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TOXOPLASMA GONDII SEROPEVALENCE IN PULMONARY TUBERCULOSIS PATIENTS

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Abstract :

This study was conducted in the Chest and Respiratory Hospital in Najaf Governorate during the period from November 2022 to October 2023. 70 sputum samples from both sexes and different ages were examined to detect tuberculosis bacteria *Mycobacterium tuberculosis* by using the traditional method (examination of sputum samples) and a Ziehl-Neelsen dye, as well as investigating their infection with the *Toxoplasma gondii* parasite using the ELISA method and the extent of the effect of this parasite and other factors on Tuberculosis.

The results showed that the traditional examination of the sputum samples taken was consistent with the clinical diagnosis made by a specialist physician at a rate of 100% of the total samples studied.

The results showed differences in the rates of males and females infected with tuberculosis. The number of males infected with tuberculosis was 40, or 57%, while the number of infected females was 30, or 43%, and it had a moral significance ($P < 0.05$).

Tuberculosis infection rates also varied according to age, and the middle age group (38-57) years was the most susceptible to infection, reaching 40%, followed by the younger age group (18-37) years, reaching 33%, and finally the oldest age group (58-77). year, reaching 27%. It had a moral significance ($P < 0.05$).

Residents of cities were more susceptible to infection with pulmonary tuberculosis than residents of rural areas, as the number of infected people from the city was 46, at a rate of 66%, and from the countryside, 24, at a rate of 34%. The results of the statistical analysis showed that there were significant differences in the rates of infection with pulmonary tuberculosis between rural and city residents ($P < 0.05$).

The results of the study noted the difference in the sensitivity of tuberculosis patients in responding to treatment and the presence of resistance of pulmonary tuberculosis bacteria to the first-line antibiotics that are usually given to the patient as the first stage of tuberculosis treatment. The number of patients resistant to the drug was 33 patients, at a rate of 47%, and the number of patients responding to the drug was 37, at a rate of 53%. With a significant difference($P=0.025$).

The results showed the seroprevalence of specific antibodies to the parasite Toxoplasma conidia*Toxoplasma gondii*In patients with pulmonary tuberculosisTB infected them at a rate of 51%, which is a high rate compared to the control group, which was infected with a lower rate of 25% of Toxoplasmosis.

The prevalence of infection was associated with the parasite Toxoplasma conidia*T. gondii*And pulmonary tuberculosis bacteria*M. tuberculosis*In females it is more than in males, 58% and 42%, respectively. Likewise, females are more infected than males, 15% and 10%, respectively, in the control group.

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Introduction

A disease results Toxoplasmosis is caused by infection with the *Toxoplasma gondii*, which is an obligate intracellular parasite. The infection produces a wide range of clinical syndromes in humans, terrestrial and marine mammals, and various bird species. *T. gondii* has been isolated from all parts of the world, except Antarctica. Nicoll and Manso first described the organism in 1908, after they observed parasites in the blood, spleen and liver of a North African rodent, Ctenodactylus gondii. The parasite was named Toxoplasma gondii (after the rodent) in 1909. In 1923, Janko reported the presence of parasitic cysts in the retina of an infant who had hydrocephalus, epileptic seizures, and unilateral microcephaly. Wolfe, Cowan, and Page (1937-1939) determined that these findings represented a syndrome of severe congenital T. gondii infection (Dubey and Beattie, 1988). There are three main genotypes of T. gondii (type I, type II, and type III) and these genotypes differ in their pathogenicity and prevalence in humans. In Europe and the United States, genotype II is responsible for most cases of congenital toxoplasmosis (Gazzinelli et. al., 1993).

Pulmonary tuberculosis is a health problem affecting many regions of the world. It causes the injury of more than eight million people ((Friend et al., 2003, and the death of about two million people annually in the world (Davis *et al*., 2007)). This disease caused the death of more than thirty million people during the twentieth century. Among the factors that increase the incidence of this disease are poverty, crowded human populations, migration from endemic areas to pure or less endemic areas, as well as infection with the immunodeficiency virus. The increase of these factors is considered a reason for its increased spread (WHO,2006).

Mycobacterium tuberculosis is the main cause for pulmonary tuberculosis, also known as pulmonary tuberculosis, as for other types *M. africanum* and *M.bovis* they are capable of causing disease in humans, but at lower rates than in humans *M. tuberculosis* (Fitzgerald & Haas,2005).

The immune response to infection agents is regulated by immune effectors and cytokinesis-producing cells such as dendritic cells.Dendritic Cells that stimulate the maturation of T cells into Th1 cells through the production of some cytokines such as (IL-12) and Interleukin-18 (IL-18).(Kadowki, 2001; Wozniak, 2006).

