

Assessments of microbial infections via cytopathological examinations in transgender people

Abstract

The oncotic cytology smear test created by George Papanicolaou is a valuable method for early diagnosis of diseases such as cervical cancer and other genitourinary tract infections. Currently, the preventive exam is periodically indicated for all women who have already had an active sexual life. In this context, transgender individuals, who do not identify with the sex assigned at birth, in addition to facing challenges of social acceptance, find it difficult to access preventive exams, such as the Pap smear. In addition, there is a lack of data and literature regarding the results and diagnoses based on the cytological evaluation of this population. Therefore, this review seeks to identify the main findings and diagnoses found in colpo-cytopathological smears of trans men, possible vulvovaginal infections (e.g. Human Papillomavirus (HPV) as well as the particularities of the results obtained, and also considering the social aspects of this portion of individuals.

Keywords: cytopathological examination, infections, epidemiology, public health, trans health, vaccination

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Introduction

Oncotic cytology smear, created in 1941 by George Papanicolaou, has established itself as a valuable method for the early diagnosis of cervical cancer and other genitourinary tract infections. Currently, the preventive exam is indicated for all women aged between 25 and 64 years who have already had an active sexual life and should be performed every 3 years after 2 consecutive years of results without abnormalities. In Brazil, this test is available free of charge by the Unified Health System (SUS) (Ministry of Health, 2022).

According to the current Brazilian Legislation, it is provided that health is a right for all and a duty of the State. However, it is possible to identify that this system faces structural flaws and that not all individuals always have access to quality health. In the case of transgender people, the lack of health care and monitoring is aggravated, since 33% of this population avoids routine health care due to persistent discrimination and disrespect.¹ In this regard, a trans man is one who at birth has a female biological sex but identifies as a man. In many cases, these men adhere to testosterone hormone therapy, promoting the development of physically masculine characteristics. However, this type of therapy can interfere with laboratory test results, as in the case of Papanicolaou smears, and occasionally lead to false diagnoses of dysplasias. According to the study published by Chiang and Shumer,² these false diagnoses mostly occur in the context of HIV-positive tests. Various cytological alterations, such as small parabasal cells and transitional cell metaplasia, can be mistaken for dysplasia in transgender men. However, these changes are representative of atrophy due to testosterone use.²

A relevant concern about the health of trans men is related to the factors that would influence, both positively and negatively, the predisposition to cervical cancer and how it would be possible to deal with this issue, taking into account the particularities involved in this process, such as the use of hormone therapy with testosterone and the difficulty of access to public health services. It is a right of all children and adolescents to access vaccination against the HPV virus, but when we relate it to the fact that a percentage of these young people are trans people, who use hormone therapy, it is necessary to think about the possible reactions and effects that immunization against such a virus can cause to the body that uses hormone therapy. It is essential to carry out further studies in this regard.³

It is essential to highlight the fact that the trans community has a low life expectancy, and greater health risks, as a result of bullying, rejection, substance abuse, body modifications without medical guidance and monitoring, depression, anxiety, and suicide, among other factors. All of this exemplifies why the health and safety of this population has become a public health problem in Brazil.¹ Therefore, this review aims to identify the main findings and diagnoses found in Papanicolaou smears of trans men, as well as the particularities of the results obtained, and also consider the social aspects of these groups of individuals.

Methodology

This is a narrative review of the literature on microbiological findings in cytopathological tests of trans men. The search was carried out using the PubMed and Scielo libraries, in addition to Google Scholar, in search of scientific articles to compose the review, using the keywords: "Papanicolaou smear"; "Infections"; "Epidemiology"; "Public health"; "Trans health"; "Vaccination". The articles that, after reading the title, abstract, and body of the text, were considered As inclusion criteria, only articles with full texts available for free, in Portuguese or English, were considered. Incomplete articles were excluded from the study. In addition, documents from international organizations, such as the World Health Organization (WHO), were consulted.

