



## **Toxoplasma gondii infection, congenital toxoplasmosis, toxoplasmic retinochoroiditis and neurotoxoplasmosis: an overview**

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### **ABSTRACT**

**Introduction:** The toxoplasmosis disease resulting from *Toxoplasma gondii* infection can manifest itself in many ways, however, congenital, ocular and cerebral forms require greater care. The infection by this protozoan is directly related to environmental and economic factors of the region. **Objective:** The present study, through a review in the literature, aimed to reinforce the knowledge about the infection caused by *Toxoplasma gondii* and its main clinical manifestations. **Methods:** This is a literature overview from academic books and scientific articles available in the Scientific Electronic Library Online, US National Library of Medicine National Institutes of Health and Google Scholar databases. To search the publications, the following descriptors were used: *Toxoplasma gondii*, toxoplasmosis, congenital toxoplasmosis, ocular toxoplasmosis and cerebral toxoplasmosis. The most relevant articles corresponding to the period from 2000 to 2017 were selected. **Development:** Toxoplasmosis may be of congenital or acquired origin after birth. The congenital form occurs during the embryonic/fetal life and through the passage of *Toxoplasma gondii* through the transplacental route. Ocular disease is common in both congenital and acquired infections and is closely associated with the presence of neurotoxoplasmosis in AIDS patients. **Conclusion:** Thus, immunocompromised patients and immunosuppressed patients are considered to be risk groups for *Toxoplasma gondii* infection.

**Keywords:** *Toxoplasma gondii*, toxoplasmosis, congenital toxoplasmosis, ocular toxoplasmosis, cerebral toxoplasmosis.

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### **1. INTRODUCTION**

*Toxoplasma gondii* (*T. gondii*) is a protozoan described in 1908 by Nicolle and Manceaux in Tunisia and by Splendore in São Paulo, Brazil. The first scientists reported the parasite in the North African rodent (the gundi) and the last, in lab rabbit (WEISS, DUBEY, 2009). The parasite was first grouped in genus *Leishmania*, and in 1909 Nicolle and Manceaux created the genus *Toxoplasma* and the *T. gondii* species (NEVES, 2004; FERGUSON, 2009). The parasitic infection, toxoplasmosis, can occur by congenital form or acquired after birth (ORÉFICE *et al.*, 2010). The congenital form occurs during embryonic / fetal life and through the passage of *T. gondii* through the transplacental route (HILL, DUBEY, 2002; MONTOYA, LIESENFELD, 2004). Acquired toxoplasmosis can occur at any stage of life after birth, through contact with infective forms of

the protozoan (ISABEL, 2006). There are known three infective stages of this parasite: tachyzoites, bradyzoites and sporozoites (Fig. 1) (SU, DUBEY, 2010).

Congenital toxoplasmosis was described in 1923 by Janku (Prague), an ophthalmologist which observed injuries in a patient eye that were related to *T. gondii* infection. Torres (1927) described a similar case in Brazil. Wolf, Cowen and Paige (1939) reported another case in a child with encephalomyelitis, with congenital transmission characteristic of the *T. gondii* infection (DUBEY, 2007, ORÉFICE *et al.*, 2010). In 1948, Sabin and Feldman described the dye test, allowing the study of laboratory and epidemiological aspects of toxoplasmosis (ORÉFICE *et al.*, 2010) following other described reactions: hemagglutination, indirect immunofluorescence, complement fixation and cutaneous sensitivity test to toxoplasmin (ISABEL, 2006).

In 1965, Hutchison recognized the role of the cat in the evolutionary cycle of the parasite, and Frenkel *et al.* (1973) described the sexed phase of *T. gondii* in the small intestine of the domestic cat, which produces typical cysts released in the stool (DUBEY, 2009).

