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Does Trichomoniasis Play Any Role in The Pathogenesis of Cervical Carcinoma?

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Summary
Trichomonas vaginalis is the causative agent of trichomoniasis, a common cause of vaginitis. Despite being a readily diagnosed and treatable sexually transmitted disease (STD), trichomoniasis is not a reportable infection and its control has received relatively little emphasis from public health STD control programs. *It* is one of the most common non-viral sexually transmitted infections worldwide. It is associated with potentially serious complications such as preterm birth and human immunodeficiency virus acquisition and transmission. Even though several studies have demonstrated the correlation between cervical cancer and trichomonas vaginalis, the pathophysiology of this relationship is still ambiguous. This review was carried out to determine the relationship between Trichomoniasis and cervical cancer.

Key: *Sexually transmitted infection, Trichomonas vaginalis, Human papillomavirus, Co-infection, Trichomonas vaginalis and cervical cancer.*

Introduction

Trichomoniasis is the most common parasitic sexually transmitted infection (STI), caused by a flagellated protozoon Trichomonas vaginalis (Sulyman and Kadir 2021). It is responsible for 143 million cases in 2012 and 110.4 million in 2018 (Organization 2018). It has only trophozoite stage; there is no cyst stage. Trophozoite has two forms: flagellated trophozoite (the infective as well as the diagnostic form) and the amoeboid trophozoite (the actively replicating form, found in the tissue feeding stage of the life cycle) (Dias-Lopes, Saboia-Vahia *et al*., 2017). T. vaginalis infections are commonly associated with other sexually transmitted diseases (STDs) and are a marker of high-risk sexual behavior (Cavallari, Ceccarelli *et al*., 2021). Unlike other STDs, which have a higher prevalence among adolescents and young adults, the rates of trichomoniasis are more evenly distributed among sexually active women of all age groups, probably as a result of a lack of an organized disease control effort for this infection (Patel *et al.,* 2018). Several studies have demonstrated the fact that at least 80% of T. vaginalis infections are asymptomatic (Lewis, Spicknall *et al.,* 2021). The asymptomatic nature of this infection tends to pose very serious public health concern. In addition to the risk of transmission to sex partners, T. vaginalis infection has been associated with as much as a 2.7-fold increase in the risk of HIV acquisition (McClelland, Sangaré *et al.,* 2007, Seña, Goldstein *et al.,* 2021). Epidemiological studies have shown that T. vaginalis infection can lead to an increased risk of cervical cancer (Lazenby, Taylor *et al.,* 2014, Kovachev, 2020).

The Parasite

Trichomonas vaginalis is a parasitic pear-shaped protozoan, with an average size of 10 × 7 μm. It has four free flagella and one recurrent flagellum, along the outer margin of the undulating membrane; a costa at the base of the undulating membrane; and an axostyle extending through the cell (Honigberg and King, 1964). T. vaginalis lacks mitochondria and instead uses the hydrogenosome to accomplish

fermentative carbohydrate metabolism, with hydrogen as the electron acceptor. The hydrogenosome appears to have a common ancestry with mitochondria based on similarities in protein import (Dyall and Johnson, 2000).

Methodology

For the conduct of this present review, online databases including Web of Science, PubMed, SCOPUS and Google Scholar were searched for articles published in the last ten years. Search keywords used included: Sexually transmitted infection, Trichomonas vaginalis, Human papillomavirus, Co-infection, Trichomonas vaginalis and cervical cancer. The PRISMA guide for publication is shown in figure 1. After the initial search, 1163 articles were identified which were deduplicated leaving a total of 189 articles for eligibility screening. Abstract screening yielded 40 eligible articles and following full text assessment, some articles were excluded leaving 26 articles, to which four articles were added due to additional information giving a total of 30 articles included in the analysis.