Infect *T. gondii* a large proportion of the world's population (perhaps a third) but uncommonly causes clinically significant disease. However, some individuals are at high risk of developing toxoplasmosis severe or life-threatening toxoplasmosis Individuals at risk for toxoplasmosis include fetuses, newborns, and immunocompromised patients (Georgie, 1994).

There is a scarcity of studies on co-infection *T. gondii* with tuberculosis. Therefore, this study aimed to determine the frequency of toxoplasmosis infection in patients with pulmonary tuberculosis

Materials and methods

Sample collection

70 blood samples were collected from pulmonary tuberculosis patientsTuberculosis, who are being followed up by government hospitals in Baghdad, Muthanna, and Najaf, and the samples were transferred to the laboratories of the College of Science, Al-Qadisiyah University, to conduct laboratory tests, in cooperation with some private clinics, during the period from November 2022 to October 2023. I also took 20 samples (control) from people who did not suffer from pulmonary tuberculosis and examined them to diagnose toxoplasmosis.

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Sample examination

A portion of the sputum was taken with a wooden stick. The festering areas were selected and then transferred to the glass slide. Then it was spread with a wooden stick over a specific area of the glass slide. Then it was left to dry and then fixed by passing the flame (3-4) times. The slide was dyed using the method of Zeal Nelson and Kalati: I poured the carbol dye. Fuchsin over the area of sputum spread on the glass slide. The dye was heated by passing a flame using a Bunsen lamp until light white vapors rose, avoiding boiling of the dye. Then I left the dye for five minutes. I washed the dye with water. I shortened the dye with alcoholic acid (95) ethanol 3.HCL) for three minutes, washing the alcoholic acid with water. The slide was immersed in methylene blue dye for two minutes. The methylene blue dye was washed off with water, the slide was dried, and it was examined microscopically with an oil lens to observe acid-fast bacilli.

Results and discussion

The results of the laboratory examination confirmed that all of them were infected with tuberculosis. The results of the statistical analysis showed that there were no significant differences between the two methods of clinical diagnosis and laboratory examination .

The sputum samples were the highest positive for microscopic examination and culture on the medium, representing 15.9% and 23.1%, respectively (Mohammed. 2017).

Prevalence Anti-Toxoplasma IgG in tuberculosis patients.

Concomitant *Toxoplasma gondii* infection was significantly more frequent among tuberculosis patients compared to the control group, as the level of antibodies Anti-Toxoplasma IgG was significantly higher (51%) among TB patients than in the control group (25%) (Table 1).

Table (1): Seroprevalence of toxoplasmosis in tuberculosis patients and the control group.

Study group	No. examined	Anti-Toxoplasma IgG	Percentage %
control	**40**	**10**	**25**
Tuberculosis patients	**70**	**36**	**51**
P-value		**0.05**	

During active TB infection, there is a decrease in cytokine productionTH1 and overproduction of TH2 cytokines (Hirsch *et al*., 1997,1999). Thus, it is this shift in the Th1 response toward Th2 responses with subsequent suppression of cell-mediated immunity against toxoplasmosis that can reactivate old lesions or increase susceptibility to new infections.

Coinfection with tuberculosis and other infections such as parasitic infections represents a serious and difficult health problem. Each of *M. Tuberculosis* and *T. gondii* they are opportunistic intracellular microorganisms widespread in developing countries. The prevalence of the parasitic disease varies widely among TB patients in different regions and different survey sites.(Li and Zhou, 2013).

The seroprevalence of Toxoplasma gondii infection among tuberculosis patients was

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significantly higher than the control group. This was consistent with (Yassin, 2015;Mashaly *et al*., 2017), who also showed that patients with active tuberculosis had a significantly higher seroprevalence of toxoplasmosis infection compared to controls. Conversely, no significant difference has been reported for Toxoplasma antibodies between controls and TB patients (Ledru *et el*., 1995). Many factors are likely to influence the co-occurrence of TB and parasitic diseases such as social demographics, decreased immunity such as in kidney transplant recipients, patients undergoing dialysis, HIV-infected patients and migration (Das et al., 2006; Ersoy et al., 2003 ;Mashaly *et al*., 2017).

Both tuberculosis and parasitic diseases are infectious diseases that cause significant harm to humans with overlap in endemic areas, which may lead to frequent co-infection in these areas. Cases of tuberculosis with intracellular parasites have been reported, as have malaria, and visceral leishmaniasis (Rajoo *et al*., 2010), and *Toxoplasma gondii* (Guneratne *et al*.,2011). A case of cerebral toxoplasmosis with disseminated tuberculosis in an immunocompetent patient has been reported. In cases of coinfection, modulation of the immune response has been suggested (Mueller *et al*., 2012).