Among the complications of *T. gondii* infection, the manifestation of ocular toxoplasmosis is common in both congenital and acquired infections (WEISS, DUBEY, 2009). The ocular lesion caused by this parasite is designated as focal necrotizing retinochoroiditis, with an exudative, yellowish-white, occasionally gray appearance and with poor limits defined (ORÉFICE, BONFIOLI, 2000). Toxoplasmosis is also known worldwide as the leading cause of infectious uveitis affecting the posterior pole of the eye (ANTONIAZZI *et al.*, 2008). Approximately two-thirds of the patients present recurrence of the disease, which may be associated with rupture of the cysts, multiplication of the parasites in the retina, reinfection and other factors (ORÉFICE, BONFIOLI, 2000).

Toxoplasmosis has a great importance for clinical disease in some risk groups. Patients with acquired immune deficiency syndrome (AIDS), when infected with *T. gondii*, may present lesions in the central nervous system and can develop neurotoxoplasmosis (FERREIRA, 2000; PEREIRA *et al.*, 2017). In addition, ocular alterations may be the first manifestation of intracranial or disseminated disease (ALVES *et al.*, 2010). Considering the importance of this theme, especially to the group of pregnant women and patients with AIDS, the present study aims to reinforce the knowledge about *T. gondii* infection and to emphasize its main clinical manifestations.

## 2. METHODS

The present study was carried out using literature review: academic books and scientific papers available in the Scientific Eletronic Library Online (SCIELO), US National Library of Medicine National Institutes of Health (PUBMED) and Google Scholar databases. To search the publications, the following descriptors were used: *Toxoplasma gondii*, toxoplasmosis, congenital toxoplasmosis, ocular toxoplasmosis and cerebral toxoplasmosis. The inclusion criteria of the study was articles published between 2000 and 2017. After the selection, a thorough reading of each material was carried out to observe the adequacy and relevance of the theme.

## 3. DEVELOPMENT

### 3.1. *Toxoplasma gondii*

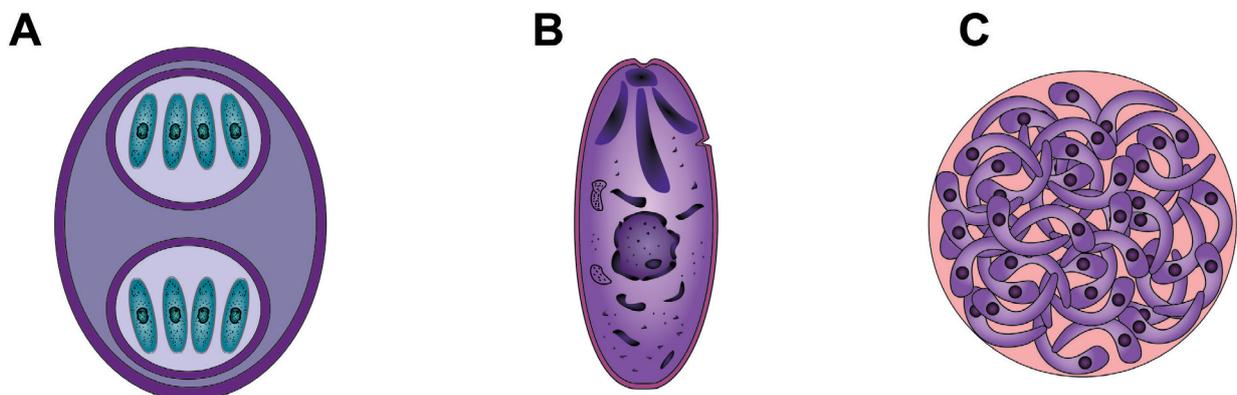
Member of the Apicomplexa phylum, *T. gondii* is an obligate intracellular parasite that can cause toxoplasmosis (MATTOS *et al.*, 2011; NETTO *et al.*, 2003). *T. gondii* has existed in Brazil for several years, and its discovery in the state of São Paulo is probably related to the climate without severe temperatures, constant humidity and the presence of definitive hosts (wild and domestic) (MELAMED, 2009).

According to Meirelles (2001), about 70% of the Brazilian population was infected by this protozoan at some point in life. The sources of contamination by *T. gondii* are diverse, from the consumption of contaminated water and food, organ transplantation, and through the environment of the felids, which are disseminators of this parasite (Fig. 2) (FERREIRA *et al.*, 2014).

