

Toxoplasma gondii immunoglobulin G in paired infant-and-mother sera

Ayling Sanjaya¹, Nurhayati Masloman¹, Rocky Wilar¹, Josef Tuda²

Abstract

Background Toxoplasmosis is a worldwide zoonotic disease caused by *Toxoplasma gondii*. Congenital toxoplasmosis (CT) is the result of vertical transmission during pregnancy that may cause pathologic effects on the newborn such as classical triad of congenital toxoplasmosis. Newborn humans are not immunologically competent and the infant must be protected by passive IgG antibodies that are selectively transported across the placenta during development. We studied the transfer of passive IgG from the mother to developing infant using blood specimen taken from the infant within one month of birth.

Objective To determine the seropositivity of IgG to *T. gondii* in paired sera of infants and mothers.

Methods A cross sectional study was carried out on 50 paired sera of infants of less than one month of age and their mothers. The study was carried out between November 2007 and January 2008 at Prof. R. D. Kandou Hospital in Manado. *T. gondii* IgG was detected using the Latex Agglutination method. The seropositivity of *T. gondii* IgG was analyzed descriptively.

Results A total of 28 mothers from 50 infant-mother pairs were seropositive for *T. gondii* IgG. Of the 28 seropositive mothers, 22 of their paired infants were seropositive. The remaining six seropositive mothers had infants that were not seropositive for *T. gondii*.

Conclusions The identification of seropositive IgG for *T. gondii* in infants less than one months age indicates that the IgGs in infants are mostly derived from their mothers. CT must be considered and further examinations are needed. [Paediatr Indones. 2009;49:65-8].

Keywords: seropositive, *T. gondii*, IgG, paired infant and mother, incidence

Toxoplasmosis is a worldwide zoonotic disease caused by the tissue cyst-forming coccidium *Toxoplasma gondii* (*T. gondii*).^{1,2} Animals in the cat family (*Felides*) are its definitive host. Human are infected either through contaminated food and water, transfusion of infected blood, organ transplantation, or vertically through the placenta.³ Once infected, humans are thought to produce IgG antibodies against *T. gondii* for life.^{4,5} Up to one third of the world's human population are believed to have been infected with the parasite.^{1,6} However, the prevalence of toxoplasmosis in human populations varies between different countries. Toxoplasmosis prevalence in England is reported to be 30%, while in Paris it is 87%.^{7,8} The prevalence for *T. gondii* in Indonesia is thought to range from 2 to 63%.⁹ A study by Clarke in the North Sulawesi showed a prevalence of 27.1%.¹⁰

Congenital toxoplasmosis can result from vertical transmission from a mother to the unborn child. The

From the Department of Child Health, Medical School, Sam Ratulangi University, Prof. R. D. Kandou General Hospital, Manado, Indonesia (AS, NM, RW).¹ From the Department of Parasitology, Medical School, Sam Ratulangi University, Prof. R. D. Kandou General Hospital, Manado, Indonesia (JT).²

Reprint request to: Ayling Sanjaya, MD, Department of Child Health, Medical School, Sam Ratulangi University, Prof. R. D. Kandou General Hospital, Jl. Raya Tanawangko, Manado 95263, Indonesia. Telp. 62-431-821. Fax. 62-431-859091. E-mail: link_anastasia@telkom.net.

parasites are transmitted during pregnancy to the fetus, which may cause pathologic effects including abortion of the fetus, intrauterine fetal death, and defects in newborn recognized as the classic triad.¹¹⁻¹⁴ Sanjaya¹⁵ reported 37% of IgG seropositivity in pregnant women in Surabaya, Indonesia. It was estimated that 40% of infected infants underwent spontaneous abortion and abnormal conditions, and the remaining 60% had asymptomatic clinical manifestations, whereas 50% developed the risk of possible sequelae in the next period of growth.¹⁶⁻¹⁹

In humans, newborn infants are not immunologically competent and must be protected by passive IgG antibody that is selectively transported across the placenta during pregnancy. In this study, possible passive IgG transfer from mothers was investigated by performing serology tests on blood samples from mothers and their infants within one month of birth.

