

Association between *Trichomonas vaginalis* and other pathogens

Hiba Riyadh Al-Abodi*

Department of Environment, College of Science, University of Al-Qadisiyah, Al Diwaniyah, Iraq

***Correspondence:**

Hiba Riyadh Al-Abodi,
hiba.al-abodi@qu.edu.iq

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There are many pathogens in the reproductive system in both women and men, which are largely responsible for the death of thousands of women as a result of incorrect diagnosis and failure to treat diseases of the reproductive system such as uterine cancer, ectopic pregnancy, acute and chronic infections of the uterus and Fallopian tubes, puerperal infections, and in the event that the patient survived death. These diseases have bad effects, including infertility, miscarriage, fetal death, birth of low-weight fetuses, fetal blindness, pneumonia, and mental retardation. These diseases are transmitted through the mucous membranes during vaginal, anal, or oral intercourse with a person who is infected or passed from mother to fetus. Wrong sexual behaviors also lead to the acquisition of genital infections. The incidence of reproductive system diseases in women is 50%, especially at an early age, compared to 25% for men, and affects them more severely. According to studies, two-thirds of cases of sexually transmitted diseases are obtained in their teens or twenties. There is limited access to health care for women infected with these diseases in developing countries, as health care is often provided in these countries through a range of services for individuals, family planning clinics, reproductive health centers, and public hospitals. However, in developing countries, untrained people provide treatment without accurate diagnosis of the disease, which increases the exacerbation of sexually transmitted diseases, whereas the situation is much better in developed countries.

Keywords: *Trichomonas vaginalis*, *Lactobacillus*, phenomenon-parasitism, STIs, pregnancy

Introduction

Micro flora of the vagina

The female genital epithelium is a complex system of bacterial colonies that are difficult to understand, highly dynamic, and clinically delusional to clinicians. These colonies are called endogenous bacterial microorganisms, and they prevent the entry of exogenous bacterial species into the vagina. These organisms are found in the vagina and cervix, where they require warmth, food, moisture, pH, and proper protection. The vaginal flora are defined as a wide range of facultatively parasitizing organisms such as *Gardnerella vaginalis*, *Mycoplasma hominis*, *Peptostreptococcus*, *Fusobacterium*, and *Lactobacillus* (1).

Lactobacillus sp. spores account for 75% of the germs in the vaginal flora. The vagina and cervix differ anatomically and physiologically. The vagina in women is acidic, ranging from 3.8 to 4.2 pH at the age of childbearing in the presence of estrogen and progesterone, and it is believed that this acidity results from breaking down of glycogen; the glycogen gene present in the vaginal mucosa is converted to lactic acid by *Lactobacillus* sp. (2). Estrogen controls the vaginal flora indirectly, increasing the amount of glycogen in the epithelial cells lining the vagina. The pH value of the vagina increases during the menstrual cycle and ranges from 4.6 to 6.5. This is because menstrual blood is highly alkaline, and this was proven by a study on women with regular menstruation who do not take any medical drugs related to hormones and were at the beginning of their first menstruation until the pre-menopause (3, 4). There are other types of vaginal

bacteria that produce hydrogen peroxide, such as *Gardnerella vaginalis*, *Mycoplasma hominis*, *Ureaplasma urealyticum*, and anaerobes such as *Prevotella*, *Mobiluncus*, and *Bacteroides*, which contribute to keeping the pH low to about 4.5 with the help of *Lactobacillus*, which leads to protecting the vagina from harmful germs. If the pH rises more than 4.5, the vagina becomes more vulnerable to bacterial vaginosis B, human papillomavirus, herpes simplex type 2, *Trichomonas vaginalis*, Neisseria gonorrhoeae, and HIV (1).

The environmental conditions of the cervix are quite different from those of the vagina. Endocervix is more alkaline compared to the vagina, approximately pH 7.8, and therefore the cervical flora contains less acidogenic bacteria than the vagina (2). It is also believed that the cylindrical epithelial cells of the inner part of the cervix, which are different from the squamous or squamous epithelium lining the neck and vagina, greatly contribute to their bacterial adherence, and this may affect the quantitative and qualitative colonies (2). Genetics also has an important role in determining the quality of the internal microflora of the vagina and cervix. It was found that women of black race are less resistant to bacteria than women of white race due to the presence of a greater number of *Lactobacillus* bacteria that produce hydrogen peroxide (2).

According to the Central of Diseases Control, the increase in bacterial growth is a normal phenomenon in the vagina, but occurs in small numbers and becomes pathological in the absence or decline of *Lactobacillus* colonies. The importance of these bacteria is as follows:

- *Lactobacillus* bacteria produce lactic acid from glucose metabolism.
- Lactic acid keeps the pH of the vagina low and thus limits the growth of other types of bacteria.
- When *Lactobacillus* colonies decline or disappear, harmful bacteria overgrow.
- *Lactobacillus* bacteria also produce hydrogen peroxide, which also maintains a low pH level and is considered a natural microbicide as it is toxic to viruses such as HIV.
- Hydrogen peroxide has the ability to kill HIV in the laboratory (1).

