REVIEW

TOXOPLASMOSIS IN MEXICO: EPIDEMIOLOGICAL SITUATION IN HUMANS AND ANIMALS

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SUMMARY

Toxoplasmosis is a parasitic disease widely distributed throughout the world, infecting a wide variety of animal species including humans. In Mexico, this parasite has been detected in different parts of the country, particularly in the tropical areas where the parasite can remain infective for long periods of time due to the environmental conditions (i.e. high temperature and humidity over the whole year). Several epidemiological studies have been conducted in both human and animal populations, but despite the wide distribution of the agent in the country, there is a significant lack of knowledge on the parasite transmission, treatment alternatives and control measures. The lack of feral cat populations and control measures in sites of meat production for human consumption are playing a role that has led to the wide spread of the disease in the country, particularly in tropical areas of Southeastern Mexico. For these reasons, this manuscript aims to review the published information on relevant epidemiological aspects of infection with *T. gondii* in humans and animals from Mexico.

KEYWORDS: Toxoplasmosis; Neglected disease; Mexico; Endemic; Zoonosis.

INTRODUCTION

Toxoplasmosis is a worldwide parasitic zoonotic disease produced by the protozoan *Toxoplasma gondii* (*T. gondii*). This intracellular parasite can infect all warm-blooded animals including humans, marine mammals and birds^{33,49,68,87}. Animals from the Felidae family play an important role in the epidemiology and maintenance of the disease since they can complete the life cycle of this parasite; they are the definitive hosts that can excrete thousands of environmentally resistant oocysts⁴⁷. Since its first description in rodents (Ctenodactylus gondii) in North Africa by NICOLLE & MANCEAUX in 1908, the parasite has been recognized as a zoonotic agent⁷⁷. At that time, the detection of *T. gondii* appeared to be only of academic interest, but when WOLF et al. found an associated encephalomyelitis in infants during 193998, T. gondii was identified as a cause of congenital disease. Currently, T. gondii is recognized as an important opportunistic pathogen of fetuses, newborns and patients with a variety of primary and secondary immunodeficiencies81. The most common source of infection for humans is through the ingestion of tissue cysts from undercooked meat, by eating food or drinking water contaminated with sporulated oocysts and congenital transmission⁸³.

Infection with the parasite can result in a broad range of clinical signs depending on the host animal species. *T. gondii* can be fatal in some species of marine mammals and marsupials⁶⁸. However, only a small percentage of exposed humans or other animals develop clinical signs

of the disease⁴⁷. The most dangerous complications of toxoplasmosis are found in patients whose immunity has been depressed by malignancies and anti-tumor therapy, those with acquired immunodeficiency syndrome (AIDS)⁵², or with immunosuppressive drugs following organ transplantation. Toxoplasmosis ranks high on the list of diseases that lead to the death of patients with AIDS⁷⁵. Additionally, in case of maternal infection acquired during pregnancy, Toxoplasma can infect the fetus with variable severity, depending on the trimester at which the pregnant woman acquired the infection, and on the efficacy of the placental barrier⁸⁹. The risk of congenital infection is lower when maternal infection occurs during the first trimester (10-15%) and higher when the infection occurs during the third trimester (60-90%)⁸⁴. However, congenital infection usually leads to more severe disease when it occurs during the first trimester⁶⁷.

The seroprevalence of human toxoplasmosis can range from 10 to 50% in temperate developed countries to over 80% in developing countries of the tropics⁷³. Mexico is among the developing countries where the infection is common due to environmental exposure. Sources of infection may vary greatly among different ethnic groups and geographical locations⁹⁴. Infective oocysts are everywhere and can contaminate water, soil, fruits or vegetables⁵³. Undercooked meat contaminated with tissue cysts may also be an important source of infection⁹⁴. In Mexico, the seroprevalence ranges from 15 to 50% among the general population⁶². Mexico is a large country with a human

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population in 2010 of more than 112 million, spread all over the country, and with very different ecological regions including subtropical areas, arid regions, temperate regions (mountains), and a very large coastal area of the Atlantic and Pacific Oceans. Areas with the highest prevalence are wet coastal regions of the Gulf of Mexico and the Pacific (64%), while the arid region scored the lowest prevalence (13%)⁹⁷. In many developing tropical countries, the presence of extensive or semi-extensive animal production systems (grazing animals) is very common, which increases the risk of contact with the agent⁷⁰. The wide differences of seroprevalence among geographical regions may be related to several factors, such as dietary habits and climate variations. The latter has a significant influence on the presence and persistence of infective oocysts, especially in tropical conditions where the temperature and precipitation can maintain the soil moisture, so that the oocysts remain viable in the environment for long periods^{76,80}.

In studies conducted on different populations of animals in Mexico, a wide distribution of the parasite has been found; reports exist on family pets (dogs and cats)^{15,31,39,63,74,85,92}, as well as animal species raised for food production (poultry, goats, sheep and pigs)^{11,34,50,60}, and wildlife species.

The aim of this paper was to review the published literature about the current status of relevant epidemiological aspects of *T. gondii* infection in humans and animals from Mexico.