Methods

A cross-sectional study was carried out on 50 mother-infant pairs, with infants of less than one month of age. The study was carried out between November 2007 and January 2008 at Prof. R. D. Hospital in Manado, Sulawesi, Indonesia. A questionnaire was used to gather information on the identity and age of the mothers, their exposure to cats, and their pregnancy and infant histories. Serology examinations of *T. gondii* IgG were performed on mother-and-infant paired sera using the latex agglutination test (LAT). Data were collected and presented descriptively.

Results

Sera from 50 paired mothers and infants were examined for *T. gondii* IgG using the latex agglutination test (LAT). Questionnaires were completed by 50 participating mothers. A total of 28 mothers (56%) had positive IgG for *T. gondii*. Of these 28 seropositive mothers, 22 of the paired infants were also seropositive for *T. gondii*. The remaining six mothers had infants who were not seropositive (Table 1).

The distribution of LAT results for all mothers with positive results, and their infants, is shown in Figure 1. The largest group of seropositive mothers

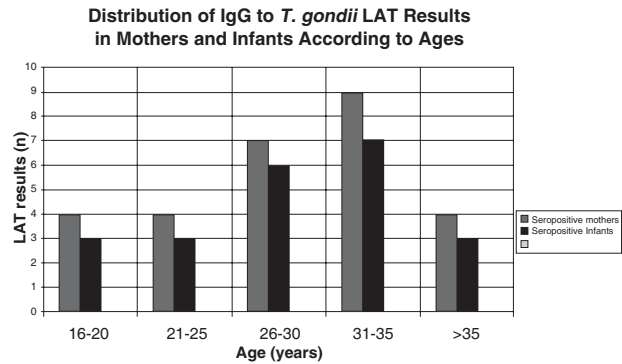


Figure 1. Distribution of IgG to *T. gondii* LAT results in mothers and infants according to ages

Table 1. LAT results for toxoplasma IgG in paired mothers and infants

Mother	Infants		Total
	Seropositive	Seronegative	
Seropositive	22	6	28
Seronegative	0	22	22
Total	22	28	50

were in the 31-35 year old age group (9/28 seropositive mothers; 32%). The largest number of seropositive infants is also in this group (7 infants, 25%).

In this study, 3/28 seropositive mothers (10.71%) had a history of abortion and two seropositive infants had mothers with history of abortion. History of neonatal jaundice was found in 2/28 (7%) seropositive mothers and one seropositive infant. History of exposure to cats was found in 17/28 (61%) seropositive mothers and 15 seropositive infants.

Discussion

High rates of IgG antibody seropositivity were observed in this study. A total of 22 (44%) infants and 28 (56%) mothers of 50 infant-mother pairs were seropositive with (IgG) *T. gondii* IgG. Out of the 28 seropositive mothers, 22 paired infants were seropositive. The remaining six seropositive mothers did not have seropositive infants. The largest group of seropositive mothers (9/28, 32%) were in the 31-35 year old age group. Seven infants of these seropositive mothers were also seropositive. Seven mothers (25%) and six infants in the 26-30 year old age group were seropositive.

Some studies showed that prevalence of seropositivity to toxoplasma increased with age suggesting long time exposure to *T. gondii*. More studies must be conducted to diminish doubts about the correlation between age and seropositivity of subjects. Inappropriately very wide or very narrow age range and sample sizes should be considered.²¹

Based on studies carried out in India, there have been considerable confusion and uncertainty concerning *T. gondii* as a cause of multiple spontaneous abortions, infertility, and other reproductive failures because most data were based on serology tests. There were several shortcomings in the reports linking habitual abortion to *T. gondii* infection, such as low number of patients, uncontrolled studies, and an absence of serologic data before pregnancy. It is necessary to establish a causal relationship between toxoplasmosis and abortion.^{20,21}

