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The Relationship Between Toxoplasmosis and Prostate Cancer Patients

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Abstract. Background: Toxoplasmosis is one of the most common global life-threatening diseases among immunocompromised persons. It is not only a disease, but also a contributing factor to several pathological disorders, such as prostate cancer. Objectives. The purpose of the presented work is determining the prevalence regarding toxoplasmosis in Iraqi cancer patients and to connect that prevalence with the type of malignancy. Patients and Methods: This study included 115 male patients (75 with prostatic tumors and 40 with normal prostate glands) from Al-Amal National Hospital for Cancer Management was enrolled between December 15, 2023and July 1, 2024. Results: The study's results showed that prostate cancer patient group with the toxoplasmosis had the greatest IgG antibody level, measuring 52.64±1.16 UI/ml. The control group had 0.306±0.05 UI/ml. According to CMIA, all groups had seronegative IgM antibody levels. However, the mean PSA of the patients in this study was 66.72±0.51 ng/ml, compared to 2.48 ±0.04 ng/ml for the healthy control groups. Measuring IL-10 levels in samples were done by ELISA method showed a group of prostate cancer patients with toxoplasmosis has highest level 19.36 ±0.15 pg/ml, while the healthy control group has the lowest level of the same assay 12.78 ±0.13 pg/ml. However, illustrated that prostate cancer patient group with toxoplasmosis higher level significantly (P≤0.01) of IFNγ in comparation of the group of healthy control. Conclusion: Prostate inflammation is caused by the common parasite T. gondii, which encysts and causes chronic inflammation in prostate of any species, according to this work. The anti-inflammatory cytokines IL-10 and IFNγ were linked to an increased risk of prostate cancer infected with toxoplasmosis.

Highlights:

1. Toxoplasmosis contributes to prostate cancer risk via chronic inflammation.
2. Analyzed IgG, PSA, IL-10, and IFNγ in prostate cancer patients.
3. Elevated IL-10, IFNγ indicate toxoplasmosis increases prostate cancer susceptibility.

Keywords: Toxoplasma gondii; IgM, IgG, Prostate cancer

Introduction

Txoplasma gondii is an apicomplexan parasite and an obligatory zoonotic intracellular opportunistic pathogen .Toxoplasmosis is not only a disease, but also a risk factor for other pathological conditions such as prostate cancer (1,2). The parasite can spread to various tissues and organs because to a compromised immune system

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(3). Prostate cancer represents a common type of cancer worldwide, including in Iraq. A PSA test or a tissue sample from affected area are utilized for the diagnosis of this type of cancer (4). Toxoplasma gondii could play a role in the mutation of parasitophorous vacuole (5).

Tachyzoites become motile and proliferative after they pass through the epithelial cells of the small intestines. Tachyzoite is released into lamina propria as well as the surrounding tissue after the multiplication of the parasite and its proliferation by endodyogeny. Parasites develop from the epithelial cells of the small intestines into proliferative, motile tachyzoites, which proceed through an asexual lytic intra-cellular development and multiplication cycle by the endodyogeny prior to rupturing and releasing into intestinal lumen and the underlying lamina propria tissues, leading to the triggering of immunological responses (6). Lung cancer, laryngeal carcinoma, and leukemia are amongst malignancies that are associated with the serologic evidence (IgM + IgG) of T. gondii infection. After the confirmation testing and appropriate treatment course, T. gondii infection's serologic evidence in cancer patients usually leads to modifications to patient group's quality of life with active toxoplasmosis. Proactive steps for the prevention of the seroconversion, which might lead to active severe toxoplasmosis, which could be beneficial as well for cancer patients who are seronegative for T. gondii infection (7,8).

The capacity of T. gondii's in the rapid crossing of the epithelial barriers of the small intestine increase its global pathogenicity. The developments in technology have provided the researchers with the ability of investigating T. gondii interaction with the host cells, which potentially results in new protective methods and therapies (9). Prostate-specific antigen (PSA) can be defined as a blood test that has the ability to detect the benign prostatic hyperplasia and prostatitis, however, it isn't a reliable prostate cancer predictor (10). This study was aimed at examining the immune modulation of the prostate cancer patients who had toxoplasmosis.