HUMAN STUDIES IN MEXICO

Adults: The toxoplasmosis situation in the adult population from Mexico has been largely explored (Table 1). In a study in Merida, Yucatán, Southeast Mexico, a significant association between 100 cases of spontaneous abortion and infection with T. gondii has been reported. Antibodies to T. gondii were found in 47% of the studied population, using a Sabin-Feldman test with titers of 1:64 and 1:12899. In another study conducted in Oaxaca (a state located in Southern Mexico), the general seroprevalence was 3.8% (124/3229), with a slight variation depending on the rural community sampled (range 1.3%-8.9%). All sampled communities were grouped in eight areas (I to VIII) based on altitude, longitude and topography. The highest prevalence rate was found in the Tehuantepec zone with 8.9% (zone VI), this area being where the highest seroprevalence was registered, whereas the coastal region of Oaxaca (with an altitude of 0 to 400 m) showed prevalence rates of 2.4, 4.6 and 5%. In the central and northern regions of Oaxaca, rates of 1.3, 2.0 and 2.7% were recorded. This large variation in the seroprevalence found in the same state is highly dependent on the geography and microclimates (humidity, altitude and temperature) of each particular region. However, the lower prevalence was associated to the almost total absence of cats and the lack of meat in their diet⁶⁴. In 1992, from 29,279 blood samples evaluated from people in all the 32 states of the Mexican Republic, the highest prevalence rate was found in coastal areas (40-65%), in people with low socioeconomic status and also in women of reproductive age97.

In another study, 350 women with high-risk pregnancies were studied. From them, 122 (34.9%) were seropositive to IgG and 76 (20.7%) to IgM *T. gondii* specific antibodies. In the same study, a group of women with recurrent spontaneous abortions were serologically evaluated and presented a seropositivity of 44.9% for IgG and 33.3% for IgM *T. gondii* antibodies⁵⁷. Moreover, in the town of Comitan Chiapas, a southern

Mexican state, a prevalence of 5% of *T. gondii* antibodies was detected in the general population and in 18% of women at risk of abortion⁹⁰.

The presence of antibodies to T. gondii in 59 cat owners through the indirect ELISA was investigated; 38 cases (64%) were positive to IgG and 70.8% of their cats were positive to IgG, 8.3% to IgM and 62.5% to IgA. Cohabitation with T. gondii infected cats, feeding them with leftovers and raw viscera, and lack of control over how to manage their feces were identified as important risk factors associated with humans becoming infected with the parasite⁵⁶.

In a public hospital in Durango, Northern Mexico, which is characterized by arid and dry environmental conditions, 343 pregnant women were evaluated for *T. gondii*. From them, 21 (6.1%) showed IgG antibodies but none (0%) IgM antibodies; a multivariate analysis showed that infection was associated with living in houses with earthen floors, residing outside the state of Durango, and consumption of turkey meat²⁴.

In another report from the same region, a comparison of the seroprevalence of IgG and IgM *T. gondii* antibodies among patients at a psychiatric hospital and a population of blood donors as a control group was performed. IgG antibodies were found in 25 (18.2%) of 137 psychiatric patients and 16 (8.9%) of 180 controls. Regarding IgM antibodies, psychiatric patients showed 4.4% compared with 2.2% in the control group¹. In the same region (Durango), a prevalence of IgG antibodies in 32 (7.4%) of 432 healthy blood donors was reported, with 8 (1.8%) of them being also positive to IgM. The infection with *T. gondii* was associated with contact with cats. It was also determined that prevalence increases with age and decreases with a higher education level¹⁹.

The prevalence of infection with T. gondii was investigated in two populations exposed to solid waste using an ELISA test. Seropositivity of IgG was 21.1% out of 90 scavengers and 8.4% out of 83 waste workers. Regarding IgM antibodies, 2.2% were presented in the waste collectors, but none (0%) in the waste workers. The seroprevalence was associated with the consumption of food found in the garbage and lack of education¹⁶. The epidemiology of infection with *T. gondii* was studied in people from three rural regions from the state of Durango, using an ELISA test. It was found that 110 (23.8%) of 463 individuals evaluated had IgG antibodies and 10 (2.2%) of these were also positive for IgM. The high prevalence of infection was observed in participants older than 70 years of age and those with good conditions in their homes. Infection was also associated with the consumption of meat from turkeys and squirrels². In another study, the usefulness of filter paper-embedded blood (FPEB) for the diagnosis of *T. gondii* in pregnant woman was evaluated; IgM, IgG and IgG avidity was determined. IgM detection in FPEB was 92% sensitive and 100% specific. The results indicated that FPEB is useful to infer the infection phase, and thus to speed clinical decisions in congenital toxoplasmosis management³⁸. In a further study conducted in nine rural communities in the state of Durango, 439 pregnant women were evaluated through a commercial ELISA. In total, 36 (8.2%) women had IgG antibodies and 10 (2.3%) were also seropositive to IgM. All IgM positive sera showed high values of IgG avidity, suggesting a chronic infection. The seroprevalence was significantly higher in women of low socioeconomic status (14%) than in those with a higher socioeconomic status (6.6%). Multivariate analysis showed that infection with T. gondii had an association with dwellings with earthen floors²⁸.