The distribution of mothers and infants with seropositive IgG to *T. gondii* in relation to history of spontaneous abortion was examined in this study. Three seropositive mothers (10%) had history of spontaneous abortion and two seropositive infants had mothers with history of spontaneous abortion. History of neonatal jaundice was observed in 2/28 seropositive mothers (7%) and one seropositive infant. Other causes of abortion and neonatal jaundice should be considered with more specific history taking and examinations.^{19,21} Although most congenitally infected children are asymptomatic at birth, they may develop some symptoms later in life. However, because these symptoms are nonspecific, postnatal toxoplasmosis is rarely diagnosed.^{18, 21}

Toxoplasmosis is not a new disease. The parasite was discovered in 1908 but its mode of transmission remained a mystery until 1970 when the full lifecycle was discovered. Cats including wild *Felidae* are the definitive host and all other warm-blooded animals including humans are the intermediate hosts. In this study, history of exposure to cats was present in 17/28 seropositive mothers (61%), and in 15 seropositive infants with seropositive mothers. Such a correlation suggested that the ingestion of oocysts might be an important mode of transmission of *T. gondii* in the population.²¹

Primary maternal toxoplasma infection exposes the fetus to the risk of parasite transmission, leading to CT (congenital toxoplasmosis).¹⁷ Seropositive

infants were detected in high numbers in this study. In humans, the newborn is not immunologically competent and must be protected by passive IgG toxoplasmosis antibody that is selectively transported across the placenta during their development. IgG in the fetus and newborn infant is derived solely from their mothers. Therefore, the IgG that was observed in our infant subjects originated from their mothers. This maternal IgG has usually disappeared by the age of nine months, by which time the infants are synthesizing their own IgG. The neonates will also produce their own IgM and IgA as these antibodies cannot cross the placenta. By the age of 12 months, the infants produce 80% of their adult level of IgG, 75% of its adult level of IgM and 20% of its adult level of IgA.²⁰ Specific IgM classes that had been formed during fetal life changed to IgG immediately through the class switching mechanisms after delivery.²²

The presence of IgG antibodies only indicates exposure. The titer of IgG may remain elevated for several years or even for the whole life, if repeated exposures are encountered. IgM antibodies are short lived and they appear before IgG antibodies. IgM serological testing appears to be less sensitive for detecting infections acquired in the first semester. However, because early infection is frequently associated with clinically apparent disease, it may be that many cases would be diagnosed on the basis of clinical examination. As the maternal antibody decreased with time, after 6-12 months, positive IgG serological examination findings in infants with seropositive mothers can be used to verify congenital toxoplasmosis.²³

In conclusion, 22 of 28 infants whose mothers had seropositive IgG to *Toxoplasma* were also seropositive, while no infants with seronegative mothers had positive IgG to *Toxoplasma*. It suggests that the IgG detected in the infants is acquired through maternal IgG placental transfer.

Acknowledgments

Our highest gratitude goes to Indonesian Pediatrician Society North Sulawesi Chapter; Freddy Y. Wagey, MD, Prof. Yoes Prijatna Dachlan, MD, Prof. Erry Gumilar Dachlan, Sukmawati Basuki, MD, Dimas Primacahyadi, Ratna Ika Susanti, Elsan, Ngurah Wandu Mastika, and Roy, for their help with laboratory analysis and data collection.