Phenomenon-Parasitism:

Parasitism is defined as a dynamic system between a host and a parasite with several strengths and weaknesses, which makes it difficult to predict the maximum limits of benefit and harm because they are unclear and unstable for both; the definitions of coexistence and exchange become meaningless because the concept of parasitism may include commensalism, mutualism, and symbiosis (5). In 1879, Luckert defined a parasite as a live plant or animal organism that spends all or part of its existence inside or on top of another organism, where it finds shelter and sustenance. Many of them are considered harmful, some are necessary for the host, and some have the ability to survive outside the host's body (6).

Parasitic infection and parasitic disease are two strikingly distinct conditions that arose from a single process, parasitism, where the parasite is a necessary but not sufficient condition to cause a parasitic disease, as certain conditions must be met in the parasite and the host to trigger the pathology. Parasites reduce the body's immunity in several ways to be able to remain in the host's body. So, the parasite can kill its host and the parasite-host relationship can remain constant so that the parasite reduces the production of members of its species and reaches a state of equilibrium with its host, which leads to the parasites remaining for a long time in the host, and this process resulted in the production of vector species responsible for the transmission of important diseases from humans to animals and insects, respectively (6).

Trichomonas vaginalis

This parasite causes what is known as trichomonosis, a urinary tract infection that affects men and women at different ages. The infection differs in whether or not it is associated with symptoms. The most important symptoms are foul odor, itching, intercourse pain, dysuria, and vaginal swelling. Trichomoniasis is of great importance as it is linked to many dangerous diseases such as AIDS, cancer, or other reproductive system diseases, as well as many complications during pregnancy (7). There is sufficient information on the host's immunity to *Trichomonas vaginalis* despite the presence of antibodies in patients' vaginal secretions, which is an immune reaction recently detected by Alderete et al. (8).

***Trichomonas vaginalis* colonization**

Trichomonas vaginalis invades the epithelial cells of the urogenital ducts and settles in women in the lower genital tract, the common genitourinary tract, and the prostate in men; man is the only known host for it (9). The presence of *Trichomonas vaginalis* in the rectum has been reported by 5% of people who reported their use of anal sex, and it may be found in the mouth due to oral sex, but there is no evidence of oral infections due to *Trichomonas vaginalis* (10). *Trichomonas vaginalis* was isolated from 72% of men whose women were infected with *Trichomonas vaginalis*, and urine and semen samples were taken. Examination of semen in addition to urine increases the detection rate of *Trichomonas vaginalis* in men by 16% (11).

Sexually transmitted infections are the second most common cause of death after pregnancy and childbirth in young women in developing countries. The World Health Organization has stated that more than 340 million people worldwide suffer from these diseases annually due to several factors, including Neisseria gonorrhoeae, Candida albicans,

Chlamydia trachomatis, and *Trichomonas vaginalis*, which constitute half of the sexually transmitted diseases and affect public health (Monteon et al., 2013). *Trichomonas vaginalis* is the causative agent of what is known as Trichomoniasis and is considered the most common non-viral sexually transmitted disease around the world (Menezes et al., 2016, 12).

The presence of *Trichomonas vaginalis* in pregnant women has a great relationship with the premature birth of fetuses with low weight and size and the occurrence of inflammation in the pregnancy membrane. Recent studies have confirmed that the *Trichomonas vaginalis* parasite is a catalyst for HIV transmission, and it also increases the chance of cervical cancer. In women's and men's prostates (13), 50% of cases infected with *Trichomonas vaginalis* are without symptoms, but women show a higher sensitivity than men with symptoms of unpleasant odor, itching, pain during intercourse, and sometimes dysuria (14). Red color in the vagina around the neck is accompanied by the appearance of some types of fungi (15).

Pathogenesis of *Trichomonas vaginalis*

The mechanism of pathogenesis has not yet been well elucidated, and this is due to the lack of a good animal model, in which the parasite behaves similarly to its behavior in humans in terms of transmission, parasitism, immune response, treatment, and vaccine development. However, the interaction of the parasite with the flora of the vagina is one of the most important factors of the disease, and the parasite, like the rest of the monocytes, shows a great ability to evade the body's immune defenses (16). It is cell detaching factors with a structure similar to trypsin, whose effectiveness depends on the pH, where a value higher than 5 is preferred, and this rise during infection increases the pathogenicity as a result of increased production of parasites and thus more enzymes (17).

It was also found that after an acute infection with *Trichomonas vaginalis*, these parasites secrete a special type of protein like excretory-secretory product similar to the exocrine secretions of cells, which has an effect on white blood cells, especially neutrophils that secrete interleukin IL-8 (Min, 2006). Laboratory studies confirmed that the parasite *Trichomonas vaginalis* has a detrimental effect on *Lactobacillus acidophilus* by several mechanisms, including its phagocytosis of acid-loving milk bacilli, and it is believed that the enzyme released by the parasite destroys these bacilli (18).

Sharing between *Trichomonas vaginalis* and other pathogens:

Frequent infections during a woman's life are often the result of a bacterial imbalance between microorganisms present in the vagina (19).