Seroprevalence of *T. gondii* among age of tuberculosis patients.

The seroprevalence of *Toxoplasma gondii* infection among tuberculosis patients was much higher in the age group (18-37) years, reaching 63.88% compared to the same category of tuberculosis patients not accompanied by *T. gondii* infection. *T. gondii* infection also decreased in the older age groups of tuberculosis and infection patients. accompanying, and the statistical analysis proved the significance of these differences, as the value was (P-Value =) as shown in Table (2).

Table (2): Seroprevalence of *T. gondii* among age of tuberculosis patients.

Age	No. examined	TB patients		TB /T. gondii		P.value
		No. Infected	(%)	No. Infected	(%)	
37-18	23	0	0	23	63.88	0.01
57-38	28	19	55.88	9	25	
77-58	19	15	44.11	4	11.11	
Total	70	34	48.57	36	51.42	

Researcher Al-Douri (2016) recorded the highest infection rate within the age group (16-25) years, and the percentage was 57%, and the lowest infection rate was 10% within the age group (36-45) years, and study (2016)Hadi et al in Al-Qadisiyah Governorate, and the highest infection rate was 45% within the age group (25-34) years, and the lowest infection rate was within the age group (35-44) years, which was 12%. The researcher Shahatha's study (2107) recorded the highest

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infection within the age group. (26-30) years, and the percentage reached 65.02%, and the researchers Abdullah and Mahmood (2017) studied in Erbil, and the highest incidence of IgG antibody was within the age group (21-30) years. The percentage of infection is 46.61%, and the lowest percentage is within the age group (20 years), which is 12.96%. Chronic disease and the study of Ali et al. (2018) in Dhi Qar Governorate. The highest rate of infection was recorded within the age group (20-24) years, which was 12.58%, and the lowest rate was within the age group (40) years, and the rate was 2.58%. 90.09% and the study of the hadith researcher (2018) in the city of Tikrit, and the highest infection rate was 42% within the age group (26-30) years, and the percentage was similar to the researchers Hadi and Al-omashi (2018) in Al-Zahra Hospital (peace be upon her) in the Holy Najaf Governorate. The study recorded the highest infection rate among The age group (21-27) years reached 42.9%.

Seroprevalence of *T. gondii* among sex of tuberculosis patients.

Males represented 70.58% of all tuberculosis cases, compared to 241% of cases among females. In the case of Toxoplasma gondii infection associated with pulmonary tuberculosis, females represented 55.55%, compared to 44.44% among males. These data were analyzed statistically and it was found that the value of (P-Value = 0.02) as shown in (Table 3).

Table (3): Seroprevalence of *Toxoplasma gondii* among sex of tuberculosis patients.

Sex	Patients (n=70)				P-Value
	TB Patients		TB / *T. gondii*		
	No. Infected	(%)	No. Infected	(%)	
Males	24	70.58	16	44.44	0.02
Females	10	241	20	55.55	
Total	34		36		

This study showed, when taking into account the sex of the person from whom the sample was taken, that the number of male tuberculosis patients infected with toxoplasmosis is 15 men, and thus the co-infection rate in males is 42%, relative to the total number of people infected with tuberculosis and toxoplasmosis together, which is 36. The number of female tuberculosis patients who are infected with toxoplasmosis is 21, and thus the percentage of women with co-infection is 58% of the total co-infection, meaning that the rate and percentage of co-infection with both diseases is higher in females than it is in males.

Seroprevalence of *T. gondii* among tuberculosis patients by residence.

Urban residents are more susceptible to pulmonary tuberculosis and *T. gondii* infection associated with pulmonary tuberculosis than residents of rural areas. These data were analyzed statistically (P-Value = 0.025) as shown in Table (4).

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Table 4: Percentages of tuberculosis and *T. gondii* infection by residence.