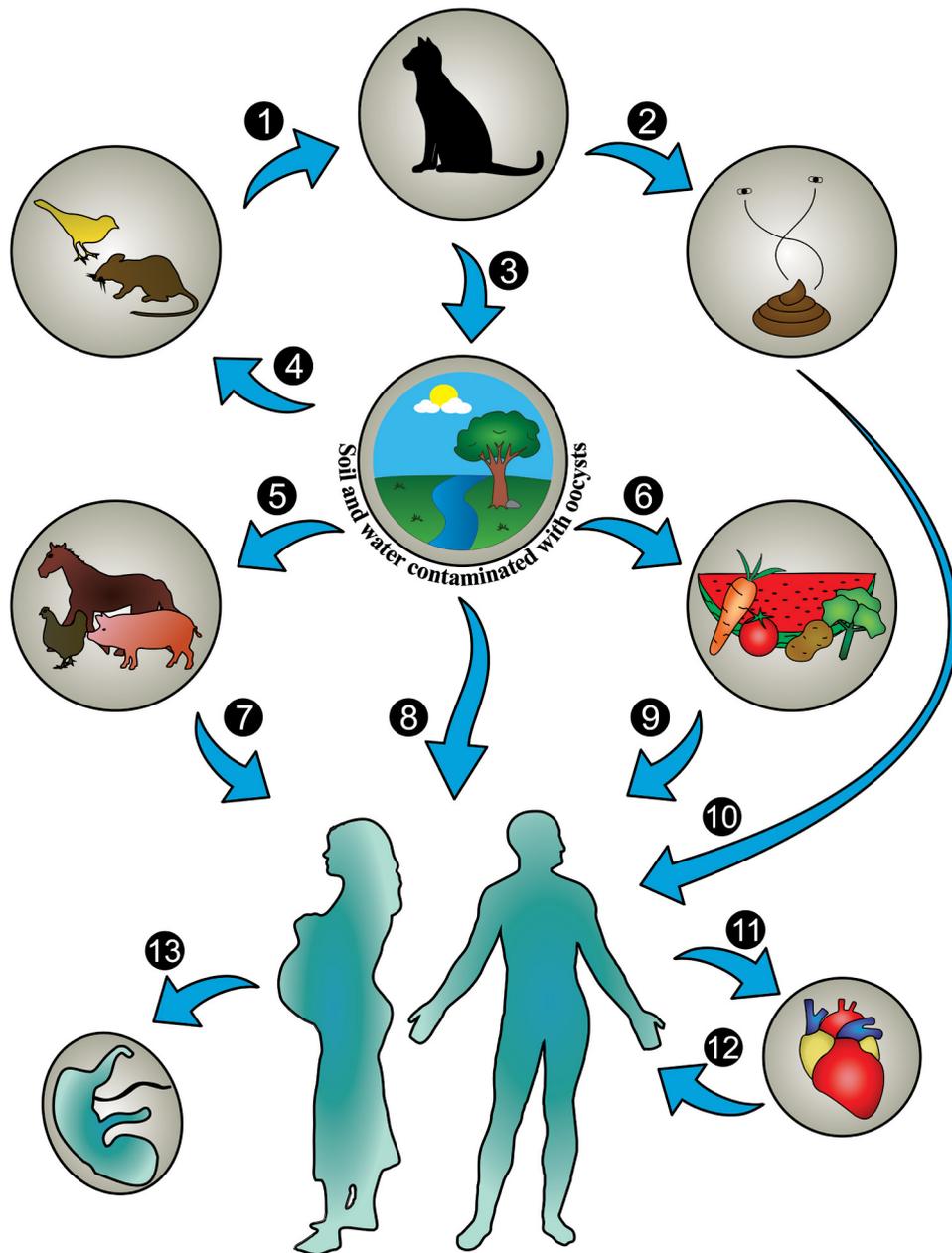
A study carried out in several localities of the state of São Paulo found that 40% of the felids presented a positive serology for *T. gondii*. The study also showed the prevalence of infection of 8.5% in pigs, 11% in cattle, 50.5% in dogs and it was not possible to find positivity in broilers, possibly because they were slaughtered with a few days of life (MEIRELLES, 2001). When infection occurs in humans and the disease installs, it is observed that congenital toxoplasmosis, toxoplasmic retinochoroiditis and neurotoxoplasmosis are the main manifestations presented by patients (BORGES, FIGUEIREDO, 2004; LEÃO *et al.*, 2004; MATTOS *et al.*, 2008).