IL-10 cytokine has several pleiotropic effects on the immunological functions and inflammation. It inhibits the co-stimulatory molecules and the T-helper1 cytokines in the macrophages (11,12,13). The dominance of the toxoplasmosis leads to producing high proinflammatory cytokine levels. Which is why, IL10 is required for the initiation of chronic toxoplasmosis infections. It prevents the antigen-presenting cells (APCs) from

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becoming inflammatory through the production of opposing costimulatory molecules (14,15,16). IL-10 leads to the inhibition of the activation of macrophage and induction of IFN-γ production during the infection with T. gondii, which results in increasing immunological suppression and intra-cellular parasite survival. Which is a benefit to the parasite as well as the host, due to the fact that it increases the ability of the parasite in producing T-helper 2 (TH2) cytokines (17). IFNγ can be described as a cytokine with a number of the biological roles, which include anti-viral, anti-cancer, and immunomodulatory characteristics. Which is why, it has a significant impact on the innate as well as the adaptive immune responses. It is helpful in the elimination of infections in an inflammatory environment through the increase of the immune responses. In addition to that, it prevents the immune system from overacting and resulting in damage to the tissues (18,19). The present study is aimed at the assessment of T. gondii impact on the immune response in patients with prostate cancer who have been infected with toxoplasmosis by examining IL-10 and IFN-γ regulatory role.

Methods

Subjects

Following the permission of the scientific ethics committee and after acquiring signed informed consent for this investigation. Between Dec. 15th, 2023, and Jul. 1st, 2024, 115 samples of blood have been collected from patients diagnosed with cancer at Al-Amal National Hospital for Cancer Management in Baghdad, Iraq, with the age groups ranging between 45 and 75. Enzyme-linked immunosorbent assay (ELISA) kits (Elabscience U.S.) have been utilized for the analysis of every sample for the detection of Toxoplasma gondii IgG and IgM antibodies as well as IL10 and IFN-γ. Sterile syringes were used to extract 3 ml of venous blood from each one of the patients, which was then evacuated in a simple tube marked with the patient's age, name, and kind of cancer. Following centrifugation, serum was extracted from blood samples and analyzed with the use of ELISA kits.

T. gondii diagnosis

As directed by the manufacturer (Architect Toxo IgM/G kit -Abbott GmbH, Germany), chemiluminescent microparticle immunoassay (CMIA) has been utilized for detecting both anti-Toxoplasma IgG/IgM antibodies in sera.

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Determination of IL-10 and IFN-γ level

Sandwich ELISA was used to quantify circulating serum levels of IL10 and IFN-γ with the use of commercial kits in accordance with manufacturer's instructions: ELISA Test Kits given by (Elabscience USA).

Statistical Analysis

The Statistical Analysis System- SAS (2018) program (20). Has been assessed Software Statistical Package for Science, Statistical significance was determined by using L.S.D. test for quantitative dated. Results were expressed as mean±S.D. Chi-square test has been utilized for comparison between percentage (P≤0.01, P≤0.05) probability in the present study

Result and Discussion

T. gondii infection in healthy hosts might occasionally cause symptoms. Toxoplasmosis is very pathogenic in immunocompromised individuals, toxoplasmosis is usually asymptomatic in immunocompetent people (21). Table (1) shows that the group of prostate patients with toxoplasmosis has the highest level of anti-Toxoplasma IgG antibody 24/25 (96.0%), followed by the Toxoplasma IgM antibody positive 7/25 (28.0%), and the IgG/IgM antibody was seropositive for anti-Toxoplasma 8/25 (32.0%).

Table1: Distribution of sample study according IgG and IgM results in patients' group

Test		No	Percentage (%)	P-value
IgG	Positive	24	96.00	0.0001 **
	Negative	1	4.00	
IgM	Positive	7	28.00	0.0057 **
	Negative	18	72.00	
IgG/ IgM	Positive	8	32.00	0.0062 **
	Negative	17	68.00	

** (P≤0.01).

Table 2 results of this study showed that prostate cancer patients with toxoplasmosis have the highest IgG antibody level 52.64 ±1.16 UI/ml followed by the group of control groups 0.306 ±0.05 UI/ml, while the level of IgM antibody was seronegative in all groups

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Table2: concentration of anti- Toxo IgG / IgM assay IU/mL in the studied groups.