Residence	No. examined	TB tuberculosis patients		TB + T. gondii		P*value
		No. Infected	(%)	No. Infected	(%)	
Urban	24	11	32.36	13	36.11	0.025
rural	46	23	67.64	23	63.88	
Total	70	34		36		

The results of the thesis were in agreement with many studies, including the study of the findings of (2018).Ali *et al*., in his study in Dhi Qar Governorate, the highest percentage in the study was the city's share at 26.5% and the rural share recorded at 16.5%. It was also inconsistent with researcher Al-Mayahi (2011) in Wasit and the highest percentage was in the countryside at 48 .56% The city had a rate of 44.33%, and the results of the study did not match the findings of the researchers Abdullah and Mahmood (2017), as the highest infection results in the study were recorded in the countryside for acute and chronic infections, and the percentage for IgG antibodies was 44.18% and for IgM antibodies was 20.39%, while the city's percentage for IgG antibodies was 30.5% and for IgM 9.03%,

The results of the current study indicated a high incidence of Toxoplasma gondii infection in cities, as most of the infections may be due to the spread of the ultimate host in cats and the egg sacs they shed, especially city dwellings, most of which are small and close together, and there are not large areas in most areas, which may limit the infection and provide a wider range of spread. Infection is in addition to negligence in handling fruits and vegetables that may be contaminated with egg sacs, or the causes of infection may be due to dietary habits and infection with tissue cysts.Tissuc Cysts in infected meat and poultry, especially after the spread and increase in quantities of imported meat and poultry or due to contaminated milk.

Some studies examining toxoplasmosis have identified a higher prevalence of infection in rural areas(Sousa *et al*., 1987; Al-Deen, 2002), while some indicated that there are no noticeable differences in toxoplasmosis infection between the countryside and the city. (Taylor *et al*., 1997; Al-Kasyi 2001), and (Al-Jubori, 2005) in Kirkuk Governorate, the rate of infection in urban areas is higher than in rural areas with intensive agricultural activity. The main reason is due to the presence of the source of infection, which is the raising of domestic cats or their roaming in those areas and their contamination of gardens and vegetables with feces containing the infectious Oocyst stage. Unpasteurized milk is another reason for transmitting the infection in these areas (Montoya and Remington, 2000).

Resistance of tuberculosis patients.

The results of the current study showed that the parasite *T. gondii*, or toxoplasmosis, has a negative impact on patients with pulmonary tuberculosis, as most people with toxoplasmosis develop tuberculosis of the resistant type. Toxoplasma gondii infection was significantly higher among tuberculosis patients sensitive to treatment compared to the treatment-resistant group (P <

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0.05), however, The level of anti-Toxoplasma IgG antibodies was significantly higher among treatment-resistant TB patients.

Studying 70 samples of patients with pulmonary tuberculosis and finding out which of them had a common infection, taking into account the sensitivity of pulmonary tuberculosis patients to the drug, it was found that these patients were divided into two parts: the first part responded to the drug (normal) and numbered 37, and the other part did not respond to the drug (resistant) and numbered 33. It was found that 3 of the patients responding to the drug had a common infection, their percentage was 8%, and 34 of them had no infection except pulmonary tuberculosis, their percentage was 92.As for the patients who did not respond to the drug, it was found that all of them were sensitive or resistant.

Through this, we conclude that it is a parasite *T. gondii*, or toxoplasmosis, has a negative impact on patients with pulmonary tuberculosis, as most people with toxoplasmosis develop resistant type tuberculosis. These data were analyzed statistically and it was found that the P-value was 0.03 (Table 5).

Table (5): The effect of concomitant *T. gondii* infection on the resistance of tuberculosis patients to treatment.

Resistance	No. Examined	TB patients (n = 34)		TB / T. gondii (n = 36)		P*value
		No. Infected	(%)	No. Infected	(%)	
Resistant	33	0	0	33	92	0.03
Non-resistant	37	34	100	3	8	
Total	70	34		36		

A cure appeared Rifampicin was used at the end of the 1960s and was used with other antibiotics to treat tuberculosis (Espinel, 2003). After the emergence of immunodeficiency virus (HIV), the incidence of multi-drug-resistant Mycobacterium tuberculosis (MDR-TB) increased (Cohn *et al*., 1997).

And he knows(MDR-TB) is defined as M. tuberculosis bacterial strains that are resistant to at least two antibiotics, including Rifampicin and Isoniazid. Bacterial resistance to antibiotics other than Rifampicin and Isoniazid is not classified as (MDR-TB) (CDC). ,2013).

As for tuberculosis bacteriaDrug resistance Extensive is a relatively rare type of resistant bacteria and is defined as bacteria resistant to the antibiotics ifampicin and isoniazid in addition to Fluoroquinolone and at least one of the second-line antibiotics that include amikacin - kanamycin - capreamycin (Kolyva and Kara Kousis, 2012), while Extremelly-drug resistant (EXDR) has been described as the end point of bacterial resistance to antibiotics and is defined as bacterial strains

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that are resistant to first- and second-line antibiotics (Andrews, 2007).

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