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CORRELATION OF *Trichomonas vaginalis* INFECTION AND PROSTATE CANCER: A SYSTEMATIC REVIEW

CORRELAÇÃO DA INFECÇÃO POR *Trichomonas vaginalis* E CÂNCER DE PRÓSTATA: UMA REVISÃO SISTEMÁTICA

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RESUMO

Introdução: A presença de *T. vaginalis* em homens deve ser investigada quanto à sua capacidade de desencadear reações inflamatórias e alterações teciduais capazes de lesar o tecido prostático. **Objetivos:** Avaliar se existe uma correlação entre a infecção por *T. vaginalis* e o risco de desenvolver câncer de próstata por meio de investigação sistemática. **Metodologia:** Estudos originais foram selecionados pelo cruzamento dos descritores em Ciências da Saúde e Termos Livres nas bases de dados PubMed, MEDLINE, LILACS e SCIELO sem limitação por ano de publicação. Artigos que abordavam a correlação entre câncer de próstata e infecção por *T. vaginalis* foram incluídos. Os estudos identificados por meio da busca eletrônica foram triados de forma independente por dois pesquisadores e os artigos em desacordo foram discutidos entre o grupo de pesquisa para inclusão ou exclusão no manuscrito final. **Resultado:** Dos 12 artigos selecionados, cinco (41,66%) indicaram associação entre infecção por *T. vaginalis* e desenvolvimento de tumores malignos de próstata, enquanto sete (58,33%) outros não relataram associação. Gravidade do câncer de próstata e morte foram desfechos associados à infecção por *T. vaginalis*. Entre os estudos que observaram associação, foi indicada relação entre tricomoníase, inflamação e mecanismos que promovem o desenvolvimento e progressão do câncer de próstata. **Conclusão:** Com base no número de artigos, não podemos concluir se há associação entre *T. vaginalis* e câncer de próstata. É importante destacar que muitos desses estudos apresentaram vieses de seleção e metodológicos, indicando a necessidade de mais estudos com grupos populacionais maiores e heterogêneos, além de metodologias diagnósticas mais específicas e sensíveis para *T. vaginalis* e câncer de próstata.
Palavras-chave: Tricomoníase; Protozoário; Câncer de próstata; Carcinogênese.

ABSTRACT

Introduction: The presence of *T. vaginalis* in men should be investigated in terms of its ability to trigger inflammatory reactions and tissue changes capable of damaging the prostatic tissue. **Objective:** To assess whether there is a correlation between *T. vaginalis* infection and the risk of developing prostate cancer through systematic investigation. **Methodology:** Original studies were selected by crossing the descriptors in Health Sciences and Free Terms in the PubMed, MEDLINE, LILACS, and SCIELO databases without limitation by year of publication. Articles that addressed the correlation between prostate cancer and *T. vaginalis* infection were included. The studies identified through the electronic search were independently screened by two researchers and the articles in disagreement were discussed among the research group for inclusion or exclusion in the final manuscript. **Results:** Of the 12 articles selected, five (41.66%) indicated an association between *T. vaginalis* infection and the development of malignant prostate tumors, while seven (58.33%) others seven did not report association. Prostate cancer severity and death were outcomes associated with infection by *T. vaginalis*. Among the studies that observed an association, a relationship was indicated between trichomoniasis, inflammation and mechanisms that promote the development and progression of prostate cancer. **Conclusion:** Based on the number of articles, we cannot conclude whether there is an association between *T. vaginalis* and prostate cancer. It is important to highlight that many of these studies presented selection and methodological biases, indicating the need for further studies with larger and heterogeneous population groups, in addition to more specific and sensitive diagnostic methodologies for *T. vaginalis* and prostate cancer.
Key-words: Trichomoniasis; Protozoan; Prostatic cancer; Carcinogenesis.