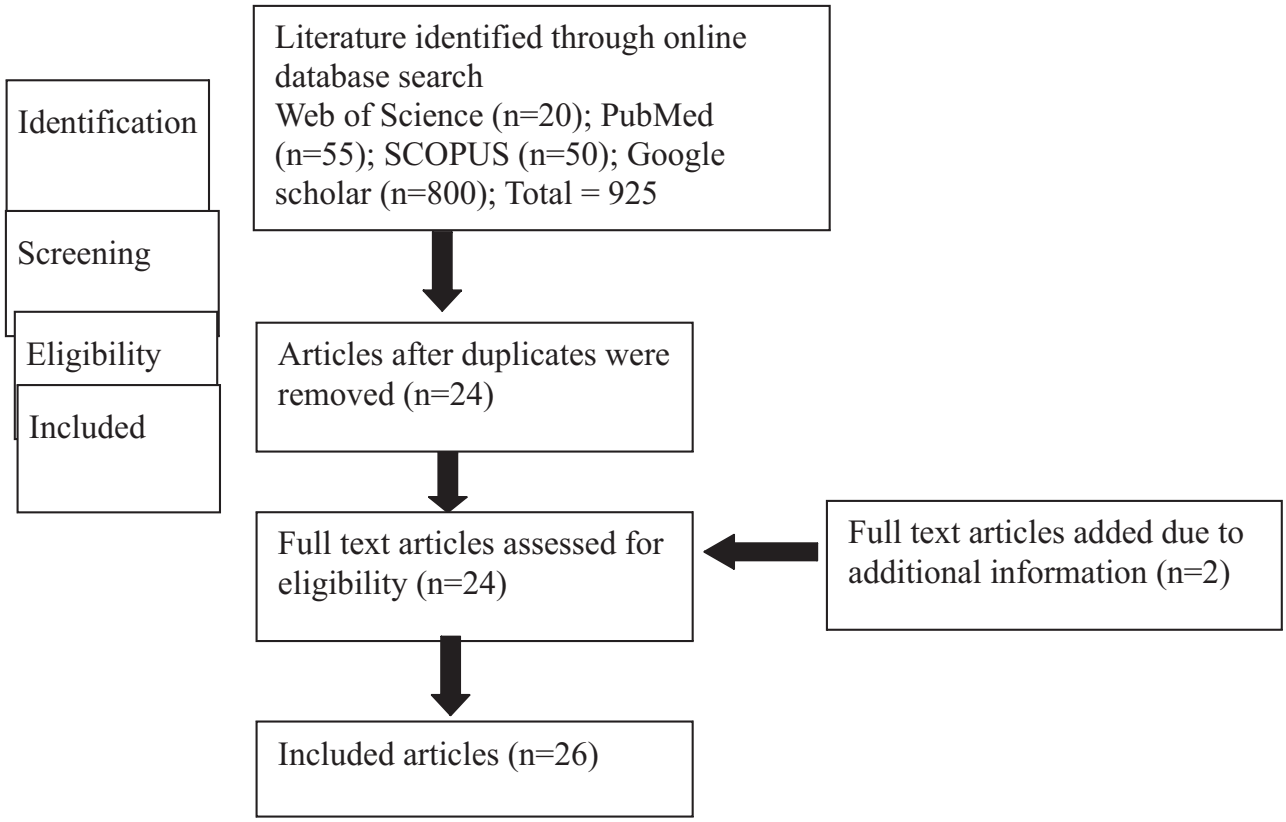

Fig. 1: Process of selection of publications (PRISMA guide) used for the review

Trichomonas vaginalis infection and the risk of cervical carcinoma

Cervical cancer is one of the most common malignant diseases worldwide (Small Jr, *et al*., 2017). It has been suggested that the aetiological agent/s are genital pathogens, probably acting synergistically. Cervical cancer is the fourth most common cancer worldwide and human papillomavirus (HPV) is a major etiological agent during its development (Ault 2006). There are several studies that suggest that some sexually transmitted infections (STIs) such as Chlamydia spp., herpes simplex virus (HSV), trichomonas vaginalis (TV), and bacterial vaginosis (BV) might play important roles in cervical carcinogenesis (Ghosh *et al*., 2017). It is believed that the inflammatory process and modulation of host metabolism caused by TV predisposes the epithelium to carcinogenesis by HPV (Castle and Giuliano 2003; Ghosh, Muwonge *et al.,* 2017; Mercer and Johnson, 2018). The organisms are said to create

