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Toxoplasmosis: An Overview

Jaita Biswas[1*], Sourav Maparu[2]
[1,2] Veterinary Officer, Animal Resource Development Department, Govt. of West Bengal, India
*Corresponding Author: Jaita Biswas, e-mail: vetjaita29@gmail.com)
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Key Points

- Toxoplasmosis is a globally important zoonotic disease caused by *Toxoplasma gondii*, with cats serving as the definitive host and humans acquiring infection mainly through contaminated food, water, or undercooked meat.
- The disease poses serious health risks for pregnant women, fetuses, and immunocompromised individuals, causing congenital abnormalities, neurological disorders, ocular lesions, and severe systemic illness.
- Early diagnosis, safe food handling, proper hygiene, and prevention of exposure to contaminated meat and cat feces remain the most effective strategies for controlling toxoplasmosis, as no licensed human vaccine is currently available.

Abstract

Toxoplasmosis is a zoonotic illness caused by the protozoan parasite Toxoplasma gondii. This parasite lacks host specificity and is widely distributed. It exclusively infects cats during the sexual stage, although it can parasitise any mammal during the asexual stage, including humans and cats. This disease is spread by drinking unfiltered water, water that contains oocysts, and water from recreational facilities. Myalgia, sore throat, myocarditis, maculopapular rash, fever, meningitis, polymyositis, muscle discomfort, malaise, pneumonia, and psychomotor abnormalities are among the symptoms of this illness. During an acute systemic infection, infected people may experience asymptomatic cervical lymphadenopathy. Different tests like Sabin-Feldman dye test, ELISA test, TORCH and PCR could be used to diagnose Toxoplasmosis. To treat toxoplasmosis, pyrimethamine is used in combination with sulfadiazine or clindamycin. There is currently no human vaccine to prevent toxoplasmosis. Hands should be properly cleaned with soap and water after handling meat, poultry, or shellfish to prevent the spread of toxoplasma to humans.

Introduction

Toxoplasma gondii is a protozoan parasite that causes the zoonotic disease toxoplasmosis (Al-Malki E. 2021). This species is an intracellular coccidian parasite from the phylum Apicomplexa (Delgado *et al.*, 2022). Animals, including household pets like dogs, cats,

and birds as well as livestock like pigs, cows, goats, and sheep, are the main carriers of this parasite. This parasite is ubiquitous and does not have host specificity. It can parasitise any animal during the asexual stage, including humans and cats, but it only infects cats during the sexual stage (Al-Malki E. 2021). The only known definitive hosts for this parasite are cats, who excrete millions of oocysts every day. These oocysts sporulate and spread to other areas. Raw or undercooked meat with Toxoplasma cysts or oocysts might spread the illness. The parasite is ready to infect if swallowed, and these cysts are resistant to stomach acid. A pregnant mother who has toxoplasma may transfer it to the foetus through the placenta without showing any symptoms. Throughout the course of the infection, the disease's clinical symptoms are both subclinical and persistent. The most noticeable sign in this infection appears during pregnancy, which raises the risk of miscarriage, stillbirth, live birth with birth defects such as hydrocephalus or microcephalus, motor difficulties, brain and retinal damage, and signs of mental disorders (Aleixo *et al.,* 2016). Because of the high frequency of human transmission, the chronic nature of the illness, its potentially fatal consequences, and the fact that many people are unaware they have the infection, toxoplasmosis infections are acknowledged as a severe public health concern.