INTRODUCTION

The prostate is a male gland that surrounds the urethra, located inferiorly the bladder and anteriorly to the rectum, being responsible for producing an alkaline pH liquid containing enzymes and mineral salts that are added to the semen produced in the testicles[1]. Numerous organic disorders can cause morphophysiological changes in the prostate tissue, which are responsible for several pathologies, including cancer[2,3]. Prostate cancer is clinically heterogeneous and its etiology is still not well understood. However, it is known that there are biological, environmental, and social risk factors, including older age, genetic predisposition, family history, African descent, obesity, and smoking[3]. Prostate cancer is the second most prevalent and the sixth leading cause of cancer death among men. It is estimated that there are currently 1.467.854 cases of prostate cancer in the world and 397.430 deaths were recorded in 2022 alone[4].

Trichomoniasis is the most important non-viral sexually transmitted infection for public health, with approximately 105 million people infected. Its etiologic agent is *Trichomonas vaginalis*, a flagellated protozoan that infects the female and male urogenital apparatus[5]. The prevalence of trichomoniasis between the different regions of Brazil reaches between 10 and 35% of the population and the incidence reaches about two million cases registered every year, especially among the younger sexually active population[6,7]. About 92% of cases of trichotomy are diagnosed in women since approximately 80% of men are asymptomatic[8,9]. Studies indicate an association with infertility, miscarriage, early birth, and the possible development of cervical câncer[10]. In men may occur purulent urethritis, dysuria, hemorrhagic penile, and prostatic lesions occasionally. By ascending route, *T. vaginalis* can reach the bladder, seminal vesicle, testes, and prostate, causing rare complications such as balanoposthitis, cystitis, prostatitis, epididymitis, and even male infertility[1,6,11,12].

Despite the low prevalence in men, the chronicity of the infection due to reinfection, and the absence or inadequate treatment are responsible for important health problems, since *T. vaginalis* can colonize and cause profound anatomical and physiological changes in different organs of the male urogenital apparatus, including prostatic tissue[13]. However, the association between *T. vaginalis* infection and prostate cancer is still controversial. Persistent *T. vaginalis* infection can cause chronic inflammation, and inflammation has been known to be implicated as a significant contributor to the initiation and progression of malignancies, including prostate câncer[14-21].

Thus, the present study, through a systematic review, aims to identify whether there is a correlation between prostate cancer and *T. vaginalis* infection.

METHODS

This is a systematic review article carried out between January and February 2023 whose search for original articles was carried out in the following databases: PubMed (National Library of Medicine), MEDLINE (National Library of Medicine), LILACS (Literatura Latino-Americana e do Caribe em Ciências da Saúde), SCIELO (Scientific Electronic Library Online). To search for articles, we performed crosses between the descriptors in Health Sciences (DECs) and Free Terms (TL), in English and Portuguese. There was no limitation for the year of publication. Search terms and key elements were combined using the Boolean operators (AND, OR, NOT) resulting in the following search algorithms: "*Trichomonas vaginalis*", "male trichomoniasis"; "trichomoniasis", "prostate neoplasm"; "prostatic; "asymptomatic carriers", prostate cancer".