 Table1

 Seroprevalence of Toxoplasma gondii in human adults from Mexico

Year	Region	State	Test	Category	Prevalence (%)	Patient tested	
1989	Southeast	Yucatán	SF	Women with miscarriages	47	100	Zavala-Velázquez et al., 1989 (99)
1991	Southeast	Oaxaca	IHA	General population	5.1	3229	Goldsmith et al., 1991 (64)
1992	Southeast Central Northern	Tabasco Estado de México Baja California Sur	IFA	General population	67.5 32.1 17.4	29 279	Velasco-Castrejón et al., 1992 (97)
1995	Central	Mexico	ELISA	Pregnant women Women with Miscarriages	34.9 IgG 20.7 IgM 44.9 IgG 33.3 IgM		Galvan-Ramirez <i>et al.</i> , 1995 (57)
1998	Southeast	Chiapas	IFA	General Population Pregnant women	5 18	50	Romero-Cabello et al., 1998 (90)
1999	Central	Jalisco	ELISA	General population owners cats	64 IgG	59	Galvan-Ramirez et al., 1999 (56)
2006	Northern	Durango	ELISA	Pregnant women	6.1 IgG	343	Alvarado-Esquivel et al., 2006 (24)
2006	Northern	Durango	ELISA	Mentally-ill patients Blood donors	18.2 IgG 4.4 IgM 8.9 IgG 2.2 IgM	137 180	Alvarado-Esquivel et al., 2006 (1)
2007	Northern	Durango	ELISA	Blood donors	7.4 IgG 1.8 IgM	432	Alvarado-Esquivel et al., 2007 (19)
2008	Northern	Durango	ELISA	Waste pickers Waste workers	21.1 IgG 2.2 IgM 8.4 IgG	90 83	Alvarado-Esquivel et al., 2008 (16)
2008	Northern	Durango	ELISA	Rural population	23.8 IgG 2.2 IgM	463	Alvarado-Esquivel et al., 2008 (2)
2009	Northern	Durango	ELISA	Pregnant women	8.2 IgG 2.3 IgM	439	Alvarado-Esquivel et al., 2009 (28)
2010	Northern	Durango	ELISA	Rural population (Mennonites)	30.3 IgG 3.3 IgM	152	Alvarado-Esquivel et al., 2010 (22)
2010	Northern	Durango	ELISA	Plumbers Construction workers Gardeners	6.6 IgG 8.4 IgG 1.4 IgM 6 IgG 2.4 IgM	61 203 168	Alvarado-Esquivel et al., 2010 (17)
2011	Southeast	Yucatán	ELISA	General population without cats contact	25 IgG 37 IgM	80	Jiménez-Coello et al., 2011 (69)
2011	Northern	Durango	ELISA	Mentally-ill patients General population	20 IgG 5.3 IgG	50 150	Alvarado-Esquivel et al., 2011 (29)
2011	Northern	Durango	ELISA	General population	6.1 IgG 2.1 IgM	974	Alvarado-Esquivel et al., 2011 (7)
2011	Northern	Durango	ELISA	Butchers General population	7 IgG 4 IgM 9 IgG 2 IgM	124 248	Alvarado-Esquivel et al., 2011 (14)
2011	Northern	Durango	ELISA	Patients with liver disease General population	13.3 IgG 2.7 IgM 10.7 IgG 3.3 IgM	75 150	Alvarado-Esquivel et al., 2011 (26)
2011	Northern	Durango	ELISA	Fruit and vegetable workers General population	7.5 IgG 1 IgM 7.8 IgG 2.8 IgM	200 400	Alvarado-Esquivel et al., 2011 (6)
2012	Northern	Durango	ELISA	Rural population	22.4 IgG 9.6 IgM	156	Alvarado-Esquivel et al., 2012 (5)
2012	Northern	Durango	ELISA	Patients with accidents at work General population	8.3 IgG 0.8 IgM 5.3 IgG 2.3 IgM	133 266	Alvarado-Esquivel et al., 2012 (27)
2012	Northern	Durango	ELISA	Elderly people	12 IgG 2.9 IgM	483	Alvarado-Esquivel et al., 2012 (13)
2012	Southeast	Yucatán	ELISA PCR	Women with miscarriages	55 IgG 20 IgM 19 PCR	100	Vado-Solís et al., 2012 (95)

ELISA: Enzyme-Linked ImmunoSorbent Assay. PCR: Polymerase Chain Reaction. SF: Sabin Feldman Technique. IFA: Indirect Fluorescent Antibody technique. IHA: Indirect Haemagglutination test.

In a community of Mennonites (ethnic German descent established in rural communities) from the state of Durango, it was found that 46 (30.3%) of 152 people had IgG antibodies to *T. gondii* and five (3.3%) also showed IgM seropositivity. The infection with *T. gondii* was associated with the presence of cats in homes, the consumption of livestock and pigeon meat, and the drinking of untreated water²².

There have been studies on workers occupationally exposed to water, wastewater and soil in the state of Durango. IgG antibodies were reported

in 4 (6.6%) of 61 plumbers, 17 (8.4%) of 203 construction workers and 10 (6.0%) of 168 gardeners; IgM antibodies were also found in three (1.5%) construction workers and four (2.4%) gardeners, but none (0%) in the plumbers. The multivariate analysis showed that infection with $T.\ gondii$ was positively associated with eating unwashed fruits and the meat of farm animals 17.

In a cross-sectional study of 80 individuals with no history of previous contact with cats, seropositivity for ELISA IgG and IgM was found in

29 (37%) and 20 (25%) of the cases respectively. From positive cases, 14 (18%) were positive to both antibodies. There was a significant association of seropositivity to IgM in individuals consuming pork and the meat of wild animals. Although participants did not have prior contact with cats, the infection was present in them⁶⁹.