Group	Means ±SE	
	IgG titer	IgM titer
Patients Cancer PSA	52.64 ±1.16	1.714 ±0.08
Control	0.306 ±0.05	0.078 ±0.01
T-test	2.133 **	0.159 **
P-value	0.0001	0.0001

** (P≤0.01).

Figure 1. mean PSA of the patients in the current study was 66.72 ±0.51 ng/ml in comparison with the healthy control groups was 2.48 ±0.04 ng/ml.

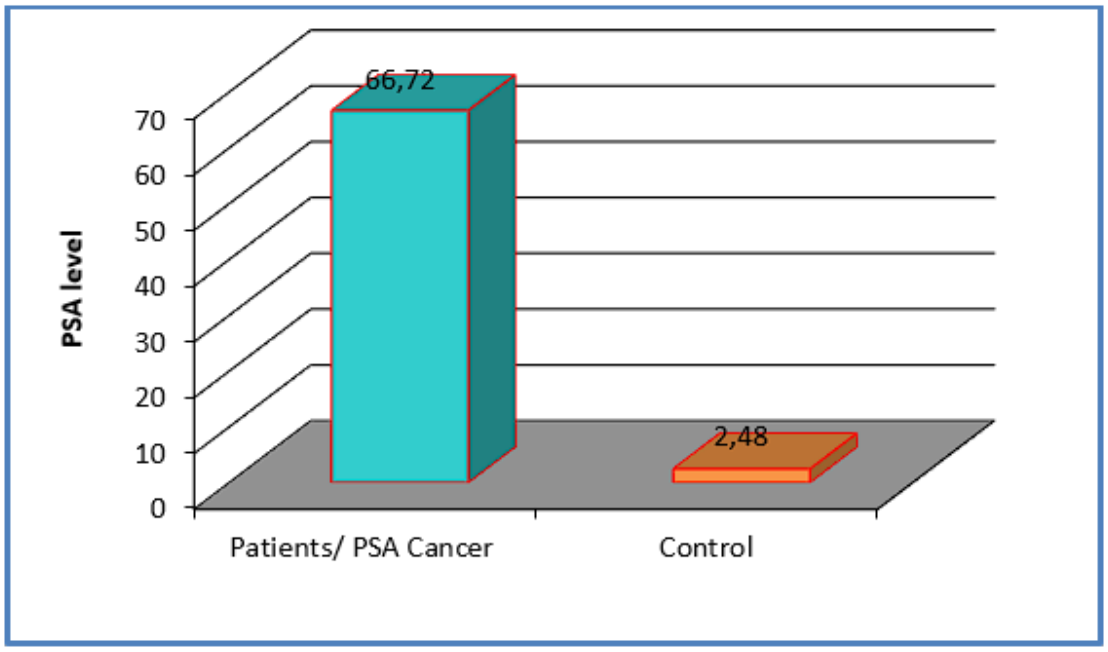

Figure 1: Comparison between patients PSA Cancer and control groups.

The current study sought to identify the prevalence and risk factors for toxoplasmosis in prostate cancer patients. Toxoplasma gondii can cause significant illness or even death in immunocompromised populations, such as pregnant women, HIV patients, organ transplant candidates, and cancer patients. Many investigations were conducted on toxoplasmosis in cancer patients (22). The rural areas were the most affected by urbanization. This is owing to the fact that the majority of conditions occur in rural areas due to poor living conditions, a lack of health care, and existing

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environmental pollutants. This finding was consistent with Bouscaren et al. (23), who discovered that 63.0% of Toxoplasmosis patients also had other significant conditions. Older men (60-75 years old) were more likely to develop prostate cancer while also afflicted with toxoplasmosis. These findings were congruent with those of Nikiforou et al. (24), who discovered that 63-year-old males exhibited the majority of the primary symptoms, including dysuria, enlarged gland size, and a high concentration of PSA (prostate specific antigen). To explore prostate cancer in patients with toxoplasmosis and a prostate tumor, several components were evaluated to assess their quantity. These changes show that Toxoplasma invaded the prostate, causing the growth of malignant tumors in the cells of the prostate tissue, as well as the occurrence of a defect and so-called prostate cancer. This is consistent with Gustavo and Travis's (25) findings, which claims that Toxoplasma infiltrates prostate cells, causing acute or chronic infections, and that the prostate tissue is exposed to the tumor, whether benign or malignant, and that the cancerous tumor developed. Toxoplasma is a factor that activates cancer cells in the prostate tissue. These findings are consistent with Seladi-Schulman's (26) conclusion that toxoplasmic ability to penetrate all host tissues may cause tissue alterations. This is consistent with Mohammad Nazar Sh (27), who established that toxoplasmosis has an effect on the conversion of the genetic sequence of the various organs of patients infected with brain and breast, and revealed that the nucleotides changed the BRCA1 gene exon 11 was amplified from malignant breast cancer tissues.