Etiology

T. gondii is a member of the Phylum Apicomplexa, Class Sporozoa, Subclass Coccidia, Family Sarcocystidae, Subfamily Toxoplasmatinae, and Genus Toxoplasma (Delgado *et al.,* 2022). The first form is a trophozoite, which is 4-6 microns long and 2-3 microns wide, with a karyosome in the center of a crescent-shaped nucleus. The brain, skeletal muscle, and heart can develop tissue cysts as a result of persistent or asymptomatic infections. After the host has died, these cysts—which can contain up to 60,000 bradyzoites—can remain in the tissue for a few days. The third type, oocysts, can withstand temperatures of 24°C for ten months or 37°C for twenty-eight days. They are usually released in the cat's faeces and are found in the intestines of cats, especially those that have sporulated (contain sporozoites). (Khairulla *et al.,* 2024)

Host

T. gondii need two distinct kinds of hosts in order to live and reproduce:

- The Definitive Hosts: The parasite's universe revolves around members of the feline family, including both domestic house cats and wild felines. The only animals on Earth that can sexually reproduce with *T. gondii* are cats.
- The Intermediate Hosts (Everyone Else): Almost any animal with warm blood can act as an intermediate host. Sheep, pigs, cattle, birds, rodents, and, of course, humans are all included in this. The parasite can only reproduce asexually in these hosts and it waits for an opportunity to re-enter a cat.

Life Cycle of the Organism

The sexual cycle and the asexual cycle are the two life cycles that *T. gondii* uses to reproduce. The sexual (enteroepithelial) cycle takes place in definitive hosts like cats, but the asexual cycle happens in hosts between humans and warm-blooded animals like birds (Al-Malki E. 2021). When the definitive host consumes infectious cysts or oocysts (cats eat mice carrying the first or third forms of *T. gondii*), the asexual stage starts. It takes three to ten days for *T. gondii* to evolve from the bradyzoite prepatent stage (second form), five to ten days for tachyzoites (first form), and twenty-four days or more for the third form to grow into oocysts. The development of merozoites into macrogametes and macrogametes in the intestinal epithelial cells marks the start of the sexual stage. A zygote is created during the fertilisation process between the two gametes, and it develops into an oocyst. Once inside the intestinal lumen, oocysts exit together with the faeces. After two to three days at 24°C, the oocysts either sporulate or turn infectious. Following an oral infection, the tachyzoites that are created mature into vacuoles of different kinds in targeted cells. The term "pseudocyst" refers to the development of eight or more tachyzoites within cells. Tachyzoites attack nearby cells when a pseudo-cyst bursts, and they travel throughout the body via lymphatic and blood flow. With the exception of those that have developed into bradyzoites in tissue cysts, tachyzoites will be eradicated by the body's response, allowing parasitemia to recur repeatedly until antibodies are produced in the plasma. (Khairulla *et al.,* 2024)

Epidemiology

There have been reports of toxoplasmosis infection in people and warm-blooded animals, as well as reports of its global expansion. This illness affects nearly all animals, including birds and mammals. Africa, the Middle East, Southeast Asia, Central Europe, Latin America, and Eastern Europe are some of the areas where toxoplasmosis is most prevalent. Toxoplasmosis is more common in warm areas and extremely uncommon in European countries due to the cold climate. Food preparation practices that affect transmission include uncooked or undercooked food (Durkovic-Dakovi O. 2017). In several countries, eating raw shellfish and oysters has been found to be a major risk factor for the transmission of toxoplasmosis. Furthermore, depending on the socio-economic status of the individuals, it seems that seroprevalence is higher in older adults. Drinking unfiltered water, oocyst-containing water, and water from recreational facilities all contribute to the spread of this disease. Due to improvements in socio-economic conditions, drinking quality water, hygiene standards, consumption of frozen meat, changes to livestock systems, and feeding autoclaved food to cats, toxoplasmosis rates have dropped in many countries during the past 20 years (Khairulla *et al.,* 2024).

Transmission

Contaminated food and water, ingesting tissue cysts or oocysts, and congenital transmission are reportedly the main ways of disease transmission. Bears, foxes, raccoons, skunks, and other carnivorous animals from natural environments can also get toxoplasmosis by eating tissue cysts (Zhu S *et al.,* 2023). Humans contract toxoplasmosis when they eat contaminated raw meat, such as lamb or pork. Bradyzoites, which are parasites, are released when eaten tissue cysts are broken down by a variety of proteolytic enzyme activity in the host's stomach. It has been demonstrated that this parasite is incredibly resistant to proteases and endures in the host organism's small intestine. Congenital transmission, which occurs during the acute phase of toxoplasmosis, has also been reported (Li J *et al.,* 2021). Tachyzoites are infectious stage of parasite that infect the foetus after crossing the placenta of mother (Khairulla *et al.,* 2024).

