

Toxoplasmosis and its Current Status in Ethiopia: A Review

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Abstract: Toxoplasmosis is one of most important worldwide zoonotic disease caused by the obligate intracellular, protozoan parasite known as *Toxoplasma gondii*. It is transmitted to humans by accidental ingestion of oocyst after cleaning an infected cat's litter box, accidental ingestion of oocyst with water and consumption of raw meat containing cyst causing fever, malaise, lymphadenopathy, pulmonary and multivisceral abnormality and encephalitis. The aim of this systemic review is to make a comprehensive document on prevalence and current status of toxoplasmosis in Ethiopia. Cats are definitive host for Toxoplasmosis but cattle, sheep and goat, poultry, pig and camel are reservoir host and facilitate the transmission of this disease to human. Toxoplasmosis common in Ethiopia and high prevalence is reported yet routine studies are needed to know accurate prevalence. Therefore, more studies in different geographical areas should be performed to design and implement appropriate intervention measures.

Key words: Toxoplasma • Toxoplasma Gondii • Obligate Intracellular

INTRODUCTION

Toxoplasmosis is one of most important worldwide zoonotic disease caused by the protozoan parasite known as *Toxoplasma gondii* [1]. It is an obligate intracellular which commonly transmitted to humans by accidental ingestion of oocyst stage of the parasite after cleaning an infected cat's litter box, accidental ingestion of oocyst with water and consumption of raw meat containing cyst [2]. Among meat producing domestic animals pigs, sheep and goats relatively often harbour *Toxoplasma gondii* cysts in edible tissues and, therefore, raw or undercooked meat from these animals constitutes a major risk to humans. In areas where goat milk is utilized, unpasteurized milk from acutely diseased goats is also an important source of infection especially to children [3].

Toxoplasma gondii can also be transmitted transplacentally from the mother to the fetus if the infection is contracted during pregnancy and cause abortion or congenital deformity [4]. *T. gondii* has a complex life cycle with asexual reproduction taking place in diverse tissues of mammals and birds (secondary hosts) and sexual reproduction taking place in digestive

epithelium of cats (primary host) [5]. Cats mainly infected by ingesting animal flesh like sheep pig mouse birds etc. encysted with *T. gondii* and rarely by ingesting oocysts directly from the feces of other cats [6]. Infected cats are usually asymptomatic and begin to shed unsporulated (noninfectious) oocysts (up to one million per day) in their feces one to two weeks after exposure [7].

Epidemiological distribution of toxoplasmosis is worldwide, but reported that very high seroprevalence of toxoplasma gondii in South America and Africa including Ethiopia [1]. Toxoplasmosis infection occurs in every individual but severe in immunocompromised patients. Individuals those have previously acquired toxoplasmosis, with or without manifestation of the disease may suffer a devastating relapse if their immune defences, particularly cell-mediated immunity are impaired as in the case of Acquired Immuno Deficiency Syndrome-AIDS [3]. The incidence of toxoplasmosis became increasing in Ethiopia, but there is only few documentation and understanding about the disease. Therefore, the objective of this paper is to review the available documents about ways of transmission to human and animal, diagnosis, treatment and control of toxoplasmosis.

Literature Review

Etiology: *Toxoplasma gondii* is the causative agent of Toxoplasmosis. It is an obligate intracellular protozoan parasite in the phylum Apicomplexa. Fyllum apicomplexa contain many genera of intracellular parasite like *Eimeria*, *Babesia*, *Theileria*, *Cyclospora*, *Isospora*, *Plasmodium*, etc. which are known to cause severe disease in animals and human [8].

T. gondii has three infective stage namely tachyzoite, bradyzoite and oocyst. tachyzoite is rapidly multiplying and invasive stage found in tissues of intermediate host (non felid domestic animal and human) [5]. Conversion of tachyzoite result Bradyzoites, which is slowly dividing in tissue cysts in muscle of intermediate host which would infect cat and the third stage an environmental stage, Oocysts (containing sporozoites) developed in intestinal wall of cat and shed with its feces [3]. These infective stages are crescent-shaped cells, approximately 5 micrometer long and 2 micrometer wide, with a pointed apical end and a rounded posterior end. They are enclosed by complex membrane called pellicle which helps to structural integrity and motility [9].