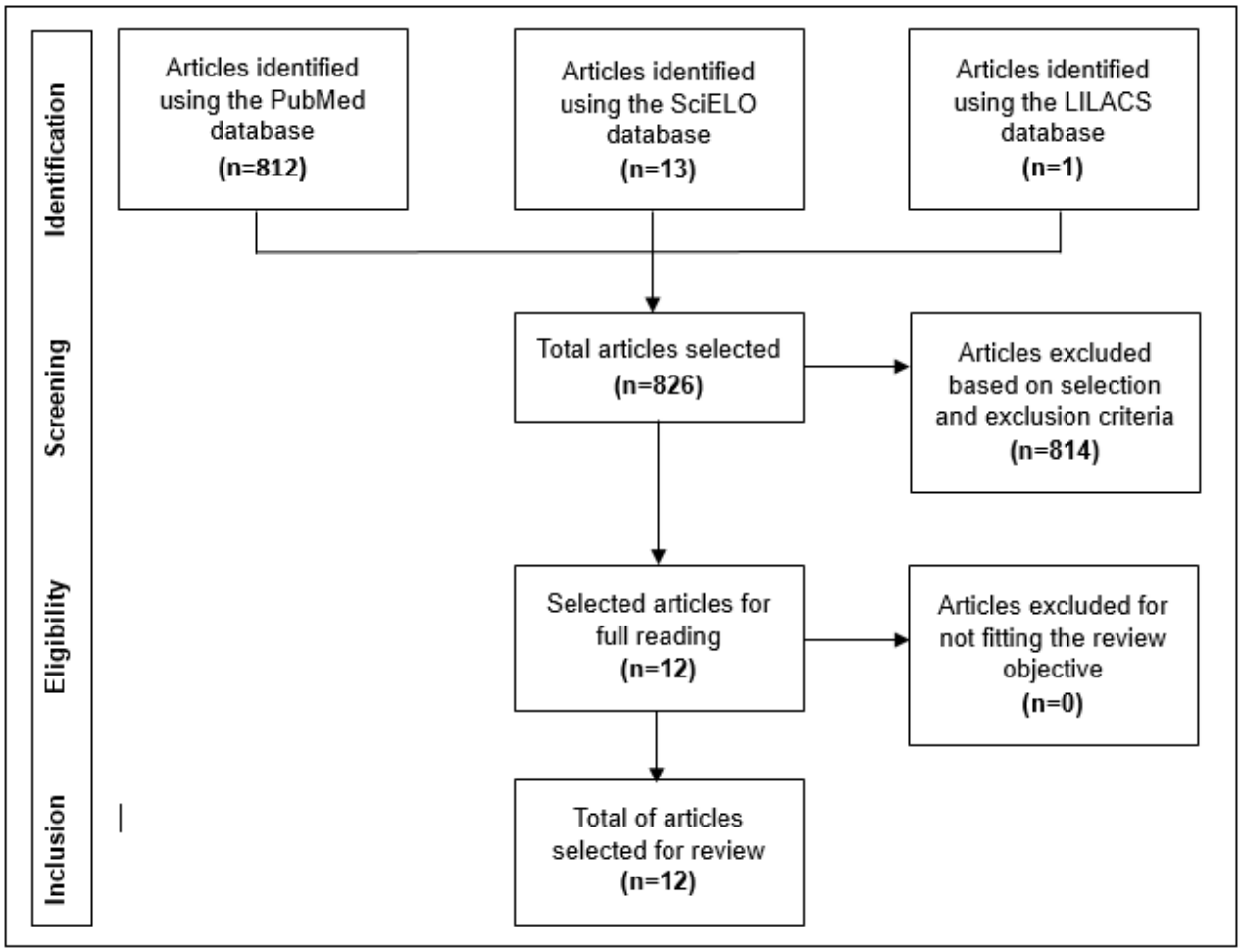
After a complete search of the articles in the databases, the following criteria were applied to meet the objective of the study: (i) exclusion of duplicate and incomplete articles in the different databases, (ii) reading of the title and abstract for the framing of the object of study and (iii) complete critical reading of the article. We hand-searched bibliographies of all recovered articles for potentially eligible studies. Articles that addressed the correlation between prostate cancer and *T. vaginalis* infection were included. The studies identified through the electronic search were independently screened by two researchers and the articles in disagreement were discussed among the research group for inclusion or exclusion in the final manuscript.

RESULT AND DISCUSSION

Figure 1 presents the articles found according to the intersection between the descriptors applied in the searched databases. In total, 826 articles were found and thus distributed according to the database: 812 articles in PUBMED, 13 articles in LILACS, and 1 article in SCIELO. After critically reading the title and abstract of all articles found, 814 did not meet the criteria used. The main causes of exclusion were articles that addressed research related to immunological aspects in trichomoniasis and/or prostate cancer, validation of diagnostic tests, therapeutic interventions, epidemiological studies, in vitro and/or in vivo experimental assays with laboratory cells or animals, and those that

addressed trichomoniasis in women in studies related to HIV/AIDS, female infertility, and cervical cancer.

Figure 1. The number of articles found according to the crossing between Health Sciences Descriptors (DECs) and Free Terms (TL) in the databases.