In a case-control study, the association between 50 schizophrenic patients and a control group of 150 individuals was made using an ELISA test. A high seroprevalence of IgG antibodies to *T. gondii* was found in 10 (20%) of 50 patients with schizophrenia compared with the eight (5.3%) of 150 control subjects. IgG levels greater than 150 IU/mL were more frequently found in schizophrenic patients than in controls (10% *vs.* 2%, respectively). In the same study, two patients were recently diagnosed with schizophrenia and one showed IgM antibodies. The seroprevalence in this study was significantly higher in patients with a history of cleaning cat feces and suffering from simple schizophrenia²⁹.

Also in the state of Durango, *T. gondii* was monitored in the general population, finding 6.1% IgG positive cases and 2.1% of IgM antibodies in 974 individuals. IgG levels from 13-99, 100-150 and > 150 IU/mL were found in 14 (23.7%), three (5.1%) and 42 (71.2%) positive cases respectively. The infection was significantly associated with the consumption of pork and squirrel meat⁷. Considering that raw meat represents a high risk for infection with *T. gondii* cysts, a case-control study evaluating 124 butchers and 248 subjects from the general population as a control group was conducted. IgG antibodies were found in eight (7%) butchers and 22 (9%) of the control subjects using an ELISA test. IgG levels were > 150 IU/mL in seven (6%) of the butchers and in 14 (6%) of the controls. IgM antibodies were found in five (4%) of the butchers and four (2%) of the controls. No statistically significant differences were found between groups¹⁴.

In order to find an association between infection with T. gondii and patients with liver disease, a case-control study using an ELISA was conducted. IgG antibodies were found in 10 (13.3%) of 75 patients and in 16 (10.7%) of 150 control subjects. IgM antibodies were found in two (2.7%) patients and five (3.3%) controls. In this study seropositivity to T. gondii did not show any association with the diagnosis of liver disease. However, seropositivity in patients was associated with consumption of deer, quail and lamb meat²⁶. In a retrospective study, a significant association between the presence of IgG antibodies and an age ≥ 50 years was reported⁸.

Recent reports showed that 7.5% of workers exposed to raw and unwashed fruits and vegetables exhibit a significant association with seropositivity towards *T. gondii*⁶. The epidemiology of *T. gondii* has been studied in Tepehuan people (indigenous ethnic group from Northern Mexico) finding IgG seropositivity in 35 (22.4%) of 156 people. Furthermore, 15 (9.6%) showed IgM antibodies using ELISA⁵.

In another case-control study, patients with recent accidents at work showed an IgG seropositivity of 8.3% while the controls had a seroprevalence of 5.3%. Seroprevalence was significantly higher in patients who have accidents at work and low socioeconomic status; a positive association with consumption of pork was also found²⁷. In senior individuals (≥ 60 years of age), the seropositivity of IgG and IgM was 12% and 2.9% respectively. The presence of cats in the neighborhood, the consumption of pork, pigeon, iguana and armadillo meat showed a

positive association with infection with *T. gondii*¹³. In a study conducted in the state of Yucatán (Southeastern Mexico) in 100 women with spontaneous abortion, it was found that 58 had antibodies to *T. gondii*; 32 were positive to IgG; two to IgM; five to both IgG and IgM; six were positive to IgG and PCR; one to IgM and PCR; and 12 to IgG, IgM and PCR. Therefore, 55% of women were seropositive to at least IgG, 20% to IgM and 19% to PCR⁹⁵.

The Mexican national seroprevalence of *T. gondii* reported from two national bank sera was 60.1% to 62.6%. Coastal states and children showed the highest prevalences, while the midwest region showed a lower number of positive cases. A positive correlation of positive cases was associated with environmental temperature from 21 states where the prevalence was higher³⁶. In a recent meta-analysis of *Toxoplasma gondii* infection among the Mexican population from 1951 until 2012, the average prevalence was 27.97% and the weighted prevalence 19.27%. The weighted prevalence was higher in women with spontaneous abortions (35.13%), immunocompromised patients (28.54%) and mental patients (38.52%). The infection with *T. gondii* among the Mexican population showed a downward trend of 0.1%/year over a period of six years, which represents a decrease in the prevalence of 5.8%⁶².

Immunodeficient patients: In a retrospective study from 1988 to 1993 in 177 patients with AIDS in Mexico City, nine (5.09%) of them developed toxoplasmosis. In two patients, the initial manifestation of HIV infection was toxoplasmic meningoencephalitis and the remaining seven had been diagnosed with AIDS, with an average of ten months between the first event and the diagnosis of toxoplasmosis. In the same study, the count of TCD4+ cells was performed simultaneously to the diagnosis of toxoplasmosis, finding a mean of 78 cells/µL. These findings are in agreement with the common features of cerebral toxoplasmosis in HIV-infected patients with CD4+ cells below 100/μL⁴³. In another study on 92 patients infected with HIV, 46 (50%) were IgG seropositive to T. gondii by ELISA test and only one case (1%) was IgM seropositive. Of the 92 patients, 53 were HIV positive and 39 had AIDS. These findings highlight the importance of monitoring patients with HIV antibodies due to the high risk of cerebral toxoplasmosis, which is the second leading cause of death in these patients⁵⁸.

In the state of Yucatán, an IgG antibodies prevalence of 47% was found in 95 patients with HIV type 1. In the same study, 69% of 100 HIV-negative blood donors were used as a control group. The high prevalence in both groups suggested that toxoplasmosis was an endemic zoonosis in the Southeast Mexico⁶⁶.