The results in figure (1) shown that the group of prostate cancer patients who have toxoplasmosis has highest IL-10 level 19.36 ±0.15 pg/ml However, the healthy control group has the lowest level of the same interleukin 12.78 ±0.13 pg/ml.

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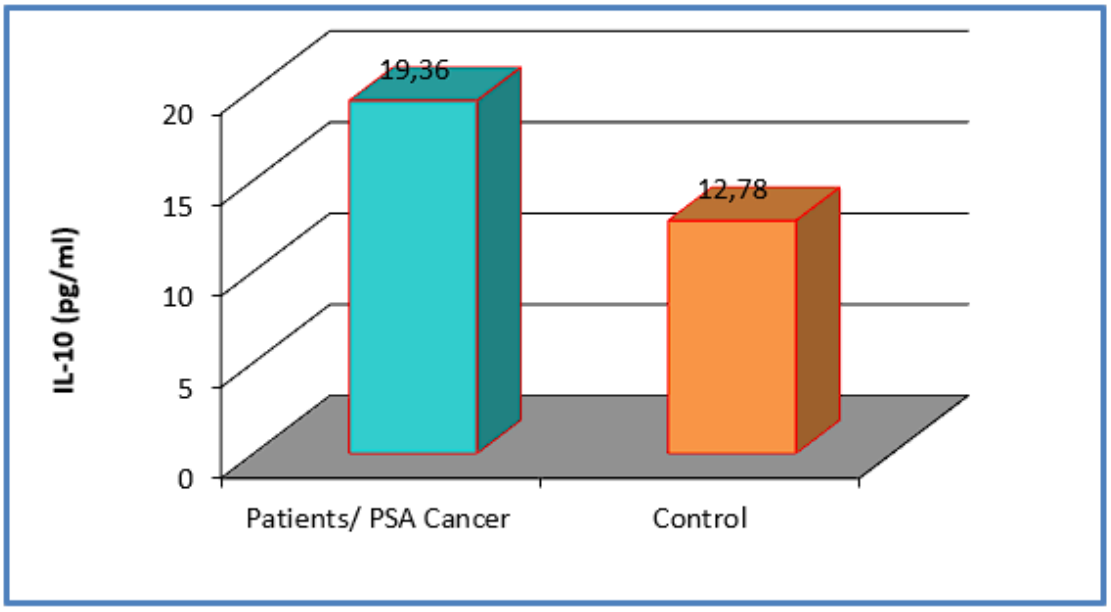

Figure 2: Comparison between patients PSA Cancer and control groups in IL-10

Interleukins are essential for the body's response to damage. IL10 secreted by T helper-2 type cells (Th2) might inhibit cell-mediated immune effector pathways that are essential for the host's defense against intracellular infections. Cytokines IL-10, IL-4, IL-12p40, and IFN-play distinct roles in toxoplasmosis disease (28). The effector response of CD8 T-cells is significantly influenced by CD4 T-cells, as demonstrated by T. gondii infection. CD8 T cell malfunction is associated with CD4 T cell depletion (29). The detrimental effects of inflammatory response, which is marked by elevated IFN, TNF-a, and NO production linked to intestinal toxoplasmosis growth, are lessened by IL-10 (30). Additionally, IL-10 is a strong anti-inflammatory cytokine that promotes iron absorption and retention in the reticuloendothelial system by blocking the synthesis of several cytokines, like IL-6, IL-1, IL-12, IL-8, TNF-a, and GM-CSF. Because it could have tumor-promoting as well as tumor-suppressive effects, IL10 plays a paradoxical role in carcinogenesis (31,32). Through promoting CD8+ T cell activation and blocking pro-inflammatory cytokines like IL6 and IL-23, IL-10 may reduce carcinogenesis [33]. On the other hand, IL-10 might suppress IFN-γ-promoting cytokines and restrict antigen presentation, which could lower anti-tumor immunity (32). Higher levels of circulating IL-10 have been linked to a decreased risk of PCa, according to previous genetic studies

