

# Infection of *Toxoplasma gondii* in Humans and Livestock Animals: An Emerging Silent Threat for Bangladesh

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## Abstract

*Toxoplasma gondii* is an intracellular, zoonotic protozoan parasite that causes toxoplasmosis. It can potentially infect almost all mammalian and avian hosts including one-third of the human population world-wide. The major target group of the parasite includes immunocompromised patients (e.g. AIDS, cancer, organ transplantation) and fetus bearing pregnant women where it develops toxoplasmic encephalitis, myocarditis, chorioretinitis and abnormal fetal brain development or stillbirths respectively. In this review, we have presented the current status of *T. gondii* infection in livestock animals and human population in Bangladesh to assess the country-wide relative risk. Although exact prevalence is difficult to predict due to the scarcity of data, nevertheless existing literature suggests that 16% - 39% humans and 8% - 70% domestic animals are infected with *T. gondii*, which implies Bangladeshi population is at high risk of toxoplasmosis. Furthermore, we have proposed a potential area of research to decipher the genetic diversity and transmission routes of *T. gondii* infection into Bangladeshi population.

## Keywords

*Toxoplasma gondii*, Seroprevalence, Livestock Animals, Humans, Bangladesh

## 1. Introduction

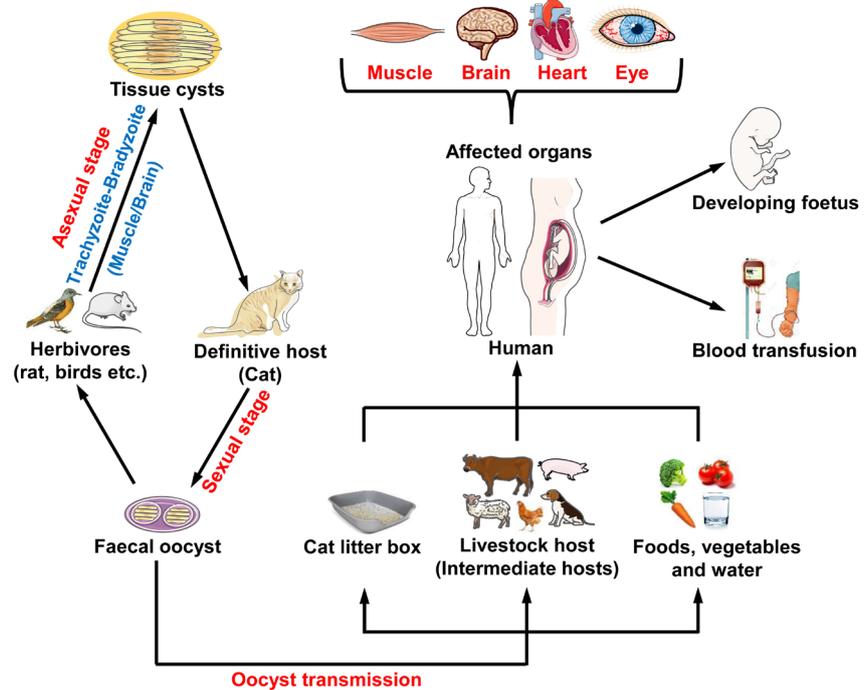
*Toxoplasma gondii* is an important zoonotic protozoan parasite that can infect any warm blooded animals including humans and causes toxoplasmosis [1]. *T. gondii* belongs to the group of phylum Apicomplexa that was first identified in African rodent "*Ctenodactylus gundii*" in 1908 by Nicolle and Manceaux at Pasteur institute of Tunis. *T. gondii* is widely distributed in nature and therefore in-

fection rate varies from 10% - 90% world-wide depending on environmental or socioeconomic factors and geographic locations [2]. Following an acute infection in healthy immunocompetent individuals, the fast replicating tachyzoite generally develops either mild flu-like symptoms and lymphadenopathy or asymptomatic clinical outcome. Importantly, active immune system can eliminate majority of *T. gondii* tachyzoite, but a portion of them undergoes developmental switching into slow replicating dormant bradyzoites particularly in skeletal muscle and brain [3] [4]. The transition from tachyzoite to bradyzoite is critical for establishing chronic and persistent infection. However, in immunocompromised patients (e.g. AIDS, organ transplantation and cancer), the parasite can be fatal by reactivation of latent infection which can cause toxoplasmic encephalitis, myocarditis and eye disease, mostly retinochoroiditis [5] [6]. In addition, pregnant women constitute special risk group, because after primary infection, the parasite can easily transmit into developing fetus and thereby causes abnormal brain development, stillbirth or even abortion of the unborn child depending on the stage of infection [7]. As *T. gondii* is capable of infecting both animal and human, this has major relevance on medical and veterinary health and economy [8].