A seroprevalence from 85 patients with hearing impairments in Durango, Mexico associated with *Toxoplasma gondii* IgG antibodies was studied, finding 8.2% positive cases. There were also positive cases in 10% of 50 patients undergoing hemodialysis, in 12.9% of 234 patients with visual impairments, and 6.8% of 103 persons at risk of immunosuppression. In total, 47 (10.0%) of 472 subjects had IgG antibodies to *T. gondii* and six (1.3%) of them also showed IgM antibodies. The infection with *T. gondii* was significantly associated with the consumption of undercooked meat, ingestion of raw cow's milk, the presence of cats in the household, and raising animals¹⁸.

Infants: The earliest report of *T. gondii* in children in Mexico dates from 1976, when five cases of fatal toxoplasmosis were reported from

the "Hospital Infantil de Mexico". In all cases, the parasite was identified in brain tissue and in some cases in the liver and lungs. Considering the early beginning of the neurological manifestations and severity of brain injuries reported, it was assumed that the five cases were of prenatal toxoplasmosis⁹¹. Likewise, in another early survey from the central region of Mexico, 667 children were reported with the presence of specific antibodies of *T. gondii*⁶⁵. Further investigations demonstrated a positive relationship between the indirect immunofluorescence (IFI) to *T. gondii* and clinical findings in a population of 328 children with cerebral palsy⁹⁰.

In a screening study conducted with 1003 newborn infants. two asymptomatic cases positive to ELISA IgM and IgG were found demonstrating that the ratio is about two cases of congenital toxoplasmosis per 1,000 newborns in Mexico City⁹⁶. A toxoplasmosis case in a 7-year-old child who received a liver transplant was described as demonstrating seroconversion to T. gondii antibodies after surgery; six months later, lesions compatible with T. gondii and CMV chorioretinitis appeared. The patient was treated and clinical manifestations improved and remained stable for 12 months until the recurrence of new lesions in the retina. These data concluded the feasibility of T. gondii transmission after organ transplantation⁵⁵. In another study IgG subclasses against T. gondii were detected in mother/newborn pairs. Antibodies of the IgG2 subclasses were more frequent among congenitally infected newborns than in non-infected. Active fetal antibody synthesis of the 4 subclasses was also demonstrated, IgG3 and IgG4 being related to clinical problems and IgG1 to protection from damage. The identification of IgG2, IgG3 and IgG4 in newborns and the comparison with the response of their mothers might be helpful to diagnose congenital transmission early after birth³⁷. This method of early diagnosis is consistent with previous studies^{82,88}. In the case of congenital transmission, *T. gondii* strain I was identified in four mothers and their newborns. These results provide information regarding the strains present in humans, but found no relationship between parasite load and genotype of T. gondii with vertical transmission. Two congenital cases of newborns showed severe disease, one fatal soon after birth and the other was born asymptomatic but developed a mild problem later on86. In a recent systematic review database, the prevalence of infection with T. gondii was 0.61% from 4833 asymptomatic newborns, whereas in 895 symptomatic newborns a prevalence of 3.0% was found⁵⁹. There are few studies concerning the genotype of T. gondii circulating in Mexico. No data on frequency in other regions about infecting genotypes is available.

STUDIES IN ANIMALS

Several studies on toxoplasmosis have been conducted in the different animal populations in Mexico, where a wide distribution of the parasite has been observed (Table 2).

Poultry: The prevalence of *T. gondii* in free breeding chickens (*Gallus domesticus*) is a good indicator of the presence of the parasite in the environment because chickens feed from the ground. In the first report made on free breeding chickens in Mexico, the presence of antibodies specific to *T. gondii* was found in 13 (6.2%) of 208 birds using a modified agglutination test. Likewise, *T. gondii* was isolated from six chickens and the genotyping of five isolates were type III and one was an isolate of type I⁴⁸.

Recent studies have reported antibodies to *T. gondii* in wild birds, using the modified agglutination test. Seropositivity was found in 17

(2.6%) of 653 birds, which included one out of two "Curve-billed thrashers" (*Toxostoma curvirostre*), two out of four ducks (one *Anas platyrhynchos* and one *Anas diazi*), one out of two eagles (*Aquila* sp), five (27.8%) out of 18 Mexican grackles (*Quiscalus mexicanus*), seven (1.3%) of 521 pigeons (*Columba livia*) and one (14.3%) out of seven quails (*Coturnix coturnix*). *T. gondii* was isolated in one out of six seropositive pigeons. The DNA obtained revealed the presence of an atypical genotype²⁰. In another study, antibodies to *T. gondii* were found in 36 (6.9%) of 519 chickens (*Gallus domesticus*) using the modified agglutination test. The seroprevalence of *T. gondii* was significantly higher in chickens raised in backyards (25.5%) than those raised on farms (4.9%)¹².

Cats: Domestic cats and wild felines are involved in the full cycle of *T. gondii*, because they can host sexually mature parasites in their gastrointestinal tract and excrete oocysts in their feces. In a study conducted between 1984 and 1999 in North, Central and South America, antibodies to *T. gondii* was found in 22.4% of 438 pumas (*Felis concolor*) and 51.7% of 58 bobcats (*Lynx rufus*)⁷⁴. In the state of Durango, a prevalence of 21% against *T. gondii* was found in 105 cats using the modified agglutination test. In this study, cats over one year of age had a significantly higher frequency of infection than younger cats (less than six months of age)¹⁵.