A dissemination form, Tachyzoites, is able to invade virtually all vertebrate cell types, where they multiply in a parasitophorous vacuole and migrate into tissue to form slow-dividing stage, Bradyzoites, which known as tissue cyst [7]. Tissue cysts are more or less spheroid in brain cells or elongated in muscular cells. They vary in size from 10 micrometer for the younger cysts, containing only two bradyzoites, to up to 100 micrometer for the older ones, containing hundreds or thousands of densely packed bradyzoites. The cyst wall consists of a limiting membrane presenting numerous invaginations and an underlying layer of electron-dense granular material [10]. Bradyzoites are resistant to the acid pepsin (1 to 2 hr survival into pepsin and HCl) allows their transmission through ingestion. Mature oocysts, containing Sporozoites, are 12 to 13 micrometers in length and ovoid shape that after sporulation contain two sporocysts, each containing four sporozoites. The oocyst wall is an extremely robust multilayer structure protecting the parasite from mechanical and chemical damages. It enables the parasite to survive for long periods, up to more than a year, in a moist environment [9].

Ways of Transmission and Life Cycle: The life cycle of *T. gondii* alternates between two hosts, definitive (sexual reproduction) and intermediate (asexual replication) hosts. The oocyst ingested by human, herbivores and chicken release sporozoites which develop into tachyzoites that can invade and multiply by sexual

reproduction and then migrate to tissues to form tissue cyst bradyzoites [11]. Humans can acquire infection in two ways, ingestion of oocyst from cat with contaminated water, food and soil and ingestion of bradyzoites in infected flesh [12]. Transplacentally, tachyzoites infect fetus in pregnant women [1].

The felids get infection when fed on the flesh of infected animal by ingesting tissue cyst bradyzoites and sexual reproduction occurs only in felids (domestic and wild cats)[5]. After the ingestion of cysts present in tissues of an intermediate host, the cyst wall is destroyed by gastric enzymes. Bradyzoites penetrate intestinal cell where they undergo a self-limiting number of asexual multiplications, characterized by the development of merozoites within schizonts [7]. Then, after this first step, it start sexual development with the formation of male and female gametes (gametogony) and oocysts formed after fertilization which liberated by the disruption of the cell and excreted as unsporulated forms in cat feces [6].

In the external environment the oocyst under goes the process of sporogony after a few days and form sporulated oocyst containing two sporocysts (each containing four haploid sporozoites) by a meiotic reduction and morphological changes [13]. Cats begin the shedding of oocysts 3 to 7 days after the ingestion of tissue cysts and may continue for up to 20 days. About more than 100 million oocysts can be released in feces infected cats. These oocysts infect a wide range of animal (intermediate host) almost all warm blooded animals including domestic ruminant and birds when ingested with food or water and also infective for cats but less efficient [9].

The parasite undergoes only asexual development in the intermediate hosts. After ingestion, sporozoites are liberated from oocyst and penetrate the intestinal epithelium, where they differentiate into tachyzoites. Tachyzoites rapidly replicate by endodyogeny inside any kind of cell and disseminate throughout the organism [14].

Tachyzoites are converted to a tissue cyst (bradyzoite) as early as 7 to 10 days postinfection and may remain throughout life in most hosts, predominantly in the brain or musculature [7]. The bradyzoites will infect the intestinal epithelium of the new host and differentiate back into the rapidly dividing tachyzoite stage for dissemination throughout the body. In addition, if the acute phase occurs during pregnancy, the parasite can cross the placenta and infect the fetus (congenital transmission). A role for this vertical transmission in maintaining high levels of infection in some species has been suggested [14, 15].

Clinical Signs of Toxoplasma Gondii Infection

Asymptomatic Infection in Human: Most persons infected by *T. gondii* after birth are asymptomatic unless immunosuppression occurs and the organism reactivates, however, some develop a mild disease or in rare cases, a more severe systemic illness [16]. Once infected, humans are believed to remain infected for life however; there is ongoing research on whether chronic *T. gondii* infection has an effect on reaction time [17].

Symptomatic Infection in Human: A minority of healthy persons infected with *T. gondii* after birth develop mild symptoms such as fever, malaise and lymphadenopathy [16]. However, in rare cases, humans who were previously healthy have developed severe and even fatal disease, including pulmonary and multivisceral involvement, possibly from more virulent types of the organism [18]. Congenital toxoplasmosis generally occurs when a woman is newly infected with *T. gondii* during pregnancy and encephalitis is the most common clinical presentation of toxoplasmosis among persons with AIDS [19].

Toxoplasmosis Manifestation in Different Livestock Species

Pig: Clinical toxoplasmosis in pigs is rare but there are cough, lack of coordination, tremors and diarrhea, with a 50% mortality rate, still-births, premature births and deaths soon after birth [20].