*T. gondii* has been found to be associated with many other diseases. A case control study has confirmed the presence IgG antibodies to *T. gondii* in patients with diabetes mellitus [9]. The authors found two folds higher rate of *T. gondii* infection in diabetic patients than healthy controls. The possible reason has been identified as *T. gondii* mediated destruction of beta cells of pancreas, which, therefore, impacts on insulin secretion [9]. Contrary, another study found a lack of association of *T. gondii* with diabetes mellitus [10]. Therefore, proofing the hypothesis “chronic *T. gondii* infection is a risk factor for developing diabetes mellitus” needs further experimental validation. In addition, *T. gondii* infection can be associated with autism [11]. Since autism affects male more frequently than female with a ratio of 4:1 (male: female), and the presence of increased concentration of testosterone in latent toxoplasmic individual than toxoplasma negative, it may suggest the possibility of association of *T. gondii* infection with developing autism spectrum disorder in male [11] [12]. From the above point of views, *T. gondii* infection can be considered as one of the major public health problems world-wide.

## 2. Life Cycle and Transmission of *T. gondii*

*T. gondii* has two distinctive stages (sexual and asexual) in their life cycle where the sexual part is accomplished in the intestine of the definitive host “Cat” and asexual reproduction occurs in an intermediate host, for instance, livestock animals or human [13]. Sexual reproduction in cat’s intestine leads to the development of *T. gondii* Oocyst which can shed into the environment through cat faeces [14] (Figure 1). Therefore, Oocysts contaminated foods and water are considered as the major transmission route of the parasite into the human [15].



**Figure 1.** Life cycle and transmission of *T. gondii* into domestic animals and humans.

However, due to the persistence of *T. gondii* in muscle and brain of warm-blooded live stock animals, the parasite can transmit into human via eating raw or undercooked meats/meat products [16]. Furthermore, developing fetus can get the infection from acutely infected mother through placental transmission [17]. In addition, the parasite may also transmit through blood transfusion particularly in  $\beta$ -thalassemic patients who require a constant supply of blood from other individuals [18] (Figure 1).

### 3. Prevalence of *T. gondii* in Major Livestock Animals and Humans of Bangladesh

Several studies have been performed on the prevalence of *T. gondii* in livestock animals (Table 1) and humans (Table 2) in Bangladesh. For the first time, Samad and colleagues have identified the presence of anti-*T. gondii* antibodies in the blood of sheep, goats and cattle at Mymensingh [19] [20]. The authors showed that 18% sheep, 12% - 38% goats and 16% cattle were infected with *T. gondii*. Another study conducted in 2011 by Shahiduzzaman M, has identified *T. gondii* antibodies in 40% sheep, 32% goats and 12% cattle. However, the highest infection rate was observed recently in livestock animals of Mymensingh in a study conducted by Rahman and colleagues who identified *T. gondii* antibodies in 70% sheep, 61% goats and 27% cattle [21]. The different infection rate might be due to either increasing the incidence of *T. gondii* with time or variation of test results in diagnostic approaches.

On the other hand, a very few studies has been conducted on human particularly in pregnant women of Bangladesh where the authors have identified anti-*T.*

**Table 1.** Prevalence of *T. gondii* in domestic animals of Bangladesh.

Host animal	Study location	Sample size (N)	Prevalence (%)	Test	Reference
Goats	Mymensingh	15	38	LAT	[19]
Sheep		17	18		
Goats	Mymensingh	306	12	LAT	[20]
Cattle		205	16		
Pigs	All over Bangladesh	200	20	HA	[22]
Sheep		15	40		
Goats	Mymensingh	17	32	Toxo-test MT	[23]
Cattle		22	12		
Sheep,		83	70		
Goats	Mymensingh	146	61	Toxo-test MT	[21]
Cattle		37	27		
Goats	Rajshahi	145	55	Toxo-test MT	[24]
Sheep	Dhaka, Mymensingh	552	12		
Goats	Sirajganj, Chittagong	300	16	ELISA	[25]
Cattle		252	8		

LAT: Latex agglutination test, HA: Hemagglutination assay, ELISA: enzyme linked immunosorbent assay.

**Table 2.** Prevalence of *T. gondii* in humans of Bangladesh.

Host	Study location	Sample size (N)	Prevalence (%)	Test	Reference
Women with Gyneco-Obstetrics problem	Mymensingh	302	16	LAT	[27]
Pregnant women	Dhaka	286	39	ELISA	[26]
Pregnant women	Dhaka	46	33	ELISA	[29]
Pregnant women	Mymensingh, Rangpur	87	25	Toxo IgG/IgM combo rapid Test	[30]

LAT: Latex agglutination, ELISA: enzyme linked immunosorbent assay.

*gondii* antibodies in the blood of 16% - 39% of pregnant women using different serological tests (Table 2). These studies confirmed that pregnant women are more susceptible to *T. gondii* infection than non-pregnant women. Furthermore, the higher prevalence rate was observed in the age group of 31 - 45 years [23] [26]. *T. gondii* infection has been found to be associated with abortion (5.3%), stillbirth (2%) and prenatal (<1%) death of fetus in pregnant women [27]. In addition, Ashrafunnessa and colleagues have confirmed that *T. gondii* infection was higher in poor women (53%) compared to women with upper socioeconomic status (22%) [26]. Recently Naheen *et al.* have confirmed that the rate of persistent infection (84% IgG) was higher than acute infection (16% IgM) in a study on thirty nine *T. gondii* positive women [28]. Altogether these data clearly indicate the presence of *T. gondii* infection in Bangladesh. Although these studies have shown the presence of anti-*T. gondii* antibodies in the blood of mostly domestic animals and to a lesser extent in human through various serological assays (Latex agglutination, Toxo-MT test, ELISA), the more accurate

detection technique, for instance, polymerase chain reaction (PCR) was not used for confirming the diagnosis. It can be stressed that the above-mentioned studies in human were carried out only on pregnant women, therefore the possibility of *T. gondii* infection on other risk groups for instance immunocompromised (HIV, cancer, transplant) or thalassemic patients has not yet been investigated.