References

1. Fransisco FDM, Souza SL, Gennari SM, Pinheiro SR, Muradiano V, Soares RM. Seroprevalence of toxoplasmosis in a low income community in the Sao Paulo Municipality SP Brazil. *Rev Inst Med Trop Sao Paulo*. 2006;48 :S167-170.
2. Tenter AM, Heckerth AR, Weiss LM. Epidemiological aspects of toxoplasmosis in school children residing in localities with urban or rural characteristics within the city of Rio de Janeiro, Brazil. *Mem Inst Oswaldo Cruz*. 1987;82:475-82.
3. Jones JF, Lopez B, Mury MAV, Wilson M, Klein R, Luby S, Maguire JH. *Toxoplasma gondii* infection in rural Guatemalan children. *Am J Trop Med Hyg*. 2005;72:295-300.
4. Montoya JG, Liesenfeld O. Toxoplasmosis. *Lancet*. 2004;363:1965-76.
5. Dubey JP. Toxoplasmosis, sarcocystosis, isosporosis and cyclosporiasis. In: Palmer SR, Soulby EJJ, Simpson DJH, editors. *Zoonoses*. Oxford: Oxford University Press, 1998; p. 579-97.
6. Tenter AM, Heckerth AR, Weiss LM. *Toxoplasma gondii*: From animals to humans. *Int J Parasit*. 2000;30:1217-58.
7. Rampengan TH, Laurentz IR. *Penyakit infeksi tropik pada anak*. 1st ed. Jakarta: Penerbit Buku Kedokteran EGC, 1997; p.245-55.
8. Thulliez P. Commentary: Efficacy of prenatal treatment for toxoplasmosis: A possibility that can not be ruled out. *Int J Epidemiol*. 2001;30:S1315-6.
9. Gandahusada. *Parasitologi Kedokteran*. 3rd ed. Jakarta: Balai Penerbit Fakultas Kedokteran Universitas Indonesia, 1998; p.153-61.
10. Rochiman Sasmita. *Toxoplasmosis penyebab keguguran dan kelainan bayi*. Surabaya: Airlangga University Press, 2006; p. 23-40.
11. Dachlan E.G. Congenital toxoplasmosis: Fetal antibodies production in amniotic fluid. *Majalah Kedokteran Tropis Indonesia*. 1999;12:S33-40.
12. Dachlan E.G. IgM anti toxoplasma dalam cairan ketuban sebagai indikator toxoplasmosis kongenital serta korelasinya dengan IgM anti toxoplasma seromaternal [dissertation]. Surabaya: Airlangga University; 1999.
13. Smith JL. Foodborne infections during pregnancy. *J Food Protect*. 1999;62:818-29.
14. Holliman RE. Toxoplasmosis. In: Cook GC. *Manson Tropical Diseases*. 21st ed. London: WB Saunders; 1996:1365-72.
15. Sanjaya A. Studi uji komparasi hasil pemeriksaan metode ELISA dan aglutinasi latex dalam pemeriksaan antibodi IgG *Toxoplasma gondii* pada wanita hamil di Puskesmas Pegirian Surabaya [thesis]. Surabaya: Airlangga University; 2006.
16. Wallon M, Kodjikian L, Binquet C, Garweg J, Fleury J, Quantin C, et al. Long term ocular prognosis in 327 children with congenital toxoplasmosis. *Pediatrics*. 2004; 113:1567-72.
17. Filisetti D, Gorcii M, Marino EP, Villard O, Candolfi E. Diagnosis of congenital toxoplasmosis, comparison of targets for detection of *Toxoplasma gondii* by PCR. *J Clin Microbiol*. 2003; 41:S4826-29.
18. Guerina NG, Hsu HW, Meissner C, Maguire JH. Neonatal serologic screening and early treatment for congenital *Toxoplasma gondii* infection. *N Engl J Med*. 1994; 330:1858-63.
19. Remington JS. *Infectious diseases of the fetus and newborn infant*. 4th ed. Philadelphia: WB Saunders, 1983; p. 140-260.
20. Male D, Brostoff J, Roth DB, Roitt I. Antibodies. In: Roitt IM, Male DK, editors. *Immunology*. 7th ed. Philadelphia: Mosby Elsevier. 2006; p. 59-86.
21. Singh S. Mother to child transmission and diagnosis of *Toxoplasma gondii* infection during pregnancy. *Indian J Med Microbiol*. 2003;21:S69-76.
22. Paul WE. The immune system. In: Paul WE, editor. *Fundamental immunology*. 5th ed. Lippincott William and Wilkins. 2003;p. 1-22.
23. Kami Kim. Time to screen for congenital toxoplasmosis. *Chicago J Clin Infect Dis*. 2006;42:1395-97.