In another study of cats in the state of Colima (west coast of Mexico), *T. gondii* antibodies were found in 28.8% of 80 domestic cats using an indirect ELISA-IgG. Prevalence among cats fed with homemade food was higher than in cats fed commercial pellets⁶³. In Mexico City, 37 (21.8%) of 169 cats were seropositive for anti-*T. gondii* IgG using an indirect ELISA. The increase in frequency was related to age. The main risk factors were female gender, feeding cats with raw meat and infrequent cleaning of the litter box³¹.

In Northeastern Mexico, a study of *T. gondii* on wild cats revealed a prevalence of 69% in 26 ocelots (*Leopardus pardalis*)⁸⁵.

In the state of Yucatán, Mexico, the seroprevalence of *T. gondii* found in domestic cats was 75.5% (166/220) of IgM antibodies and 91.8% (202/220) to IgG. From the 220 studied cats, 79% (173/220) were PCR positive. The number of cats per household and low body condition is associated with reactivation of chronic infection³⁹.

Rabbits: In domestic rabbits, an isolated study reported the prevalence of antibodies to *T. gondii* as 26.9% from 77 out of 286 animals from three different farms, using an ELISA test⁵⁴.

Dogs: In dogs, antibodies to *T. gondii* were found in 52 (51.5%) of 101 dogs in the state of Durango, using the modified agglutination test⁴⁵. Frequencies have also been reported in 61.7% of stray dogs from Oaxaca, using indirect ELISA⁴⁰, although this species is not considered relevant in the epidemiology of the parasite, and these animals are considered as incidental hosts.

Pigs: The transmission of *T. gondii* to humans has usually been attributed to the ingestion of raw or undercooked meat. Pork meat in particular is considered as one of the most common sources of infection. A study conducted on 48 samples of pork meat from butchers in the state of Jalisco, Mexico revealed that all samples studied were negative following histopathology, and were PCR negative. However, IgG and IgM

 $\begin{tabular}{ll} \textbf{Table 2} \\ \textbf{Seroprevalence of } \textit{Toxoplasma gondii} \ \textbf{in animals from Mexico} \\ \end{tabular}$

Year	State	Animal	Specie	Prevalence (%)	Test	Reference
2004	State of Mexico	Chickens	Gallus domesticus	6.2	MAT	48
2011	Durango	Wild birds	Toxostoma curvirostre Anas platyrhynchos Anas diazi Aquila sp	2.6	MAT	20
			Quiscalus mexicanus Columba livia			
			Coturnix coturnix			
2012	Durango	Chickens	Gallus domesticus	25.5	MAT	12
			Raised in backyards Raised on farms	25.5 4.9		
2004	Mexico	Pumas	Felis concolor	16.7	IHA	74
2004	Mexico	Lynxes	Lynx rufus	66.6	ILAT	/4
2007	Durango	Domestic cats	Felis silvestris catus	21	MAT	15
2007	Colima	Domestic cats	Felis silvestris catus	28.8 IgG	ELISA	63
2008	Mexico City	Domestic cats	Felis silvestris catus	21.8 IgG	ELISA	31
2012				69	ILAT	85
2012	Tamaulipas Yucatan	Ocelots Domestic cats	Leopardus pardalis Felis silvestris catus		ELISA	39
		-		75.5 IgM 91.8 IgG		-
2006	State of Mexico	Rabbits	Oryctolagus cuniculus	26.9 IgG	ELISA	54
2007	Durango	Dogs	Canis familiaris	51.5	MAT	45
2012	Oaxaca	Stray dogs	Canis familiaris	61.7 IgG	ELISA	40
2011	Yucatan	Pigs	Sus scrofa	100 IgG	ELISA	79
2011	Durango	Pigs	Sus scrofa	32.1	MAT	9
2012	Oaxaca	Pigs	Raised in backyards Raised on farms	17.2 0.5	MAT	4
2008	Puebla-Veracruz	Sheep	Ovis aries	77-84 IgG	ELISA	35
2008	Colima	Sheep	Ovis aries	29.1 IgG	ELISA	34
2012	Durango	Sheep	Ovis aries	15.1	MAT	10
2013	Oaxaca	Sheep	Ovis aries	23.1	MAT	3
2011	Durango	Goats	Capra hircus	31	MAT	11
2013	Michoacan	Dairy Goats	Capra hircus	15.2	MAT	25
2012	Durango	Horses	Equus caballus	6.1	MAT	21
2012	Coahuila	Deer	Odocoileus virginianus	13.9 IgG	ELISA	78
	Nuevo Leon Tamaulipas					
2012	Quintana Roo	Dolphins	Tursiops truncatus truncatus	87.3	MAT	23
	Mexico City	Sea lions	Tursiops truncatus gillii Zalophus californianus			
2005	Mexico City	Opossums	Didelphis virginianus	23.9	CF	92
2003	mente only	Ringtail cat	Bassariscus astutus	20.7	01	7-
		Spotted skunks	Spilogale gracilis			
		Weasel	Mustela frenata			
		Rock squirrels	Spermophilus variegatus			
		Gray squirrels Feral cats	Sciurus aureogaster Felis catus			
		Feral dogs	Canis familiaris			
2009	Durango	Dogs	Canis familaris	45.3	MAT	50
		Cats	Felis catus	9.3		
		Opossums	Didelphis virginianus	16.6		
		Rats	Rattus spp.	0.8		
		Mice	Mus musculus	3.1		

ILAT: Latex agglutination test. MAT: Modified agglutination test. IHA: Indirect agglutination test. CF: Complement fixation. ELISA: Enzyme-Linked ImmunoSorbent Assay.

antibodies were found in one of 48 mice inoculated through an ELISA. The frequency in the pork was 2.1%, which was lower than expected but similar to that found in other regions⁶⁰.