### 3.2. CONGENITAL TOXOPLASMOSIS

The individual may develop toxoplasmosis from contact with sporozoites obtained from the hatching of oocysts released from feline stools, by ingestion of tecdial cysts containing bradyzoites present in raw or undercooked meat, by ingestion of raw milk containing tachyzoites, and other forms of infection (SARTORI *et al.*, 2011; FERREIRA *et al.*, 2014). However, there is another route of infection, which occurs through acute maternal infection during the gestational period or by exacerbation of a previous infection (TLAMCANI *et al.*, 2017; MATTOS *et al.*, 2008). During this time, tachyzoites may be transmitted to the embryo / fetus via transplacental route (JONES *et al.*, 2003). This episode is called congenital toxoplasmosis and can lead to possible neurological, ocular, auditory



**Figure 1. Infectious forms of *Toxoplasma gondii*.** (A) Oocysts sporulated. (B) Tachyzoite (C) Cysts of bradyzoites.



**Figura 2. Forms of *Toxoplasma gondii* transmission.** (1) Tissue cysts containing bradyzoites in prey. (2) Fecal oocysts. (3) Fecal oocysts in environment. (4) Oocysts sporulated ingested by wild animals. (5) Oocysts sporulated ingested by domestic animals. (6) Oocysts sporulated on fruits and vegetables. (7) Tissue cysts containing bradyzoites in undercooked or raw meats. (8) Oocysts sporulated. (9) Oocysts sporulated on unwashed fruits and vegetables. (10) Oocysts sporulated. (11) Organs containing bradyzoites in tissue cysts. (12) Organs containing bradyzoites in tissue cysts. (13) Tachyzoites transmitted to fetus.

and even intrauterine complications depending on the gestational period (WEISS, DUBEY, 2009; TORGERSON, MASTROIACOVO, 2013).

In the fetus, the parasite will host in cells of the phagocytic-mononuclear system, giving rise to so-called pseudocysts. Pseudocysts spread through the blood or lymphatic system to the organs or tissues, being mainly found in the eyes and the nervous system (SILVA *et al.*, 2015). In Brazil, it is estimated that approximately sixty thousands of children are born annually with the disease (NASCIMENTO *et al.*, 2002). Of the women infected with *T. gondii* during pregnancy, only 39% will transmit the disease to the embryo / fetus. Of these, 26% may have subclinical manifestations as visual impairment, hearing

loss or learning deficit, and the other 13% can have clinical symptoms as hydrocephalus, microcephaly, cerebral calcification and mental retardation (DIAS *et al.*, 2011).

Due to the fact that the disease is mostly asymptomatic, prenatal care is of great importance to reduce sequelae or even to prevent transmission of the parasite to the child (SOUZA *et al.*, 2010). The types of sequelae caused by congenital toxoplasmosis can be related directly to the gestational period. During the first trimester, there is a greater chance of miscarriage, and in the second trimester there is a probability of developing Sabin's tetrad symptoms. However, when the infection occurs during the third trimester of gestation, the child may be born without evidence of the disease, and may present them years later

(JONES *et al.*, 2003; SOUZA *et al.*, 2010). The main manifestation observed in congenital toxoplasmosis is the toxoplasmic retinochoroiditis, being present in 80% of cases (SOARES *et al.*, 2011). However, brain calcifications, mental retardation, hydrocephalus, with macro and microcephaly may also be present in patients who develop this condition (VIDIGAL *et al.*, 2002).