microulcerations in the genital mucosa by direct contact, mediated by surface proteins (Zhang *et al.,* 2020).

In women, it is the squamous epithelium of the vagina that is infected (Zhang *et al.,* 2020). Cervical epithelium disruption is due to the inflammation process caused by T. vaginalis, which facilitates the entry of Human Papillomavirus (HPV) into the basal layer of the epithelium. As a result, it leads to the integration of viral DNA into the host DNA and the overexpression of viral oncogenes that contribute to the activation of carcinogenic mechanisms (Mercer and Johnson 2018; Nikas, Hapfelmeier *et al.,* 2018; Belfort, Cunha *et al.,* 2021).

Another study showed that T. vaginalis releases lytic enzymes that reduce the protective mucus layer of the vaginal wall, leading to a reduction in vaginal fluids (Lazenby *et al.,* 2014). This can lead to the development of micro lesions in the epithelium, thereby increasing virulence of the HPV and favoring the integration of the DNA into the host cell, subsequently leading to host cell DNA damage and initiating the process of carcinogenesis (Ghosh *et al.,* 2017). The inflammatory process can also lead to rupture of basal layer of the cervical epithelium and subsequently promote its persistence in the cervical-vaginal epithelium tissue (Mercer and Johnson, 2018).

Persistent infection by viral types of high oncogenic risk, mainly by HPV types 16 and 18, is one of the main factors for the development of cervical cancer. The extent of the inflammatory response to the parasite may determine the severity of the symptoms (Slaughter,2021). Factors that influence the host inflammatory response are not well understood but may include hormonal levels, coexisting vaginal flora, and strain and relative concentration of the organisms present in the vagina (Slaughter, 2021). In one study, it was demonstrated that HPV is a risk factor for TV, suggesting that there is a possible cooperation between both microorganisms, contributing to cellular microenvironment changes (Belfort, Cunha *et al.,* 2021). There are several studies that found an association between T. vaginalis infection, cervicitis, and vaginal infections in the increased risk of squamous intraepithelial lesions and/or cervical intraepithelial neoplasia (CIN) (Noël, Fayt *et al.,* 2010; Menon, Broeck *et al.,* 2016).

The scientific explanation of association between cervical dysplasia and persistent HPV infection in the presence of coinfection with sexually transmitted infections is the changes caused by the inflammation of the cervical epithelium. When this inflammation induced by the sexually transmitted infections disrupt the epithelium, high-risk HPV (HR HPV) can penetrate to the basal layer and alter multiple cell activity (Castle and Giuliano, 2003; Watts, Fazarri *et al.,* 2005; Lu, *et al.,* 2015; Mercer and Johnson, 2018; Nikas *et al.,* 2018). In a study from rural Tanzanian women who presented for cervical cancer screening, Trichomonas vaginitis was significantly associated with high-risk HPV infection (specifically type 16) (Lazenby *et al.,* 2014). It can be deduced that T. vaginalis is merely a surrogate marker of exposure to HPV, which can be influenced by promiscuous sexual behavior. Serological test could be applied to identify women with serum antibodies to TV as being at higher risk of developing cervical cancer. Developing this diagnostic test for testing both serum anti-T. vaginalis as well as E6 and E7 proteins of HPV types 16 and 18 antibodies may reduce the incidence of cervical cancer.