Thus, only 12 articles were used for this review, all indexed in PUBMED and published between 2006 and 2023 (Table 1). The articles used were cross-sectional case-control, prospective case-control, and a study with secondary data (sample files of prostatic tissue in paraffin). Of the 12 articles, 11 used the Enzyme-Linked Immunosorbent Assay (ELISA) as a test for the detection of *T. vaginalis*, and only one study, carried out by Yow *et al*., used the Polymerase Chain Reaction (PCR) for the parasite DNA extraction[18]. Of the total number of articles, five (41.66%) associated *T. vaginalis* infection with prostate cancer, while the others (seven, 58.33%) reported no association (Table1).

Table 1. Summary of the content of the articles used in this review.

Title	Authors Year /Country [Ref]	Population Number of participants	Objective	Main results	Conclusion. Correlation between TV and PC
Plasma antibodies against *Trichomonas vaginalis* and subsequent risk of prostate cancer.	Sutcliffe 2006/EUA [22]	Male health professionals 1.382	To investigate the relationship between trichomoniasis and incident PC through a nested case-control study.	Thirteen percent of cases and nine percent of controls were seropositive for trichomoniasis (adjusted odds ratio, 1.43; 95% confidence interval, 1.00-2.03).	Serologic evidence of a history of trichomoniasis was positively associated with PC incidence. Yes
Trichomonosis and subsequent risk of prostate cancer in the Prostate Cancer Prevention Trial.	Sutcliffe 2009/EUA [16]	Male ≥55 years of age no evidence of PC at enrollment. 1.232	To investigate the association of Tv infection with PC through a prospective study.	About 21% of cases and 24.8% of controls had low seropositivity, and 15.2% and 15.0% had high seropositivity. Compared to seronegative men, the odds ratio (OR) of PC for men with low seropositivity was 0.83, and that for men with high seropositivity was 0.97.	No association was observed between Tv serostatus and PC. No
Prospective study of *Trichomonas vaginalis* infection and prostate cancer incidence and mortality: Physicians' Health Study.	Stark 2009/EUA [23]	Male physicians aged 40 – 84. 1.346	To investigate the association between Tv serostatus and PC incidence.	Tv seropositivity was not associated with total PC risk or high-grade disease. Serological evidence of Tv infection was associated with a increase in the risk of a diagnosis of advanced-stage PC (OR = 2.17) and in the risk of cancer that would ultimately progress to distant metastases or cancer-specific death (OR = 2.69).	There is an association between Tv serostatus and aggressive PCr. Yes
Prospective study of effect modification by Toll-like receptor 4 variation on the association between *Trichomonas vaginalis* serostatus and prostate cancer.	Chen 2013/EUA [17]	Male ages 40 to 75 years. 1.400	To investigate the effect of modification by TLR4 SNP, rs4986790, on the association between Tv serostatus and PC risk.	A non-significant suggestion of effect modification was observed by rs4986790 carrier status on the association between Tv serostatus and PC risk (p=0.07). No association was observed among men homozygous wildtype for this SNP (OR =1.23). A positive association was observed among variant carriers (OR=4.16).	TLR4 influence the association between serostatus to Tv and PC, the hypothesis that inflammation plays a role in this association. Yes