Discussion

Although there are scarce data and literature that portray the main findings in the Papanicolaou smear results of trans men, this article surveyed studies that portray this theme, and from this, it was possible to identify and list the results that were most frequently obtained in this portion of the population. The literature about cytological findings in preventive exams of trans men describes that in most cases patients highlighted varied conditions of atrophy, due to the use of testosterone therapy, since atrophy is a physiological response resulting from decreased estrogen stimulation, which leads to thinning of the immature cervicovaginal squamous epithelium.⁴ Also according to the same study, transitional cell metaplasia is considered a common finding in cervicovaginal cytology of transgender people undergoing exogenous testosterone therapy, being observed in up to 88.2%. Alterations in the vaginal micro flora of these patients are also

observed, evidencing a decrease in the count of lactobacilli, which are generally dominant structures in the healthy vaginal microflora during the reproductive years. This effect can also be explained and associated with hormone therapy, which decreases estrogen making the vaginal environment less conducive to the proliferation of lactobacilli.⁵

The vaginal microbiota has numerous different microorganisms, which protect the vaginal epithelium against contamination by pathogens. However, it can be affected by several physiological conditions, such as age, menstrual cycle, sexual activity, gestational status, use of contraception and even use of medications, such as hormone therapy, in the case of transgender people. These changes in the vaginal microbiota may be responsible for the emergence of genital infections, which leaves the population of trans men even more exposed to health problems, considering the lifestyle habits that can interfere with their microbiota. Studies show positive results in the use of probiotics for vaginal health, even acting with antifungal properties. These probiotics seem to be a good option to help the vaginal health of the trans population, which is more fragile due to several aspects related to lifestyle habits, even improving their immunity.⁶

The cervicovaginal smear exam allows the identification of possible pathological conditions of the individual, pointing out low- or high-grade lesions, cancers, and microbiological infections.⁷ In this case, the infectious agents that can compromise the gynecological tract are bacteria, fungi, protozoa, and even viruses. Some examples of disease-causing bacteria are coccibacilli of *Gardnerella vaginalis*, *Actinomyces*, *Chlamydia trachomatis* and the filamentous ones called *Leptothrix vaginalis*. Fungi, on the other hand, can be listed mainly of the genus *Candida*, and can be found in the form of pseudohyphae or spores. Also in this context, it is possible to observe protozoa that affect the region, such as Trichomoniasis, caused by the species *Trichomonas vaginalis*, and viral infections are mainly caused by *genital herpes simplex* and the Human Papillomavirus (HPV).⁸ It should be considered that trans men who have a uterus and cervix may be equally affected by these conditions, but face additional challenges in accessing prevention and diagnosis. The invisibility of this population in screening protocols can lead to the underdiagnosis of cervical infections and neoplasms, reinforcing the need for sensitive and welcoming approaches by health professionals. In addition, the use of hormone therapy with testosterone can induce changes in the vaginal mucosa, such as atrophy, which impact the local immune response and increase susceptibility to infections.

On the other hand, *Gardnerella vaginalis* is one of the main etiological agents of bacterial vaginosis, characterized by a decrease in the amount of bacteria that produce lactic acid in the vaginal canal.⁹ Also according to Kavita, the individual with bacterial vaginosis has thin fluids with a foul odor, alkaline vaginal pH, smear with variable Gram, and few Döderlein's lactobacilli. *Actinomyces* bacteria, on the other hand, are anaerobic and filamentous, requiring an anaerobic microenvironment to proliferate.¹⁰ Chlamydiosis, which occurs with the causative agent *Chlamydia trachomatis*, is one of the most common sexually transmitted infections in the world, where the microorganism is obligatorily intracellular, which means that the bacteria lodges in a host cell and if not treated correctly, can cause infertility.¹¹ It is essential to emphasize that trans men who practice sex without barriers or who have vaginal atrophy due to the use of testosterone may have an increased risk for infection since the thinning of the mucosa reduces its ability to protect against pathogens, and therefore they are more exposed to this type of infection.

Another vulvovaginal condition within the context of possible findings in laboratory tests in transgender people is Trichomoniasis, which is caused by the protozoan *Trichomonas vaginalis*. This can present with symptoms of itching, increased secretions, and irritation in the vulvovaginal region, which can lead to urethritis.¹² Additionally, it is possible to observe cases of *Leptothrix vaginalis* often associated

with infections caused by the protozoan *Trichomonas vaginalis*.¹³ In addition, a study by Kissinger¹⁴ shows that the complications of this disease involve infections in the Skene's and Bartholin's glands (responsible for lubricating the genitalia) and even a greater predisposition to contract the Human Immunodeficiency Virus (HIV) since *T. vaginalis* implies an increase in the number of HIV target cells and impairs the mechanical barrier against the virus since protozoa can cause hemorrhages in the region.

