., Bienvenu, E., & Giglio, D. (2018). Screening for human papillomavirus, cervical cytological abnormalities and associated risk factors in HIV-positive and HIV-negative women in Rwanda. *HIV medicine*, *19*(2), 152–166. https://doi.org/10.1111/hiv.12564

18. Tompkins EL, Beltran TA, Gelner EJ, Farmer AR. Prevalence and risk factors for Trichomonas vaginalis infection among adults in the U.S., 2013-2014. PLoS One. 2020 Jun 16;15(6):e0234704. doi: 10.1371/journal.pone.0234704. PMID: 32544192; PMCID: PMC7297358.