The prevalence of congenital toxoplasmosis may vary in the population, dietary habits, according to age, level of schooling, and socioeconomic conditions (DIAS *et al.*, 2011; SARTORI *et al.*, 2011; LOPES-MORI *et al.* 2011; FERREIRA *et al.*, 2014). In order to control the number of infected individuals, maternal care and diagnosis are necessary (SARTORI *et al.*, 2011). It is essential that pregnant women become aware of the primary prevention measures (information about the sources of infection) and secondary (serological screening for anti-*T. gondii* antibodies during prenatal care) (LOPES-MORI *et al.*, 2011). A correct prenatal care enables the early identification of the pregnant women with acute infection and allows her to receive appropriate medical / therapeutic intervention (BOYER *et al.*, 2005).

Prenatal screening, added to prevention programs, respecting the epidemiological and cultural characteristics of each region, has solidified in several places as an important tool to strike congenital toxoplasmosis (SARTORI *et al.*, 2011). In places where are the investigation of IgG and IgM antibodies against *T. gondii* in pregnant, the rate of disease per 1,000 pregnancies reaches irrelevant levels as: 0.5% in Sweden, 1.7 % in Norway and 6.6% in Paris (SANDRIN *et al.*, 2012).

In Brazil, the "Mãe Curitiba" program gains a prominent role. It was implemented by the Municipal Health Department of Curitiba, Paraná, and guarantees pregnant women a higher quality care. The serological test, which detects IgM and IgG antibodies, is performed at the first visit and in the second and third trimesters of pregnancy. Moreover, can be performed if the previous results of the test is negative or if the patient presents high risk for the infection. However, if the pregnant is considered to be at low risk, the serology is repeated between the 26th and 28th week of gestation, and in the patients with reactive serology for IgG and IgM, the result is confirmed by the IgG avidity test (LOPES-MORI *et al.*, 2011).

### 3.3. TOXOPLASMIC RETINOCHOROIDITIS

Ocular toxoplasmosis, also known as toxoplasmic retinochoroiditis, is the main cause of infectious uveitis reaching the posterior region of the eye (ANTONIAZZI *et al.*, 2008). It may be accompanied by anterior uveitis (ORÉFICE, BONFIOLI, 2000). The ocular lesions caused by *T. gondii* are characterized by focal necrotizing retinochoroiditis (ATMACA *et al.*, 2004), with an exudative, yellowish-white, occasionally gray appearance and with poor limits defined (ANTONIAZZI *et al.*, 2008; ORÉFICE, BONFIOLI, 2000).

The parasites reach the eye through infected leukocytes and it is believed that *T. gondii* can also reach the eye through the optic nerve after primary intracranial infection. About eight days after infection, tissue cysts are formed, which can persist throughout the host's life without inducing immune response, or suffer intermittent ruptures and cause

recurrence of infection (ORÉFICE, BONFIOLI, 2000).

The pathophysiology of the disease is linked to the action of the parasite directly at the site of infection, as well as the parasite load and strain type. There are different strains according to the region, and in Brazil the type 1 strain is directly involved with the severity of retinochoroiditis. The ocular lesions are mainly present at the birth of children with congenital toxoplasmosis, but the individual who becomes infected during the gestational period can also develop eye lesions throughout life (SOARES *et al.*, 2011). When the infection occurs in the postnatal period, the eye damage can appear during the acute phase or years after the systemic disease. The retinochoroiditis is the main clinical manifestation of postnatal ocular disease, but may also present some other symptoms as neuritis, vitreitis, iridocyclitis and vasculitis (ORÉFICE *et al.*, 2010).

### 3.4. NEUROTOXOPLASMOSIS

Neurotoxoplasmosis is characterized as an accumulation of abscesses in the brain region with presence of *T. gondii* (BARSOTTI *et al.*, 2005). The prevalence of the disease varies according to the geographic area, in a rate of 3% to 50% of patients with this disease (BORGES *et al.*, 2004). In most of the cases, the neurotoxoplasmosis occurs due to a reactivation of a previous infection by *T. gondii*. Thus, to identify the patients who present the infection is very important, especially in the case of immunocompromised individuals (BARSOTTI *et al.*, 2005).