Cattle: Although cattle are considered a poor host for *T. gondii* can be successfully infected with *T. gondii* oocysts but due to innate resistance the parasite is eliminated or reduced to undetectable levels within a few weeks [21]. There is no confirmed report of clinical toxoplasmosis in cattle but there is an assumption as it causes abortion in cattle [22].

Camel: Acute toxoplasmosis is observed in camel with dyspnea, many tachyzoites can be found in lungs and plueral exudates and *T.gondii* can be isolated from camel meat using cat biopsy [23].

Poultry: Toxoplasmic chickens show clinical signs like encephalitis, chorioretinitis, peripheral neuritis, torticollis, an inability to stand and lateral recumbancy [24].

Sheep and Goat: *Toxoplasma gondii* causes abortion and neonatal mortality in sheep and goat, congenitally-infected lambs that survive the first week after birth usually grow asymptomatic and can be a source of infection for humans while adult goats can develop

clinical toxoplasmosis involving liver, kidneys and brain [25]. In sheep and goats a primary infection established during pregnancy may result in apparent infertility or in stillbirths and abortion, according to the stage of pregnancy at which infection was initiated. In a typical case of abortion, a ewe or doe infected in mid-gestation produces a stillborn lamb/kid a few days earlier than the predicted end of pregnancy. The aborted fetus is often accompanied by either a weak sibling or a 'mummified' fetus [26].

Pets: *Toxoplasma gondii* infection in cats is clinical significant, most severe in congenitally infected kittens and affected cats may appear depressed and anorexic and die suddenly with no obvious clinical signs [27]. Pneumonia is the most important clinical manifestation of feline toxoplasmosis and other common clinical manifestations are hepatitis, pancreatic necrosis, myositis, myocarditis, uveitis, dermatitis and encephalitis [28]. Primary toxoplasmosis in dogs is rare but common clinical manifestations of toxoplasmosis in dogs are pneumonia, hepatitis and encephalitis [29].

Diagnosis of Toxoplasmosis: The diagnosis of *T. gondii* infection or toxoplasmosis can be established by serologic tests, amplification of specific nucleic acid sequences by PCR, histologic demonstration of the parasite and/or its antigens by immunoperoxidase stain or by isolation of the organism [30].

Serologic Tests: The use of serologic tests for demonstration of specific antibody to *T. gondii* is the initial and primary method of diagnosis [31]. A combination of serologic tests is required to measure different antibodies that possess unique patterns of rise and fall with time after infection [32]. *Toxoplasma* Serological Profile (TSP), ELISA and AC/HS tests are used to determine infection acquired in the recent or more distant past [33].

PCR: PCR amplification is very important for detection of *T. gondii* DNA in body fluids and tissues PCR enables an early detection of *T. gondii* DNA in brain tissue, cerebrospinal fluid (CSF), Vitreous and aqueous fluids, bronchoalveolar lavage (BAL) fluid and blood [34].

Histologic Diagnosis: Demonstration of tachyzoites in tissue sections or smears of body establishes the diagnosis of the acute infection [30]. The immunoperoxidase technique, rapid and simple, which uses antisera and Wright-Giemsa stain, is both sensitive

and specific to demonstrate the presence of the parasite in the central nervous system (CNS) or in impression smears of biopsy tissue in acute infection or reactivation of latent infection [33].

Isolation of *T. gondii*: Isolation of *T. gondii* from blood or body fluids establishes that the infection is acute [35]. Attempts at isolation of the parasite can be performed by mouse inoculation or inoculation in tissue cell cultures of virtually any animal tissue or body fluid [36].

Treatment: The most effective treatment of toxoplasmosis is a combination of the oral antibiotic drugs pyrimethamine and sulfadiazine plus the B vitamin folic acid [37]. Pyrimethamine is tolerated by most people, but it has some side effects like nausea, vomiting and diarrhea in the first few days of treatment while Sulfadiazine also causes skin rashes, itching and sensitivity to light, joint pain, fever and chills [38]. Some times, the combination of pyrimethamine + sulfadiazine may not be appropriate for everyone, therefore, another treatment option includes: pyrimethamine + clindamycin (IV) + folic acid [39]. For people who cannot tolerate pyrimethamine, sulfadiazine or clindamycin, the combination of: pyrimethamine + azithromycin, atovaquone + pyrimethamine and atovaquone + sulfadiazine can be used [40].