Still, under the aspect of microbiological infections, Genital Herpes, caused by the HSV-2 virus, and HPV, caused by the Human Papillomavirus stand out among the Brazilian trans population. HSV-2 enters the individual through lesions of the genital epithelium and the strains reach the nerve ganglia, where they will remain in a state of latency¹⁵ and when symptoms manifest, painful and numerous ulcers can be observed¹⁶ HPV, on the other hand, is an oncogenic viral infection that can be prevented through vaccination.¹⁷ Another study, carried out by Tim¹⁸ followed women born between 1988 and 1996 and concluded that those who were vaccinated between 12 and 13 years of age did not have any record of cervical cancer.

In addition, cervical cancer resulting from the Human Papilloma Virus (HPV) is considered one of the most common neoplasms diagnosed and leading to death in several countries around the world. This type of disease, which refers to a slowly progressing sexually transmitted infection, usually has no signs or symptoms in its initial phase. Its early detection is essential through cytopathological examination, which detects the presence of neoplastic lesions. However, the lack of preparation of health professionals to meet the demands and needs of the trans population, such as the approach and use of inclusive language in the screening process also including structural prejudice, leaves this population even more vulnerable and susceptible to this type of neoplasm. In addition, the fact that performing the Papanicolaou smear triggers gender dysphoria in many cases has been discussed, a factor that prevents many from undergoing the procedures.¹⁷

As an alternative to this fact, many countries have employed the self-collection method, which can make the patient more comfortable performing the test. On the other hand, there is concern about the effectiveness of sample quality. The best option would be to perform the procedure by a professional who has a good relationship with the patient and is qualified to meet the demands of trans men.³ Recent studies reveal that the lack of access to preventive exams, as well as the lack of medical advice, are key factors in the proliferation of bacterial infections in transgender people, which causes damage to the health of the individual and partners.^{19,20} According to Blondeel¹⁹ there is a high number of diseases among specific subpopulations of sexual and gender minorities (SGM), such as HIV and sexually transmitted infections (STIs), mental health conditions, high rates of violence, as well as cancers associated with STIs.

Currently, one of the forms of prevention of cervical cancer in Brazil has been carried out through the vaccination of children and adolescents against the HPV virus, one of the main causative agents of this type of neoplasia. Since 2017, the National Health Surveillance Agency (ANVISA) has authorized the use of three types of HPV vaccine. The immunizer is offered free of charge by the Unified Health System (SUS) for boys from 11 to 14 years old and girls from 09 to 14 years old. In immunosuppressed women, vaccination is allowed up to 45 years of age, with an interval of 6 months between two doses, while for men the maximum limit is up to 26 years of age, even with some type of concomitant immunosuppression (BRAZIL, 2021). However, there are few studies related to HPV vaccination in transgender people. The recommendations of the Ministry of Health are based on the sex assigned at birth, not taking into account the specificities of this group. It should be noted that the transgender population has a high risk of acquiring HPV, which can lead to precursor lesions of cancer.²¹

According to the Joint United Nations Programme on HIV/AIDS (UNAIDS) in 2019,²² the risk of contracting HIV was 13 times higher among trans people than in the rest of the adult population, as access to HIV-related services is more difficult for transgender people than for the rest of the population. The acronym HIV refers to the human immunodeficiency virus, which causes acquired human immunodeficiency syndrome (AIDS) that attacks the immune system, leaving it weakened. Currently, there is still no cure for the disease, but there is a treatment based on antiretroviral drugs, which improves the quality of life and reduces the chances of transmitting the virus (Ministry of Health, 2024). It is known today that there is no harm to hormone therapy for those who use antiretroviral drugs (ART). However, many trans men worry about the drug interaction between PrEP (Pre-Exposure Prophylaxis), PEP (Post-Exposure Prophylaxis), and testosterone therapy, that is, whether these drugs will disrupt the effects of harmonization or vice versa. More research is needed on this issue concerning PrEP and PEP, although it is initially believed that there is no harm to the use of PrEP or PEP and hormone therapy (Ministry of Health, 2024).