This disease corresponds to the clinical manifestation present in about half of the patients with ocular damage and AIDS (ALVES *et al.*, 2010). People with AIDS often develop neurotoxoplasmosis resulting from lesions of the central nervous system, possibly due to reactivation or rupture of cysts present in the brain (FERREIRA, 2000). *T. gondii* is one of the main opportunistic microorganisms that infect immunocompromised individuals (CARRUTHERS, 2002). In addition, patients with toxoplasmosis in the neurological form have a 10% to 20% of chance to present the ocular form of the disease (ALVES *et al.*, 2010).

The difficulty in diagnosing neurotoxoplasmosis is related to its clinical similarity compared to other opportunistic diseases, such as viral and fungal encephalitis, neurotuberculosis, among others. Therefore, the use of devices such as computed tomography of the cranium and magnetic resonance imaging are important to the diagnosis of neurotoxoplasmosis. These image tests enable the observation of the disease characteristics in 90% of the cases, together with the serology of IgM / IgG antibodies against *T. gondii* (BORGES *et al.*, 2004).

### 4. CONCLUSION

This study reinforces the knowledge about *T. gondii* infection and emphasizes its main clinical manifestations. The prevalence of infection varies between countries, geographical areas and ethnic groups living within a specific region and can reach more than 80% of individuals. The high prevalence worldwide is correlated to environmental risk factors and socioeconomic factors. Risk factors range from contaminated food to vertical transmission. Most of the time, the disease has an asymptomatic course, however, when symptoms are present, it can be observed from mild to severe complications.

When a woman becomes infected during the gestational period, there is a strong likelihood that the embryo / fetus will also become infected. In this sense, there is a special concern with this group of women, because once the child becomes infected, it can develop from jaundice until it evolves to intrauterine death. The main manifestation of congenital toxoplasmosis is toxoplasmic retinochoroiditis; however, this ocular alteration may also be of postnatal origin and can be considered the main cause of infectious uveitis reaching the posterior region of the eye. In addition, ocular disease is closely associated with the presence of neurotoxoplasmosis in patients with AIDS. It is found that immunocompromised patients and immunosuppressed patients may develop the more severe forms of toxoplasmosis due to *T. gondii* infection.

#### CONFLICT OF INTEREST

The authors declares that there is no conflict of interest regarding the publication of this paper.