Detection of infectious organisms in archival prostate cancer tissues.	Yow 2014/ Australia [18]	Histopathologically confirmed tissue blocks for aggressive or non-aggressive PC. 128	To identify the presence of DNA from microorganisms in PC tissues to assess whether PC is associated with common genital infections.	Tv DNA was not detected in any sample of cancerous prostate tissue.	Low prevalence of detectable DNA makes it unlikely that persistent infection by microorganisms contributes to PC risk. No
Trichomonas vaginalis infection and risk of advanced prostate cancer.	Shui 2016/EUA [19]	Male with advanced (metastatic or fatal) PC and age-matched controls. 327	To assess whether Tv serostatus is associated with advanced or fatal PC.	Tv serostatus was not associated with an increased risk of metastatic or fatal PC (ORs<1).	The study does not support an increased risk of advanced or fatal PC in men seropositive for Tv. No
A prospective study of *Trichomonas vaginalis* and prostate cancer risk among African American men.	Fowke 2016/EUA [20]	Male at age 40-79. About 85% of the population was african american. 793	To determine the prospective relationship between Tv infection and PC risk among African American (AA) men.	Mean antibody response levels were similar between cases and controls (all p > 0.05). There was no significant association between Tv and PC in the total study population, or when restricted to AA men.	No evidence of a prospective association between baseline Tv infection and PC risk in AA men. No
Trichomonas vaginalis infection and risk of prostate cancer: associations by disease aggressiveness and race/ethnicity in the PLCO Trial.	Marous 2017/EUA [21]	Caucasian and African American men previously diagnosed with PC. 2.342	To examine possible correlation between Tv and PC, including separate analyses for the aggressive cases and African American men.	No associations were observed for risk of Gleason 7 (odds ratio (OR) = 0.87, 95% confidence interval (CI) 0.55-1.37) or more advanced (OR = 0.90, 95% CI 0.58-1.38) PC in Caucasian men, or for risk of any PC (OR = 1.06, 95% CI 0.67-1.68) in African-American men.	The findings do not support an association between Tv infection and PC. No
Comparison of seropositivity to *Trichomonas vaginalis* between men with prostatic tumor and normal men.	Kim 2019/ South Korea	Male benign prostatic hyperplasia and men with PC. 241	To identify seropositivity to Tv in men with prostate tumors treated at Hanyang University Hospital.	Seropositivity to Tv in patients with prostatic diseases was 19.7% (BPH: 18.7%, PC: 22.7%) and it was significantly higher than the 1.7% of the comparing healthy group (P = 0.001).	The prostatic tumor showed higher seropositivity against Tv than normal men. Yes

	[15]				
Trichomonas vaginalis infection and prostate-specific antigen concentration: Insights into prostate involvement and prostate disease risk.	Langston 2019/EUA [33]	Young male U.S. active duty military members 732	To investigate the relation between Tv antibody serostatus and serum prostate-specific antigen (PSA) concentration	42.5% of men with high seropositive scores Tv had a PSA concentration ≥ 0.70 ng/mL compared to 33.2% of seronegative men. Although slightly larger, no significant differences were found in the distribution of PSA by Tv serostatus.	Not predict prostate involvement during Tv infection, although suggestive of higher PSA concentrations that do not completely exclude this possibility. No
Trichomonas vaginalis serostatus and prostate cancer risk in Egypt: a case-control study.	Saleh 2021/ Egypt [34]	Male at age 40-75, diagnosed with PC and different types of cancers. 445	To investigate if Tv can be a risk factor for PC in Egypt and its possible relationship with cancer prognostic factors and overall survival.	The seropositivity for Tv in control group was 8.3%, compared with 19% of PC patients (P = 0.015). No significant correlations were detected between seropositivity of Tv and other prognostic factors or overall survival in those patients.	Chronic Tv infection may be associated with PC, but it does not seem that this STI aggravates the cancer status. Yes
No Association of *Trichomonas vaginalis* Seropositivity with Advanced Prostate Cancer Risk in the Multiethnic Cohort: A Nested Case-Control Study	Nagata 2023/EUA [35]	Male at age 45-75, with advanced PC. 940	To assess the relationship between Tv seropositivity and advanced PC risk	Seropositivity to Tv was observed in 35 of 470 (7.4%) cases and 26 of 470 (5.5%) controls (unadjusted OR = 1.47, 95% CI 0.82–2.64; adjusted OR = 1.31, 95% CI 0.67–2.53).	The findings do not support a role for Tv in the etiology of advanced PC. No

Tv = *Trichomonas vaginalis,* PC = Prostate cancer, BPH = Benign prostatic hyperplasia, PSA = Prostate Specific Antigens