In a cohort study conducted in 64 newly weaned pigs, from two farms with different densities of cats, on the farm with higher cat density (FA), 97.5% of 31 pigs were seroconverted in the second sampling and 100% in the third sample, while in the second farm (FB) (with lower cat density) all pigs were seroconverted in the fourth sampling, using an indirect ELISA. The true incidence rate (TIR) was 0.67 and 0.43 for FA and FB respectively, during the first four weeks at risk. The relative risk (RR) was 1.5. Animals from FA had a higher risk of infection compared to FB; however, in the end, all pigs showed antibodies against *T. gondii*. These results suggested a major environmental contamination with oocysts, since the study area is located in an endemic area⁷⁹.

In another study, 136 (12.7%) of 1074 evaluated pigs from Durango State showed antibodies against T. gondii, using the modified agglutination test. In this study, the seroprevalence varied according to the geographic regions in which they were bred; in the mountainous region a significantly higher seroprevalence (32.1%) was found compared to those raised in the valley (13.0%) and semi-desert regions (14.0%). In pigs reared in backyards, the seropositivity was 37.9% from 337 evaluated animals, while only one (0.5%) of 188 pigs raised on farms showed antibodies against T. gondii. The higher seroprevalence of T. gondii from the backyard pigs was found in animals ≥ 9 months of age (40%), in females (40%), in pigs from the isthmus region (33.3%), and those raised in tropical climates (65%). The results confirm that the management system (outdoor vs. interior with biosecurity) is a key factor in the epidemiology of swine toxoplasmosis⁴.

Sheep: In a study located in Eastern Mexico, a frequency range of 77-84% of anti-T. gondii antibodies was found in 103 sera of sheep, using an indirect ELISA. The higher prevalence of toxoplasmosis in environments with warm and humid climates was attributed to the high viability of the T. gondii oocysts35. In another study conducted in the coastal, mountainous and hill regions in the state of Colima, serum samples of 351 sheep were tested using a previously standardized indirect ELISA. The frequency of IgG antibodies depended on the altitude, being higher than 1200 meters above sea level, and the size of the flock, with a higher frequency being found in the largest³⁴. In Northern Mexico, a T. gondii seropositivity of 15.1% was found in 511 animals tested using a modified agglutination test. Seroprevalence significantly increased with age, indicating transmission soon after birth¹⁰. In Southern Mexico, a seroprevalence of 23.1% was found in sheep, using the modified agglutination test. The seroprevalence was significantly higher in sheep reared under semi-intensive (grazing cultivated pasture and hay) conditions than those reared under semi-extensive (grazing lands with natural grass) conditions. Additionally, the seroprevalence of T. gondii was higher in mixed breed sheep than in purebreds³.

Goats: Few studies have been conducted on the seroprevalence of *T. gondii* in goats. Antibody seropositivity evaluated from 562 domestic goats, using the modified agglutination test, showed a prevalence of 31%. In this study, seroprevalence was widely distributed in the geographic region studied, and increases with age and race. Goats reared in the semi-desert (Nubian) had a significantly higher seroprevalence (32.7%) than those raised in the mountains (18.6%) (mixed breeds). Positivity

was found in all 12 (100%) farms sampled¹¹. In dairy goats, the seropositivity found was 15.2% from 341 examined animals. An increase in seroprevalence was found in goats 13-24 and 49-86 months of age (25% and 22.9% respectively). Additionally, goats from warm-humid climates and at 1,700 meters above sea level had higher seroprevalence (62.1%)²⁵.

Horses: In horses from the Northwest Mexico, seroprevalence to T. *gondii* was reported in 30 (6.1%) of 495 animals, using the modified agglutination test (MAT). Seroprevalence was higher in horses from rural areas (7.8%) compared to those living in urban areas (0%) 21 .

Monkeys: Toxoplasmosis causes a fatal, multi-systemic disease in New World primates, such as impaired respiratory and multifocal necrotic lesions. Two fatal cases of acute toxoplasmosis in squirrel monkeys (*Saimiri sciureus*) were found; the main pathological findings included pulmonary edema, interstitial pneumonia, hepatitis, and necrotizing lymphadenitis. In addition, structures similar to tachyzoites of *T. gondii* by histopathology in these organs were described. The diagnosis was confirmed by immunohistochemistry, transmission electron microscopy, and real time PCR. Quantification of the parasite load was < 14 and 23 parasites/mg tissue and genotyping was similar to the reference strain type I⁴¹.

Deer: In white-tailed deer from Northern Mexico, a seroprevalence of 13.9% (74/532) was found using an ELISA test. These results were associated with management factors on farms, such as the number of deer per hectare and the geographic location⁷⁸.

Marine mammals: Toxoplasmosis in marine mammals is of great importance since these animals serve as sentinel organisms for the level of oocyst pollution in the seas. A study in Central and Southern Mexico was conducted on 75 marine mammals in captivity through the modified agglutination test. Antibodies to T. gondii were found in 55 (87.3%) of 63 Atlantic bottlenose dolphins (Tursiops truncatus truncatus), in three Pacific bottlenose dolphins (Tursiops truncatus gillii), in two out of four California sea lions (Zalophus californianus), but not in three West Indian manatees (Trichechus manatus) or two Patagonian sea lions (Otaria flavescens). All marine animals sampled were found in healthy conditions and have had no records of cases of clinical toxoplasmosis in at least the last 15 years²³.