#### REFERENCES

- Alves, J.M., Magalhaes, V., Matos, M.A.G., 2010. Retinocoroidite toxoplásmica em pacientes com AIDS e neurotoxoplasrose. *Arq Bras Oftalmol* 73, 150-154.
- Antoniazzi, E., Guagliano, R., Meroni, V., Pezzotta, S., Bianchi, P.E., 2008. Ocular impairment of toxoplasmosis. *Parassitologia* 50, 35-36.
- Atmaca, L.S., Simsek, T., Batioglu, F., 2004. Clinical features and prognosis in ocular toxoplasmosis. *Jpn J Ophthalmol* 48, 386-391.
- Barsotti, V., Moraes, A.T., 2005. Neurotoxoplasrose como primeira manifestação da Síndrome de Imunodeficiência Adquirida. *Rev Fac Ciênc Méd Sorocaba* 7, 133-141.
- Borges, A.S., Figueiredo, J.F.C., 2004. Detecção de imunoglobulinas IgG, IgM e IgA anti-*Toxoplasma gondii* no soro, líquido e saliva de pacientes com síndrome da imunodeficiência adquirida e neurotoxoplasrose. *Arq Neuro-Psiquiatr* 62, 1033-1037.
- Boyer, K.M., Holfels, E., Roizen, N., Swisher, C., Mack, D., Remington, J., Withers, S., Meier, P., McLeod, R., 2005. Risk factors for *Toxoplasma gondii* infection in mothers of infants with congenital toxoplasmosis: Implications for prenatal management and screening. *Am J Obstet Gynecol* 192, 564-571.
- Carruthers, V.B., 2002. Host cell invasion by the opportunistic pathogen *Toxoplasma gondii*. *Acta Tropica* 81, 111-122.
- Dias, R.C.F., Lopes-Mori, F.M.R., Mitsuka-Breganó, R., Dias, R.A.F., Tokano, D.V., Reiche, E.M.V., Freire, R.L., Navarro, I.T., 2011. Factors associated to infection by *Toxoplasma gondii* in pregnant women attended in Basic Health Units in the city of Rolândia, Paraná, Brazil. *Rev Inst Med Trop* 53, 185-191.
- Dubey, J.P., (2007). The history and life cycle of *Toxoplasma gondii*. In: Weiss, L.M., Kim, K., editores. *Toxoplasma gondii: The model apicomplexan: perspectives and methods*. Amsterdam, Elsevier/ Academic Press.
- Dubey, J.P., 2009. History of the discovery of the life cycle of *Toxoplasma gondii*. *Int J Parasitol* 39, 877-882.
- Ferguson, D.J.P., 2009. *Toxoplasma gondii*: 1908-2008, homage to Nicolle, Manceaux and Splendore. *Mem Inst Oswaldo Cruz* 104, 133-148.
- Ferreira, M.S., 2000. Infections by protozoa in immunocompromised hosts. *Mem Inst Oswaldo Cruz* 95, 159-162.
- Ferreira, A.I.C., Mattos, C.C.B., Frederico, F.B., Meira, C.S., Almeida Jr. G.C., Nakashima, F., Bernardo, C.R., Pereira-Chiocola, V.L., Mattos, L.C., 2014. Risk factors for ocular toxoplasmosis in Brazil. *Epidemiol Infect* 142, 142-148.
- Hill, D., Dubey, J.P., 2002. *Toxoplasma gondii*: transmission, diagnosis and prevention. *Clin Microbiol Infect* 8, 634-640.
- Isabel, T.F., Toxoplasrose aguda em gestantes de Araraquara-SP: Avaliação da aplicabilidade do teste de avidade de IgG anti-Toxoplasma. São Paulo, 2006.
- Jones, J., Lopes, A., Wilson, M., 2003. Congenital Toxoplasmosis. *Am Fam Physician* 67, 2131-2138.
- Leão, P.R.D., Meirelles-Filho, J., Medeiros, S.F., 2004. Toxoplasrose: soroprevalência em puérperas atendidas pelo Sistema Único de Saúde. *Rev Bras Ginecol Obstet* 26, 627-632.
- Lopes-Mori, F.M.R., Mitsuka-Breganó, R., Capobianco, J.D., Inoue, I.T., Reiche, E.M.V., Morimoto, H.K., Casella, A.M.B., Bittencourt, L.H.F.B., Freire, L.R., Navarro, I.T., 2011. Programas de controle da toxoplasrose congênita. *Rev Assoc Med Bras* 57, 594-599.
- Mattos, C.C.B., Cintra, J.R., Ferreira, A.I.C., Spejorin, L.C.J.F., Galisteu, K.J., Machado, R.L.D.M., Mattos, L.C., 2008. Lack of association between ABO histo-blood groups, secretor and non-secretor phenotypes, and anti-*Toxoplasma gondii* antibodies among pregnant women from the northwestern region of São Paulo State, Brazil. *Arch Med Sci* 4, 254-258.
- Mattos, C.C.B., Spejorin, L.C.J.F., Meira, C.S., Silva, T.C., Ferreira, A.I.C., Nakashima, F., Pereira-Chiocola, V.L., Mattos, L.C., 2011. Anti-*Toxoplasma gondii* antibodies in pregnant women and their newborn infants in the region of São José do Rio Preto, São Paulo, Brazil. *Sao Paulo Med J* 129, 261-266.
- Meireles, L.R., Estudo das fontes de infecção da toxoplasrose humana em diferentes localidades do Estado de São Paulo. São Paulo, 2001.
- Melamed, J., 2009. Contributions to the history of ocular toxoplasmosis in Southern Brazil. *Mem Inst Oswaldo Cruz* 104, 358-363.
- Montoya, J.G., Liesenfeld, O., 2004. Toxoplasmosis. *Lancet* 363, 1965-1976.
- Nascimento, I., Carvalho, S., Cardozo, N., Asfora, S., Campos, A., Menezes, S., Simões, J., Schaer, R.E., Meyer, R., 2002. Estudo da prevalência de anticorpos anti-*Toxoplasma gondii* em mulheres grávidas no Estado da Bahia. *Rev Ci Méd Biol* 1, 12-15.
- Netto, E.G., Munhoz, A.D., Albuquerque, G.R., Lopes, C.W.G., Ferreira, A.M.R., 2003. Ocorrência de gatos soropositivos para *Toxoplasma gondii* Nicolle e Manceaux, 1909 (apicomplexa: toxoplasmatinae) na cidade de Niterói, Rio de Janeiro. *Rev Bras Parasitol Vet* 12, 145-149.
- Neves, D.P., (2004). *Parassitologia humana*. São Paulo, Atheneu.
- Oréfice, F., Bonfioli, A.A., (2000). Toxoplasrose. In: Oréfice, F., editor. *Uveíte clínica e cirúrgica: texto e atlas*. Rio de Janeiro, Cultura Médica.