Cancer and *Trichomonas vaginalis*

Scientists believe that there is a significant relationship between *Trichomonas vaginalis* and cervical cancer in women or prostate cancer in men. It was found that the antibodies to *Trichomonas vaginalis* are somehow related to prostate cancer. It is believed that inflammation within the prostate is a catalyst factor later on for the occurrence of cancer. Infection with the parasite in men aged 15–40 years is often without symptoms, and there is a relationship between infection with *Trichomonas vaginalis* at an early age, a high percentage of antibodies, and the presence of chronic non-accidental infections, which if left untreated will reach the prostate and cause cancer (20–22).

Trichomonas vaginalis parasite and fungi

Studies have confirmed that the parasite *Trichomonas vaginalis* phagocytosis germs and cells, including epithelial cells, leukocytes, erythrocytes, and *Saccharomyces cerevisiae* present in the vagina (23). There is a close relationship between the parasite and fungi, especially *Candida albicans*, which are present in small numbers in the vagina in a non-pathogenic manner. However, the change in pH value leads to the multiplication of these fungi greatly, and thus the pH reaches nearly 6, which is the appropriate degree for the growth of most types of vaginal bacteria (24).

Trichomonas vaginalis and HIV

Many studies have confirmed the existence of a close relationship between the *Trichomonas vaginalis* parasite and the AIDS virus or HIV (25, 26). A 2015 study demonstrated that the risk of HIV infection is increased by the presence of a parasite.

Trichomonas vaginalis is due to the following three reasons (9):

1. The inflammatory response caused by *Trichomonas vaginalis* increases the appearance of target cells of the AIDS virus.
2. Infection with *Trichomonas vaginalis* weakens the mechanical barrier in HIV infection through mucosal hemorrhage.
3. Infection with *Trichomonas vaginalis* changes the vaginal flora and makes it more suitable for harmful germs, which increases the chance of acquiring HIV.

Several other studies conducted on AIDS-positive and HIV + /TV + -positive patients showed that in a society where the percentage of people infected with *Trichomonas vaginalis* is high, it was found that 20% of HIV patients are attributable to *Trichomonas vaginalis*, and 6.2% of all

HIV cases in women in the United States of America can be attributed to *Trichomonas vaginalis* (9). Studies in Africa indicated that infection with *Trichomonas vaginalis* increases the chance of transmission of the virus by about two to threefold, especially in African Americans. Infection with the parasite stimulates an inflammatory immune response, and this leads to the infiltration of a large number of leukocytes, including HIV target cells such as CD4 + - bearing T-helpers, lymphocytes, and macrophages (27).

In an HIV-negative person, these immune cells are infiltrated by the action of the *Trichomonas vaginalis* parasite, which increases and enlarges the gate of entry for the AIDS virus by increasing the number of target cells for the virus, and it facilitates the arrival of the virus directly into the bloodstream. In a person infected with HIV, inflammation and bleeding increase the level of fluid in the body, resulting in more virus-laden cells and more virus-infected lymphocytes, which are abundant in the inflammatory area. There is an increase in the number of free viruses and leukocytes carrying the virus, thus increasing the chance of transmitting them to an uninfected partner (28).

In addition, this parasite has the ability to break down a compound secreted by leukocytes called leukocyte protease inhibitor that hides target cells from the HIV, and this phenomenon may enhance virus transmission. Because most patients with *Trichomonas vaginalis* do not develop symptoms, it is likely that infected individuals will remain sexually active (28). The damage caused by *Trichomonas vaginalis* facilitates the entry of the AIDS virus into the body, and during the outbreak of the virus in the body, the cells of *Trichomonas vaginalis* capture the virus endocytosis and facilitate its transmission to another host, so that the virus is released 2–6 days after the parasite enters the host either after the parasite's death or the parasites are released through the recycling route of the endocytic pathway, and this is evidence that the virus has the ability to replicate within *Trichomonas vaginalis*.

Pregnancy and *Trichomonas vaginalis*

Pregnancy is a special physiological phenomenon that a woman's body goes through, in which significant hormonal changes occur and the body becomes more sensitive and susceptible to diseases, especially in the genital area. Infection with *Trichomonas vaginalis* during pregnancy is a major problem that may lead to premature birth of low-weight and small fetuses, inflammation of the membrane of pregnancy, and conjunctivitis in premature infants in a state of natural birth (29).

Studies have indicated that the incidence of vaginal infections during pregnancy has a relationship with the gestational age. In other words, the incidence increases with an increase in the stage of pregnancy. Vaginal infections are more common in the second half of pregnancy than in

the first half, and this may be due to the increase in the percentage of secretions and difficulty in movement and, therefore, a lower personal hygiene ratio (30, 31). Although infection with *Trichomonas vaginalis* during pregnancy is common, recent studies have confirmed that the fetus born naturally to a mother infected with *Trichomonas vaginalis* may develop genital infections. *Trichomonas vaginalis* was isolated from the bronchi of fetuses < 3 weeks old and from genitourinary methods as well. The fetus is highly susceptible to eye infections (30, 32).

Author contributions

The author confirms being the sole contributor of this work and has approved it for publication.

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