A cross-sectional case-control study conducted by Sutcliffe *et al*. [22] used prostate cancer-positive cases and controls who had at least one prostate-specific antigen test and who were free of prostate cancer. In this study, serological identification of *T. vaginali*s in cases and controls was performed by ELISA, and these authors identified seropositivity in 13% of cases and 9% of controls. In view of the results, the authors concluded that there was an association between infection by *T. vaginalis* and prostate cancer. In addition, these authors report that this was the first study investigating *T. vaginalis* infection and prostate cancer by serology, highlighting the importance of further studies to confirm this association and of new guidelines for the prevention of prostate cancer, including early diagnosis and treatment for *T. vaginalis*[22]. On the other hand, in 2009, the same research group by Sutcliffe *et al*.,[16] when carrying out a prospective case-control study to evaluate the association of trichomoniasis with prostate cancer, using serological diagnosis for *T. vaginalis*, concluded that there is no association between infection and cancer. According to this study, in *T. vaginalis* seronegative men, the odds ratio of developing prostate cancer when compared to men with low seropositivity was 0.83 (95% confidence interval ((CI): 0.63-1.09) and for men with high seropositivity of 0.97 (95% CI: 0.70-1.34). The hypothesis for this divergence of results can be attributed to the fact that in the study carried out in 2006, the included cases of prostate cancer were diagnosed by biopsy in patients with elevated Prostate Specific Antigens (PSA) or Digital Rectal Examination (DRE) changed. In the study published in 2009, cases with prostate cancer were diagnosed through biopsy regardless of the results of PSA or DRE tests, indicating that in this study not all cases of prostate cancer were detectable by laboratory and clinical screening, and therefore, it probably included cases with less potential for progression. Added to this methodological bias is the exclusion of men with benign prostatic hyperplasia (BPH). On the hypothesis that *T. vaginalis*-mediated inflammation is a risk factor for the development of cancer, the exclusion of positive cases diagnosed with BPH could reduce the positive association between prostate cancer and *T. vaginalis* infection[16].

Stark *et al*.[23] investigated whether *T. vaginalis* infection was associated with prostate cancer incidence, progression, and mortality. The authors concluded that there was no association with the development of cancer (OR = 1.23, 95% confidence interval [CI] = 0.94 to 1.61). However, a statistically significantly increased risk was reported for advanced-stage cancer and cases with the endpoints of progression to metastases (OR = 2.17, 95% CI = 1.08 to 4.37) or prostate cancer-specific death (OR = 269, 95% CI = 1.37 to 5.28) associated

with *T. vaginalis* seropositive status. Furthermore, these correlations were established independent of body mass index, smoking, age at diagnosis, and tumor stage and grade [23]. On the other hand, according to Xu *et al*.[3], it is known that obesity, smoking, men aged over 50 years, and late diagnosis for the more advanced stage are risk factors for prostate cancer. Also in this study, during the 5-year follow-up period of cases and controls, cases with cancer diagnosed with trichomoniasis had a higher positive correlation to develop lethal prostate cancer than men seronegative for *T. vaginalis* (OR = 6.4, CI 95% = 1.5 to 27.9)[3].

T. vaginalis is an extracellular cavitary protozoan, but its presence in epithelial cells and subepithelial tissues suggests that it can invade cells and tissues through mechanisms of inflammatory activation, including upregulation of antiapoptotic gene expression[24,25,26]. Studies investigating the association of *T. vaginalis* and prostate cancer report that in chronic prostatic infection, trichomoniasis may contribute to the development of cancer by several distinct but synergistic mechanisms. *T. vaginalis* secretes a pro-inflammatory cytokine, the *T. vaginalis* macrophage migration inhibitory factor (TvMIF), which is 47% similar to human macrophage migration inhibitory factor (HuMIF). TvMIF has a similar affinity to HuMIF with the extracellular receptor CD74 and, like the human homolog, activates signaling cascades of cell proliferation and activation of effector proteins involved in the inflammatory response. In addition, TvMIF also participates in survival pathways and increased invasiveness of tumor cells, such mechanisms being promoters of prostate cancer development and progression[27].