Conclusion

Prevention of HPV infection with vaccines and screening for STDs (including TV) may work together to decrease the high rates of cervical cancer (Campos *et al.,* 2012). Because of associations between HPV co-infections with several sexually transmitted diseases, early diagnosis and treatment of these STIs may also reduce the incidence cervical cancer.

References

Ault, K. A. (2006). "Epidemiology and natural history of human papillomavirus infections in the female genital tract." *Infectious Diseases in Obstetrics and Gynecology*;2006 Suppl:40470. doi: 10.1155/IDOG/2006/40470.

Belfort, I. K. P., A. P. A. Cunha, F. P. B. Mendes,

L. V. Galvão-Moreira, R. G. Lemos, L. H. de Lima Costa, P. Monteiro, M. B. Ferreira, G. R. B. Dos Santos and J. L. Costa (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): 1-8.

Campos, N. G., J. J. Kim, P. E. Castle, J. D. Ortendahl, M. O'Shea, M. Diaz and S. J. Goldie (2012). "Health and economic impact of HPV 16/18 vaccination and cervical cancer screening in Eastern Africa." *International Journal of Cancer*;130(11): 2672-2684.

Castle, P. E. and A. R. Giuliano (2003). "Chapter 4: Genital tract infections, cervical inflammation, and antioxidant nutrients—assessing their roles as human papillomavirus cofactors." *Jnci Monographs*; 2003(31): 29-34.

Cavallari, E. N., G. Ceccarelli and G. D'Ettorre (2021). Sexually Transmitted Infections and Risk Behaviors in the Adolescence. *Pediatric and Adolescent Andrology*: 201-212.

Dias-Lopes, G., L. Saboia-Vahia, E. T. Margotti, N. d. S. Fernandes, C. L. d. F. Castro, F.O. Oliveira, J. F. Peixoto, C. Britto, F. C. Silva and P. Cuervo (2017). "Morphologic study of the effect of iron on pseudocyst formation in Trichomonas vaginalis and its interaction with human epithelial cells." *Memórias do Instituto Oswaldo Cruz;* 112: 664-673.

Dyall, S. D. and P. J. Johnson (2000). "Origins of hydrogenosomes and mitochondria: evolution and organelle biogenesis." *Current Opinion in Microbiology; 3(4)*: 404-411.

Ghosh, I., R. Muwonge, S. Mittal, D. Banerjee, P. Kundu, R. Mandal, J. Biswas and P. Basu (2017). "Association between high-risk human papillomavirus infection and co-infection with Candida spp. and Trichomonas vaginalis in women with cervical premalignant and malignant lesions." *Journal of Clinical Virology ;87*: 43-48.

Honigberg, B. and V. King (1964). "Structure of Trichomonas vaginalis Donne." *The Journal of Parasitology*: 345-364.

Kovachev, S.M. (2020). "Cervical cancer and vaginal microbiota changes." Archives of Microbiology; 202(2): 323-327.

Lazenby, G. B., P. T. Taylor, B. S. Badman, E. Mchaki, J. E. Korte, D. E. Soper and J. Y. Pierce (2014). "An association between Trichomonas vaginalis and high-risk human papillomavirus in rural Tanzanian women undergoing cervical cancer screening." *Clinical Therapeutics*; 36(1): 38-45.

Lewis, F. M., Spicknall, I. H., Flagg, E. W., Papp, J. R. and Kreisel, K. M. (2021). "Incidence and Prevalence of Trichomonas vaginalis Infection Among Persons Aged 15 to 59 Years: United States, 2018." *Sexually Transmitted Diseases;* 48(4): 232-237.

Lu, H., Jiang, P.C., Zhang, X.D., Hou, W.J., Wei, Z.H., Lu, J.Q., Zhang, H., Xu, G.X., Chen, Y.P. and Ren, Y. (2015). "Characteristics of bacterial vaginosis infection in cervical lesions with high-risk human papillomavirus infection." International *Journal of Clinical and Experimental Medicine*;8(11): 21080.