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[34–35]. IL-10 polymorphism −592A > C, which is associated with elevated peripheral IL-10 levels, was observed to reduce the risk of PCa in a meta-analysis (36).

The findings in figure (2) showed that, in comparison to the group of healthy controls, the group of prostate cancer patients with toxoplasmosis had a significantly (P≤0.01) greater level of IFNγ.

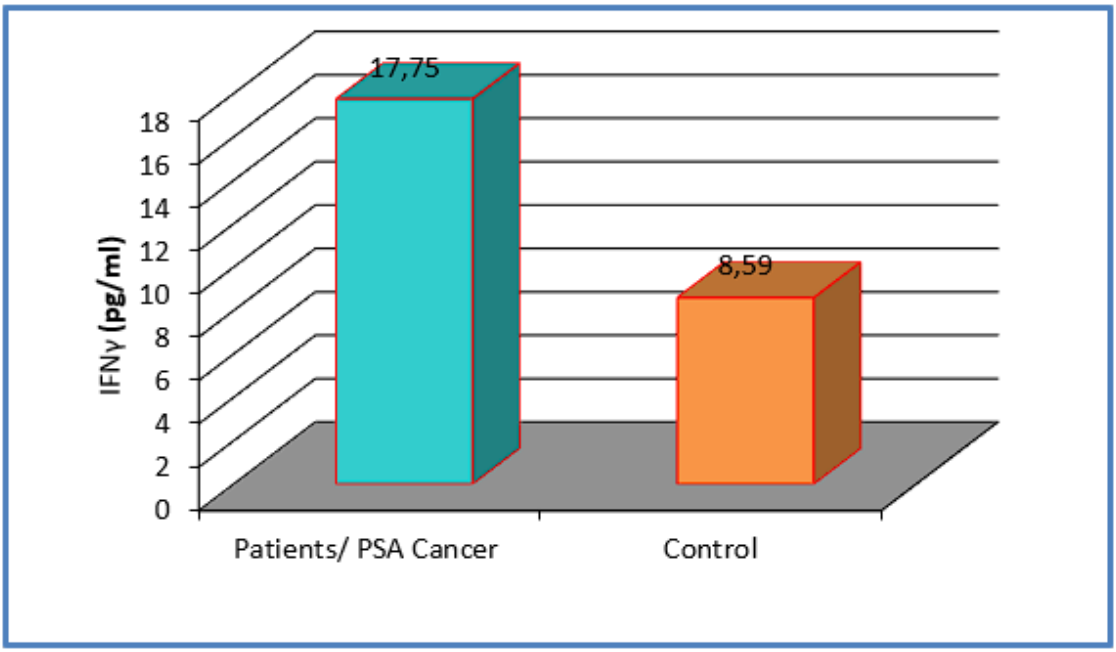

Figure 2: Comparison between patients/ PSA Cancer and control groups in IFNγ

IFNγ is the upregulation of the expression of major histocompatibility class-I (MHC-I) gene. This leads to improved tumor antigen processing and presentation in the setting of cancer, which improves T-cell cytotoxicity and identification (37).The findings of a phase clinical trial of systemic IFN-γ were published by Zhang et al. (38) in 2 other immunological cold tumors, myxoid/round cell liposarcoma and synovial sarcoma. According to the study, intratumoral tumor infiltrating lymphocytes (TILs) exhibited reduced worn-out phenotypes, enhanced tumor antigen presentation, and considerable T-cell infiltration as a result of IFNγ.

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Conclusion

Prostate inflammation is caused by the common parasite T. gondii, which encysts and causes chronic inflammation in prostate of any species, according to this study. The anti-inflammatory cytokines IL-10 and IFNγ were linked to an increased risk of prostate cancer in cases of toxoplasmosis infection

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