Clinical Symptoms

Although both competent and immunocompetent persons can get the disease, especially retinochoroiditis, most immunocompetent people would not have symptoms for the rest of their lives. In addition to symptoms similar to infectious mononucleosis, such as myalgia, sore throat, myocarditis, maculopapular rash, fever, meningitis, polymyositis, muscle pain, malaise, pneumonia, and psychomotor disorders, infected individuals may have asymptomatic cervical lymphadenopathy during an acute systemic infection.

Ocular Toxoplasmosis: Ocular toxoplasmosis (OT) often causes discrete, localised, white-looking retinal lesions that are usually less than 1,000 microns in size. The distinctive "headlights in the fog" picture is caused by a substantial vitreous inflammatory response. Retinochoroidal inflammation usually lasts two to four months with primary or recurrent eye infections (Aleixo *et al.,* 2016).

Toxoplasmic Encephalitis: Even in the age of extremely aggressive antiretroviral therapy, toxoplasmic encephalitis (TE), which is usually brought on by the reactivation of latent infections, remains a major cause of morbidity and death in AIDS patients. Seizures, ataxia, dementia, and lethargy are among the nonspecific symptoms that are noted. The emergence of many brain abscesses is the most distinctive symptom of *T. gondii* infection in AIDS patients; however, it is not pathognomonic. The brain regions most frequently affected by *T. gondii* are the corticomedullary junction and basal ganglia (Khairulla *et al.,* 2024).

Congenital Toxoplasmosis: Newborns with congenital toxoplasmosis may have no symptoms or develop retinochoroiditis and central nervous system damage. Although the risk of vertical transmission is greater in the latter stages of pregnancy, the infection is usually more severe if it is transmitted early in pregnancy. The commonly observed signs of the infection in a pregnant

woman are increasing the risk of abortion, stillbirth, live births with birth defects such hydrocephalus or microcephalus, motor problems, brain and retinal damage, and signs of mental illness. The retinal lesions in congenitally infected newborns are frequently found in the macula, the area responsible for central vision The children who develop blindness or nearsightedness as a result of toxoplasmosis will be disabled for years as congenital Ocular toxoplasmosis (OT) is typically more dangerous for vision than acquired infections (Li J *et al.,* 2021).

Diagnosis:

For early discovery, prevention of transmission, and as a guide for treatment options for pregnant infected women, diagnostic evaluation is crucial. Serological testing is the first diagnostic method used to detect both current and past illnesses. Immunoglobulin G (IgG) and immunoglobulin M (IgM) antibodies are detected in maternal blood samples using serum markers. An infection with *T. gondii* is indicated by these antibody markers. Numerous serological testing methods, include Sabin–Feldman dye tests, indirect fluorescent antibody tests, and enzyme immunoassay tests, can be used to identify them. To distinguish between acute and chronic infections, it is crucial to carefully assess IgM and IgG titers. IgM titers grow sharply in response to acute sickness five days to weeks after the original exposure (Khairulla *et al.,* 2024).

In pregnant women, antibodies against *Toxoplasma gondii* are detected by the Toxoplasmosis test in a TORCH panel to evaluate serious congenital issues like vision loss, intellectual problems, and seizures of expected infants. Pregnant individuals with positive toxoplasmosis test results may undergo amniocentesis. An amniocentesis should be performed four weeks after a suspected infection and no earlier than 18 weeks of pregnancy. One common diagnostic method is polymerase chain reaction (PCR) fluid testing (de Oliveira *et al.,* 2016). PCR testing has a nearly 100% positive predictive value. In the past, cordocentesis-based foetal blood sample was regarded as the gold standard for diagnostic testing. Cordocentesis is no longer used since it poses greater risks to the foetus than amniocentesis. The most recent diagnostic research used foetal ultrasonography. For women who are suspected of or have been diagnosed with an acute infection, ultrasound is advised. Foetal ultrasonography examines the developing nervous system for abnormalities (Khairulla *et al.,* 2024).