- Oréface, F., Cunha-Filho, R., Barbosa, A.L., Oréface, J.L., Calucci, D., 2010. Toxoplasmose ocular adquirida – toxoplasmose ocular pós-natal. *Rev Bras Oftalmol* 69, 184-207.
- Pereira, N.M.D., Shah, I., Lala, M., 2017. Toxoplasmosis with chorioretinitis in an HIV-infected child with no visual complaints-importance of fundus examination. *Oxf Med Case Reports* 01, 1-3.
- Sandrin, L.N.A., Ponzi, C.C., Binda, G., Nardi, A., 2012. Perfil epidemiológico de toxoplasmose em gestantes. *Rev Bras Clin Med* 10, 486-489.
- Sartori, A.L., Minamisava, R., Avelino, M.M., Martins, C.A., 2011. Triagem pré-natal para toxoplasmose e fatores associados à soropositividade de gestantes em Goiânia, Goiás. *Rev Bras Ginecol Obstet* 33, 93-98.
- Silva, J.V., Araújo, M.D., Gomes, T.C., Transmissão vertical na toxoplasmose: uma revisão na literatura. Goiânia, 2015.
- Soares, J.A.S., Násser, L.S., Carvalho, S.F.G., Caldeira, A.P., 2011. Achados oculares em crianças com toxoplasmose congênita. *Arq Bras Oftalmol* 74, 255-257.
- Souza, C.O., Tashima, N.T., Silva, M.A., Tumitan, A.R.P., 2010. Estudo transversal de toxoplasmose em alunas de um curso superior da região de Presidente Prudente, Estado de São Paulo. *Rev Soc Bras Med Trop* 43, 59-61.
- Su, C., Dubey, J.P., (2010). Toxoplasma. In: Liu, D., editor. *Molecular detection of foodborne pathogens*. Boca Raton, CRC Press.
- Tlamcani, Z., Yahyaoui, G., Mahmoud, M., 2017. Prevalence of immunity to toxoplasmosis among pregnant women in University Hospital Center Hassan II of FEZ city (Morocco). *Acta Medica International* 4, 43-45.
- Torgerson, P.R., Mastroiacovo, P., 2013. The global burden of congenital toxoplasmosis: a systematic review. *Bull World Health Organ* 91, 501-508.
- Uzorka, J.W., Arend, S.M., 2017. A critical assessment of the association between postnatal toxoplasmosis and epilepsy in immune-competent patients. *Eur J Clin Microbiol Infect Dis* DOI 10.1007/s10096-016-2897-0.
- Vidigal, P.V.T., Santos, D.V.V., Castro, F.C., Couto, J.C.F., Vitor, R.W.A., Brasileiro Filho, G., 2002. Prenatal toxoplasmosis diagnosis from amniotic fluid by PCR. *Rev Soc Bras Med Trop* 35, 1-6.
- Weiss, L.M., Dubey, J.P., 2009. Toxoplasmosis: a history of clinical observations. *Inst J Parasitol* 39, 895-901.