Prevention and Control: There is no effective vaccine to prevent *T. gondii* infection in animals and humans; therefore, practicing good hygienic measures is the best option to minimize transmission of *T. gondii* to humans [41]. Oocysts are almost indestructible but tissue cysts in meat can easily killed by freezing meat in a household freezer and by cooking until the internal temperature reaches 66°C [20]. Avoiding the handling of stray cats, especially pregnant women and keeping cats indoors are good prevention measures [6].

Current Status of Toxoplasmosis in Ethiopia

The Status in the Animal: Some studies conducted in different geographical location of Ethiopia indicated a high seroprevalance of *toxoplasma gondii* infection in sheep, goat and pig. The early studies on has reported overall seroprevalance of 19.5% [42] and 24.1%[43] of toxoplasma antibodies in goats using indirect haemagglutination test (IHAT-2) and modified agglutination test (MAT) respectively. The serological survey conducted in central and southern regions of Ethiopia by Teshale *et al.* [44] indicated 74.9% of overall prevalence of *Toxoplasma gondii* in goat using modified agglutination test.

Recent study conducted in southern Ethiopia reported the overall seroprevalance of 26.09% *toxoplasma gondii* antibodies in sheep and goats using Indirect Enzyme Linked Immunosorbent Assay (ELISA) as a diagnostic tool [45]. The data reported on seroprevalance of *toxoplasma gondii* in pig in Ethiopia is very rare, but Mulisa [8] indicated the overall seroprevalance of 32.7% in pig farms in and around Addis Ababa using modified agglutination test.

In definitive host, cat, the recent study conducted in Addis Ababa by Dubey *et al.* [46] reported that there were 33 seropositive cats (which are 91.6%) among 36 randomly sampled cats. Also they carried out the isolation of toxoplasma gondii from the heart of 26 cats in which 25 of which was seropositive and 1 was seronegative by the process of homogenization and inoculation to mice and this study was recorded as the frist study that isolated toxoplasma gondii from any host in Ethiopia.

Status in Human: In Ethiopia the highest prevalence (95.1%) from Butajira from patients found in 15-49 age groups, it is also reported that toxoplasmosis gondii is severe HIV/AIDS patients with 94% prevalence from Tikur Anbessa Specialized Hospital, Addis Ababa while minimum prevalence is reported from Adama (Table 1).

Study Area or Hospital	Population subjected in the study	No. sample	Serological test, cut-off titre	% of prevalence	References
Adama Hospital	People aged 15 days–65 years	65	MAT, 32	60.0	[3]
Butajira,					
Addis Ababa	Patients aged 15–49 years,	456	ELISA-VI	95.1	[47]
Addis Ababa	Hospitalized Patients	330	ELISA-BC	90.0	[48]
Addis Ababa	Pregnant women		LAT, 10	85.4	[49]
Jimma town, Southwestern Ethiopia	pregnant women	201	ELISA	83.6	[2]
Tikur Anbessa					
Specialized Hospital, Addis Ababa	HIV/AIDS patients	150	Human-ELISA, Germany	94	[50]
Mettu Karl Hospital, Ethiopia	HIV/AIDS Patients	120	different model checking and model diagnostic test	60	[51]

LAT, latex agglutination test (Eiken Co., Japan); MAT, modified agglutination test; ELISA, enzyme-linked immunoabsorbent assay; ELISA-IN, ELISA in house ; ELISA-BC, ELISA (BioCheck Inc., USA); ELISA-VI (Viro-immuno Diagnostica GmbH, Germany).

CONCLUSION

Toxoplasmosis is one of most important worldwide zoonotic disease caused by the protozoan parasite, *Toxoplasma gondii* which commonly transmitted to humans by accidental ingestion of oocyst after cleaning an infected cat's litter box, accidental ingestion of oocyst with water and consumption of raw meat containing cyst. *Toxoplasma gondii* can also be transmitted transplacentally from the mother to the fetus and cause abortion or congenital deformity and severe in immunocompromised patients. Studies conducted in different geographical location of Ethiopia from 2007 to 2015 indicated a high seroprevalance of *toxoplasma gondii* infection in human, sheep, goat and pig.

Recommendations: Since *T.gondii* is zoonotic and its oocysts can be acquired from infected cat litter care should be taken. Consumption of raw meat and drinking contaminated water should be avoided. Further routine studies should be carried out in Ethiopia to estimate true prevalence in different geographical area using sophisticated diagnostic tools. Appropriate prevention designs should be made and mitigation measures should be implemented.

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