Public Health Importance

Nearly all warm-blooded animals, including humans, domestic animals, and wild animals, are affected by the zoonotic protozoan parasite *T. gondii* (Al-Malki E. 2021). The first human sickness linked to *T. gondii* was discovered in the late 1930s. The prevalence of human infection varies globally, according to reports. A human toxoplasma infection can have

disastrous effects, especially for those with compromised immune systems, pregnant women, HIV/AIDS patients, children, and people with co-occurring illnesses. Toxoplasmosis is the primary cause of death for AIDS patients. In addition to miscarriage and other birth abnormalities, infection during pregnancy can result in retinochoroiditis, hydrocephalus, cerebral calcification, and congenital infections of the foetus.

Treatment

Dihydropteroate synthetase and dihydrofolate reductase inhibitors are recommended to treat toxoplasmosis (Hopper *et al.,* 2019)). Pyrimethamine is one of the dihydrofolate reductase inhibitors used to successfully treat this illness. This infection is also treated with drugs like trimethoprim and sulfamethoxazole (Konstantinovic N *et al.,* 2019). Nearly all prescription drugs are more effective against the tachyzoite stage than against bradyzoite-containing cysts (Khairulla *et al.,* 2024). Bradyzoite reactivation is commonly observed in immunocompetent patients, and cysts in the retina or uvea stay dormant (Cerutti *et al.,* 2020). There is no record of oocyst elimination with a trustworthy treatment. Pyrimethamine is used in conjunction with clindamycin or sulfadiazine to treat toxoplasmosis, which can occasionally cause ocular damage. Pyrimethamine and sulfadiazine together are believed to be beneficial when the immune system is failing. An alternative to it is sulfadiazine combined with pyrimethamine. Recombinant anti-Toxoplasma antibodies prevent early parasite invasion or tachyzoite multiplication. Up until the sixteenth week of pregnancy, expectant mothers can benefit from spiramycin, and various combinations of sulfadiazine, pyrimethamine, and folinic acid are recommended. Spiramycin has been widely used to reduce transmission from mother to child (Khairulla *et al.,* 2024).

Prevention & Control

After handling meat, poultry, or seafood, hands should be washed thoroughly with soap to prevent the spread of toxoplasma to people. Cutting boards, sinks, knives, and other objects that come into contact with raw meat should also be cleaned with soap and water. Either heating the meat to 67°C or cooling it to -13°C will remove meat tissue cysts. Exposure to 0.5 kilorad of gamma radiation also kills toxoplasma in tissue cysts. Women who are pregnant should avoid handling cats, touching dirt, and eating raw meat. Pet cats should only be fed cooked, canned, or dried food to stop the spread of this parasite. Pregnant ladies should refrain from emptying their cat's litter box on a daily basis.

A veterinary vaccination based on the live attenuated S48 strain was developed in recent years, marking a significant advancement in the development of toxoplasmosis vaccines (Chu KB *et al.,* 2021). Nevertheless, this immunisation has a short shelf life, is costly, and has adverse consequences. Additionally, this vaccine may result in pathogenic strains, making it

unsuitable for human usage. It is possible to develop a vaccine to prevent human toxoplasmosis, as several experimental studies have shown.

Conclusion

Human health is seriously threatened by toxoplasmosis, particularly for expectant mothers. For early detection, transmission prevention, and, as a guide, treatment options for pregnant infected women, diagnostic evaluation is crucial. As of right now, there is no human vaccination to prevent toxoplasmosis. To treat toxoplasmosis, inhibitors of dihydrofolate reductase and dihydropteroate synthetase are advised. Toxoplasma transmission to humans can be avoided by thoroughly cleaning hands with soap and water after handling meat, poultry, or shellfish.

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