Lemos and Amaral[28] demonstrated, in a systematic review, a positive correlation between the association of *T. vaginalis* and cervical cancer. Kucknoor *et al*.[26] report that, in women, the adhesion of *T. vaginalis* to the vaginal mucosa modifies the gene expression of epithelial cells, including genes related to pro-inflammatory cytokines, such as Interleukin 8 (IL-8) and Monocyte Chemotactic Protein (MCP -1), involved in the chemotaxis of T cells, neutrophils, monocytes and macrophages to the site of infection. These inflammatory cells secrete reactive oxygen and nitrogen-based molecules that can damage cellular DNA and cause lysis in adjacent cells. In damaged epithelium, inflammatory cells also stimulate cell renewal to replace lysed cells through the release of cytokines that stimulate cell proliferation[26]. Mechanisms that are similar to what occurs in prostatic tissue in the presence of *T. vaginalis*, and if uncontrolled can cause hyperproliferation of prostatic epithelial cells with potentially genotoxic mutations[25,26].

Evidence suggests that *T. vaginalis* may provoke inflammation, at least in part, through activation of the innate immune response receptor Toll-like receptor 4 (TLR4)[29]. In

this regard, *T. vaginalis*-stimulated HeLa cells and *T. vaginalis*-infected female genital tract tissue samples expressed elevated levels of TLR4[30]. Regarding inflammation in the prostatic tissue induced by the presence of *T. vaginalis*, Chen *et al*.[17] found that seropositivity for *T. vaginalis* was associated with the risk of prostate cancer (OR = 4.16, 95% CI: 1.32-13.1) among TLR4 polymorphisms carriers, although no association was observed between wild-type TLR4 homozygous males (OR = 1.23, 95%, CI: 0.86–1.77). These authors support the hypothesis that these carriers produce a less effective innate immune response against *T. vaginalis* when compared to homozygotes. Thus, they could increase the probability of developing persistent *T. vaginalis* infections that ultimately ascend to the prostate. Thus, prostatic inflammation or *T. vaginalis* prostatic infections could increase the risk of prostate cancer[17].

A study by Yow *et al*.[18] sought to detect, through PCR, the presence of DNA from infectious organisms, including *T. vaginalis*, in cancerous prostatic tissue embedded in paraffin blocks. Despite the detection method being more sensitive and specific when compared to serology by ELISA, *T. vaginalis* DNA was not detected in any tissue sample. On the other hand, using the PCR technique, Lee *et al*.[31] detected *T. vaginalis* in 21.2% of Korean patients complaining of lower urinary tract symptoms, and 71.4% of them have chronic prostatitis. Despite the techniques employed for DNA detection presenting sensitivity and specificity close to 100% for *T. vaginalis*, they are not routinely used in diagnostic laboratories due to their high cost for processing and specific equipment, in addition to the low demand by health professionals. In routine, the diagnosis is performed directly by staining and microscopic analysis of fresh preparation and/or culture of secretion samples, but these techniques have low sensitivity for samples collected from men, due to the low parasite load and the anatomy of the male urogenital system itself. Furthermore, the culture requires between 5 to 7 days for analysis and release of the diagnostic result[7].

Several diagnostic methods have been developed for the detection of anti-*T. vaginalis* antibodies. However, in addition to the high cost, low sensitivity and specificity for acute and chronic cases make these methods less than ideal for the detection of *T. vaginalis* infections and should not be used for the routine diagnosis of trichomoniasis without performing the direct examination and culture[7]. For serological tests, the agreement observed in the articles is considered good, as they reached 89 - 94% agreement. The serological diagnostic value over time for detecting trichomoniasis was investigated by Sutcliffe *et al*.[32]. The authors observed that after 3 years of confirmation of the first positive diagnosis, 76% of these men were still seropositive and about 4.4% seroconverted. According to the authors, these data

are similar to those observed for other Sexually Transmitted Infections (STIs) investigated about prostate cancer risk[32].