McClelland, R. S., Sangaré, L., Hassan, W. M., Lavreys, L., Mandaliya, K., Kiarie, J., Ndinya-Achola, J., Jaoko, W. and Baeten, J. M. (2007). "Infection with Trichomonas vaginalis increases the risk of HIV-1 acquisition." *The Journal of Infectious Diseases;195(5)*: 698-702.

Menon, S., Broeck, D. V., Rossi, R., Ogbe, E., Harmon, S. and Mabeya, H. (2016)."Associations between vaginal infections and potential high-risk and high-risk human papillomavirus genotypes in female sex workers in western Kenya." *Clinical Therapeutics ;38(12)*: 2567-2577.

Mercer, F. and Johnson, P. J. (2018). "Trichomonas vaginalis: pathogenesis, symbiont interactions, and host cell immune responses." *Trends in Parasitology*; 34(8): 683-693.

Nikas, I., Hapfelmeier, A., Mollenhauer, M., Angermeier, D., Bettstetter, M., Götz, R., Schmidmayr, M. Seifert-Klauss, V., Muckenhuber, A. and Schenck, U. (2018). "Integrated morphologic and molecular analysis of Trichomonas vaginalis, Mycoplasma hominis, and human papillomavirus using cytologic smear

preparations." *Parasitology Research;117(5)*: 1443-1451.

Noël, J.C., Fayt, I., Munoz, M.R.R., Simon P. and Engohan-Aloghe, C. (2010). "High prevalence of high-risk human papillomavirus infection among women with Trichomonas vaginalis infection on monolayer cytology." *Archives of Gynecology and Obstetrics; 282(5)*: 503-505.

Organization, W. H. (2018). "Report on global sexually transmitted infection surveillance 2018."

Patel, E. U., Gaydos, C. A., Packman, Z. R., Quinn T. C. and Tobian, A.A. (2018). "Prevalence and correlates of Trichomonas vaginalis infection among men and women in the United States." *Clinical Infectious Diseases; 67(2)*: 211-217.

Seña, A. C., Goldstein, L.A., Ramirez, G., Parish, A. J. and McClelland, R.S. (2021). "Bacterial Vaginosis and Its Association with Incident Trichomonas vaginalis Infections: A Systematic Review and Meta-Analysis." *Sexually Transmitted Diseases;48(12)*: e192-e201.

Slaughter, C. (2021). "Trichomonas vaginalis Induced Toll-like Receptor Gene Expression in Cervical Epithelial Cells." Office of Undergraduate Research – SURF, 2021.

Small Jr, W., Bacon, M. A., Bajaj, A., Chuang, L.T., Fisher, B.J., Harkenrider, M.M., Jhingran, A., Kitchener, H.C., Mileshkin, L.R. and Viswanathan, A.N. (2017). "Cervical cancer: a global health crisis." *Cancer; 123(13)*: 2404-2412.

Sulyman, M.E. and Kadir, M. A. (2021). "Detection and Comparison of Size of Trichomonas Vaginalis In Direct Smear and Culture Media." *World Bulletin of Public Health*; 3: 4-8.

Watts, D.H., Fazarri, M., Minkoff, H., Hillier, S. L., Sha, B., Glesby, M., Levine, A.M., Burk, R. Palefsky, J.M. and Moxley, M. (2005). "Effects of bacterial vaginosis and other genital infections on the natural history of human papillomavirus infection in HIV-1–infected and high-risk HIV-1–uninfected women." *The Journal of Infectious Diseases;191(7)*: 1129-1139.

Zhang, Z., Li, Y., Wang, S., Hao, L., Zhu, V., Li, H., Song, X., Duan, Y., Sang, Y. and Wu, P. (2020). "The Molecular Characterization and Immunity Identification of Trichomonas vaginalis Adhesion Protein 33 (AP33)." *Frontiers in Microbiology; 11*: 1433.

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