Another limitation that seriously hindered the assessment of the country-wide prevalence of *T. gondii* infection is scarcity of country-wide data. Our analysis revealed that only the small-scale prevalence studies were conducted restricted to a certain geographical locations within Bangladesh seriously hampering the precise estimation of the actual prevalence of *T. gondii* infection in Bangladesh. For instance certain geographical locations such as Dhaka, Mymensingh, Rangpur and Rajshahi are over represented and the whole southern and north-eastern part of Bangladesh is either under-represented or missing altogether. This incomplete data makes the prevalence estimation incorrect and more importantly may lead us to underestimate the prevalence of overall *T. gondii*. It is likely that certain geographical area in Bangladesh may serve as hot-spot for *T. gondii* infections. Moreover the usage of serological assays for the diagnosis of *T. gondii*, make it prone to underestimation of *T. gondii* infection since molecular assays are required to diagnose the parasite in distinct developmental stages. Therefore, it is very difficult to conclude the exact prevalence of *T. gondii* infection in Bangladesh. However, it can be said that the infection rate may be even higher than that found by previous studies in this country and further studies on other risk groups may address this. In addition, there is no data available on the genotyping of the *T. gondii* strain in Bangladesh. To the end it can be concluded that further research has to be performed to find out the exact prevalence and types of *T. gondii* strain present in Bangladesh.

#### **4. A Possible Link between *T. gondii* Infection and Stillbirths/Neonatal Deaths Rates: A Grand Challenge for Bangladesh**

Bangladesh has made giant leaps toward achieving the Millennium Development Goals (MDGs). However to attain Sustainable Development Goals (SDGs), certain areas demand for urgent attention including reproductive, maternal, newborn and child health. In a recent study Abir *et al.* analyzing the data from the Bangladesh Demographic and Health Surveys for four years identified 29,094 cases of stillbirths and estimated rate of stillbirth in Bangladesh as 28 in 1000 births (95% CI: 22, 34) [31]. Although the authors tried to correlate the cases of stillbirth with various social parameters such as education of mother, majority of the cases remains unexplained implying that natural causes like parasite infection can also be responsible for certain fraction of the stillbirth cases. In this circumstance, it is of utmost importance to identify the etiology of stillbirths. Therefore an epidemiological survey of parasitic infections including *T. gondii* infection may reveal the hidden association of parasite infection and stillbirth in Bangladesh.

Although neonatal death rate has decreased significantly in Bangladesh in last 25 years (23.3 per 1000 live birth (LB) [32], the number is still high compared to other middle income countries. In this context, identifying the causes of neonatal deaths would be immensely beneficial to adopt a strategy to lower the death rates. In this context the prevalence of *T. gondii* infection in pregnant woman can enlighten to assess the risk of *T. gondii* infection for stillbirths and neonatal mortality.

## 5. Prevention Strategy of *T. gondii* Infection

Since *T. gondii* is mainly transmitted through eating undercooked or raw meats and meat-products, therefore the infection rate can be prevented by proper management of meat processing including use of gloves, washing cooking surface and utensils etc, ingestion of well cooked meats and meat products. Furthermore, *T. gondii* infection can be prevented by thoroughly washing oocyst contaminated foods and vegetables before eating. In addition, awareness of people particularly pregnant women could be done not to change cat litter without using proper safety. Extra precaution for instance screening of *T. gondii* infection in blood can be performed before blood transfusion. Currently, a live vaccine, S48 strain of *T. gondii* (Toxovax) is used for sheep but there is no vaccine available against *T. gondii* infection for human.

## 6. Conclusion

The current study has compiled enough evidence that indicates the presence of *T. gondii* infection in livestock animals and humans in Bangladesh beyond any reasonable doubt. The review also underpinned the urgent demand for using molecular approach, such as polymerase chain reaction (PCR) for confirming *T. gondii* diagnosis, to identify the strains and dissecting possible transmission routes of *T. gondii* in human and domestic animals. Such large scale molecular diagnosis based studies encompassing all the geographical regions in Bangladesh are required to estimate the true prevalence of *T. gondii*. One of the benefits of such large-scale studies includes the adaptation of potential strategies to reduce incidence and prevent the diseases associated with *T. gondii* in Bangladesh. This review is sought not only to provide the current status of *T. gondii* infection in Bangladesh and but also to encourage government and non-government organizations (NGOs) to undertake large scale studies to gain deeper insight into the association of *T. gondii* infection and stillbirths/neonatal deaths in Bangladesh.

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## Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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