Hormone therapy with testosterone used by trans men seeks to guarantee individuals typically masculine physical characteristics such as hair and beard growth, deepening of voice, and muscle gain. People who received hormone therapy reported significant improvements in gender dysphoria, including reduced discomfort with their body and increased satisfaction with their physical appearance, as well as reduced depression and anxiety. Therapy can be given by injection, gel, patch, or subcutaneous implant. The recommended dosage varies according to age, weight, metabolism, and form of administration, which should be supervised by a qualified health professional.²³ However, it is important to note that the use of these medications can cause side effects on health and depend directly on the medication, dosages, and health conditions of the patient, such as water and sodium retention, the development of hypertension, the increase in erythropoiesis, the decrease in high-density lipoprotein, the increase in low-density lipoprotein, the elevation of liver enzymes, acne, mental disorders, and emotional affections.²⁴

In addition, there is concern about the development of endometrial and ovarian cancer, as reproductive tissues can continue to respond to hormonal stimuli, even after menstrual suppression. Therefore, regular medical follow-up is essential to monitor for liver changes and possible signs of malignancy.²⁵ In addition, one of the main challenges faced by many trans men is the fact that most of them still have a uterus and, therefore, can become pregnant. However, there is limited knowledge about the side effects and risks to the health of the pregnant person and the healthy development of the baby associated with the use of testosterone. For those who wish to become pregnant, it is essential to suspend the use of the hormone, as it can cause anomalies in the urogenital development of the female fetus.²⁶

The optimal time to stop using the hormone is debatable. There are no well-established guidelines that determine the optimal interval between testosterone suspension and the beginning of pregnancy. It is not known whether trans male individuals are at higher risk of obstetric complications. However, current fertility counseling for individuals undergoing gender-affirming hormone therapy is generally unclear and consistent. Many people are advised to preserve their fertility before starting therapy or to stop treatment, as there is a prevailing belief that T-therapy leads to infertility.²⁷ On the other hand, there is no evidence of a significant association between the duration of testosterone cessation and the number of mature oocytes or total oocytes in transgender patients undergoing assisted reproductive technology (ART).²⁸

This reality, however, is not homogeneous. While several cities lack specialized services and trained professionals, others demonstrate remarkable advances. The city of Poços de Caldas (Minas Gerais, Brazil), for example, stands out for the creation of the

“Translation Outpatient Clinic”, a multidisciplinary service dedicated to the comprehensive health of transgender people. According to data provided by the municipality of Poços de Caldas,²⁹ a positive impact of this initiative can be detected, with 265 medical consultations, 360 psychotherapy sessions, and 72 consultations with social assistance in one year. In addition, dozens of meetings were held with the network for training and guidance on the rights of the trans population. The partnership with civil society entities, such as the city’s LGBTQIAPN+ Community and the LGBTQIAPN+ Collective, strengthens access to Primary Care, resulting in 36 matrix support in the Family Health Team units, expanding knowledge about the health of this population and strengthening the bond with the community.

Conclusion

Access to health care for the Trans population is still a considerable challenge, marked by gaps in professional training and social prejudice, both in the public and private spheres. Insufficient medical care for transgender individuals highlights a major deficiency in medical care, resulting in lower participation in preventive exams, such as Papanicolaou smears, and greater vulnerability to infections. Also, the lack of specific protocols and the lack of training of health professionals make the early diagnosis of cervical lesions more challenging, increasing the probability of progression to cervical cancer. In addition, guidelines for HPV immunization are based on sex assigned at birth, ignoring the high exposure of the transgender population to the virus and limiting access to vaccination and health services. Besides, hormone therapy affects the vaginal microbiota and cervical epithelium, increasing the risk of infections such as bacterial vaginosis, candidiasis, and trichomoniasis, in addition to influencing the vaginal microbiota and even the fertility of the person. Hence, while the journey towards a more inclusive and equitable health system is ongoing, initiatives such as the “Translation Outpatient Clinic” represent an assertive crucial initiative, offering hope and opportunities for trans people to live with health, dignity, and respect.

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Conflicts of interest

The authors declare that they have no conflicts of interest.

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