Other species: In wild mammals such as opossums (Didelphis virginiana), ring-tailed cats (Bassariscus astutus), spotted skunks (Spilogale gracilis), weasels (Mustela frenata), rock squirrels (Spermophilus variegatus), gray squirrels (Sciurus aureogaster), feral cats (Felis catus), and feral dogs (Canis familiaris), a 23.9% seroprevalence of T. gondii has been reported. Later studies conducted in the state of Durango showed antibodies to T. gondii in 11 (16.6%) of 66 opossums (Didelphis virginianus), two (0.8%) of 249 rats (Rattus spp.), four (3.1%) of 127 mice (Mus musculus) and 0 (0%) of 69 squirrels (Spermophilus variegatus). Additionally, viable T. gondii cysts were isolated from tissue (brain and heart) in three of 28 seropositive dogs and five of eight seropositive cats but no isolations were obtained in other animal species studied.

Genotyping of Toxoplasma gondii in animals from Mexico: Very few reports reveal predominant genotypes of *T. gondii* present in animals. In 2004, *T. gondii* was isolated from six chickens and all six isolates were avirulent for mice. Genotyping of chicken isolates of *T. gondii* using

the SAG2 locus indicated that five were type III and one was type I⁴⁸. In another study, viable *T. gondii* was isolated in tissues from three of 28 seropositive dogs and five of eight seropositive cats and four isolates from free-range chickens from Mexico, previously isolated. The PCR-RFLP identified five genotypes. One genotype (the four chicken isolates) belongs to the clonal Type III lineage, three genotypes were reported in previous reports, and are different from Type I, II and III lineages that predominate in North America and Europe, and one genotype is unique⁵⁰. Two cases of lethal acute toxoplasmosis in squirrel monkeys (*Saimiri sciureus*) from Mexico City were studied, where digestion of the *SAG3* gene amplicon showed similar bands to type I reference strains⁴¹. Recent studies found a new atypical genotype of *T. gondii* in a wild puma (*Felis concolor*) that was virulent for mice, this is the only study from wildlife in Mexico⁴⁴.

Analysis: The highest seroprevalence of toxoplasmosis found in human adults from the southeastern states of Mexico such as Yucatán, Tabasco and Jalisco, could be due to the climatic conditions found in those areas, characterized by their tropical climates (high temperature and humidity) which promote the survival of the parasite oocysts in the environment^{56,64,97,99}. However, the low seroprevalence reported in some areas, like in Oaxaca State, may be related to a low density of cats and low consumption of meat in the diet of the general population⁶⁴. Even when located in a tropical region, the humidity, temperature and presence of cats play an important role in the transmission of this parasite. The seroprevalence found in the northern regions of Mexico (i.e. Durango state) is lower than that from other regions of Mexico; the differences between the two regions could be explained by the dry climate and relatively high altitude in the region and probably the characteristics of the studied populations. Seroprevalence, particularly in breeding animals (pigs and sheep), is much higher in tropical areas, which is also related to the climatic conditions. It is noteworthy that Yucatán state is an endemic region where animals and humans are constantly exposed to the parasite due to the high contamination of the environment with infective oocysts³⁹.

CONCLUSION

Reports of T. gondii in Mexico indicate that this neglected disease is widely distributed in humans and domestic and wild animals throughout the country, with increased prevalences in tropical regions. A high seroprevalence is commonly found in farm animals in the tropical areas of Mexico where T. gondii is endemic; in these endemic areas T. gondii is maintained viable for a long time in the soil and water, which are critical for its transmission to animals. This agent is usually found in meat produced for human consumption, which could be a major source of infection. Fetuses of susceptible pregnant women (i.e. those having not been previously exposed to the parasite) and immunocompromised patients are at high risk of developing clinical signs associated with the agent such as abortion, malformations and fatal cases of meningoencephalitis respectively. Efforts in the field of education should be oriented towards the importance of hygiene when handling and preparing food. It is vital to implement control and surveillance programs for the prevention and control of toxoplasmosis in Mexico at the farm level for meat production, reducing the environmental oocyst load and maintaining a low incidence of positive cases in animal production species for meat consumption and, consequently, reducing the spread to the human population.

RESUMEN

Toxoplasmosis en México: situación epidemiológica en humanos y animales

La toxoplasmosis es una enfermedad parasitaria ampliamente distribuida en todo el mundo y puede infectar a una gran diversidad de especies animales y a los humanos. En México, esta parasitosis ha sido detectada en diferentes partes del país, en particular en las zonas tropicales en donde debido a las condiciones ambientales (ej. alta temperatura y humedad a lo largo todo el año), el parásito puede mantenerse infectante por largos períodos de tiempo en el medio ambiente. Se han realizado diversos estudios epidemiológicos tanto en poblaciones humanas como en animales y se observa que a pesar de la amplia distribución y buen establecimiento del agente en el país, existe un importante desconocimiento desde la epidemiologia, tratamientos alternativos o las medidas de control. La falta de control de las poblaciones ferales de felinos así como el establecimiento de medidas de control en unidades de producción de carne de diferentes especies para consumo humano están jugando un papel primordial que ha favorecido la amplia diseminación de la enfermedad en el país, principalmente en las zonas tropicales del sureste mexicano. Por lo que este manuscrito tiene como objetivo revisar la información publicada hasta ahora que nos describe aspectos epidemiológicos relevantes de la infección por T. gondii en humanos y animales de México.

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