Interestingly, Shui *et al*.[19] estimated that *T. vaginalis* seropositivity would be a protective factor against prostate cancer. In this study, seropositive men had a non-statistically significant decreased risk of fatal prostate cancer (OR: 0.57; 95% CI: 0.30–1.08) and a statistically significant decreased risk of advanced prostate cancer (OR: 0.51; 95% CI: 0.28- 0.93). However, the authors point out that these results, in part, can be attributed to the study population, since 89% of the cases were Caucasian men and, in the study, there were not enough African American men to perform subgroup analysis. In this context, in the same year, a prospective study was published to assess the association between *T. vaginalis* and prostate cancer in African-American men, in which Fowke *et al*.[20] found no significant association in the total study population or when restricted to African-American men. The study conducted by Marous *et al*., did not observe any association between *T. vaginalis* seropositivity and Gleason 7 (score used to measure the aggressiveness of prostate cancer) or more severe stage of prostate cancer in Caucasian participants or full-blown prostate cancer in African-American participants[21].

Seropositivity for *T. vaginalis* was 19.7% in patients with prostatic diseases, and 18.7% and 22.7% for patients with benign prostatic hyperplasia and prostate cancer, respectively[15]. The results were significant (P = 0.001) when compared to the healthy control group that exhibited 1.7% seropositivity for *T. vaginalis*. The authors emphasize that these results can, in part, be attributed to the age difference between the groups, of which the case had a mean age of 66.2 ± 0.06 and the control was 40.4 ± 0.15[15], Corroborating with the studies by Xu *et al*.[3]. Langston *et al.*[33] reported that of 732 study participants, 341 (46.6%) had low *T. vaginalis* seropositive, 198 (27.0%) had high, and the remainder were seronegative, when investigating the relationship between *T. vaginalis* infection and prostate specific antigen concentration. This results highlighting high seropositivity for *T. vaginalis,* but there were no statistically significant differences in PSA concentration between men. Specifically, 42.5% of men with high seropositive had PSA ≥ 0.70 ng/ml compared to 33.2% of seronegative men. According to the authors, while these findings offer limited evidence of *T. vaginalis* infection involvement in prostate cancer, the observed increase in PSA levels suggests that the possibility cannot be entirely excluded[33]. In this study, we highlight that seropositivity was higher among African-American men, corroborating with the literature[3,20,21].

In a case-control study conducted by Saleh *et al*.[34], the seropositivity rates for *T. vaginalis* were statistically higher in prostate cancer patients compared to normal controls (19% vs. 8.3%, respectively, P<0.05), which could suggest the possibility of an association between trichomoniasis and prostate cancer. Furthermore, there were positive associations between the levels of PSA and tumor stage with the levels of IgG for *T. vaginalis* among the seropositive cases (P<0.001 and <0.05, respectively), which shows an association between trichomoniasis and prostate cancer. On the other hand, the authors report no significant correlations between seropositivity for *T. vaginalis* and other prognostic factors or overall survival in these patients. In contradiction, the findings of Nagata *et al*.,[35] do not support *T. vaginalis* infection in the etiology of prostate cancer, since their results for *T. vaginalis* seropositivity were 7.4% among cases and 5.5% of controls. Different populations, demographic characteristics, *T. vaginalis* strains, methods of detecting *T. vaginalis* infection and prostate cancer diagnosis may contribute to explaining the discrepancy between the results of the studies presented[20,21,33,34].

CONCLUSION

In the review presented, five (41.66%) articles considered infection by *T. vaginalis* as a risk factor for the development of prostate cancer, highlighting patients diagnosed with cancer with trichomoniasis having a greater chance of progression to metastasis or cancer-specific death, in addition to indicating that immune system evasion mechanisms applied by *T. vaginalis* may also promote the development and progression of prostate cancer. However, seven (58.33%) of the studies did not report an association between infection by the protozoan and the development of cancer. The number of studies that observed an association is very close to the number that did not, and therefore it is not possible to reach a conclusion regarding this association. It is also important to highlight that many of these studies had biases such as selection bias, since many of the samples obtained in these studies used only men from a single country, only Caucasian men or only African-American men, for example. Methodological biases were also presented in some studies, such as the exclusion of men with benign prostatic hyperplasia and the sensitivity of diagnosis for both prostate cancer and *T. vaginalis* infection.

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